MODULE-1: INTRODUCTION TO GENERAL HISTOLOGY

Learning outcomes

At the end of this module the learner will be able to know about tissues and its types.

GENERAL HISTOLOGY

- A *tissue* is an aggregation of cells that are similar in structure and function to perform a specific function.
- Intercellular substance and fibres are the non-living parts of a tissue. In between the cells is the *intercellular substance*, produced by the cells themselves.
- The intercellular substance generally consists of a homogenous ground substance or matrix. Fibres are embedded in the ground substance.
- The structure, shape, size, and arrangement of the cells, the bio-chemical and physicochemical properties of the ground substance, and the nature of fibres when present are different in the various types of tissues. Further the proportion between the cells and the intercellular substance also differs from one type of tissue to another.
- Different types of fundamental tissues are evolved in the body based on the basic property of the protoplasm to perform a specific function.
- The *Organ* **(e.g. liver)** is made-up of a combination of one or more of the fundamental tissues to perform a specific function. Several organs with a common function form the *Organ System* **(e.g. digestive system)** in the body. Different organ systems join to form the individual.
- There are four types of elementary or fundamental tissues in the animal body in the adult and the organ systems are made up of one or more of these varieties of tissues arranged in a specific and characteristic way in each organ.
- The elementary or fundamental tissues are,
    - Epithelium
    - Connective tissue
    - Muscular tissue
    - Nervous tissue

MODULE-2: EPITHELIUM

- Learning outcomes
- At the end of this module the learner will be able to know about epithelium and its classifications.

EPITHELIUM

Definition

Epithelium is composed *primarily of cells* between which a *very little amount of intercellular substance* exists. It is an unilaminar or multilaminar sheet of cells which covers the body surface and lines the body cavities or tubular passages.

Shape and arrangement of epithelial cell

- The shape of epithelial cells varies from a very flat type – squamous, a tall rod-like columnar cell and an intermediate between the two are cuboidal cells, which may be low or high.
- When an epithelium is lined by one layer of cells, it is called simple epithelium; when it is lined by two are more layers of cells it is stratified epithelium.
- In the stratified epithelium, the basal layer of cells rest on a basement membrane and only the uppermost cells have a free surface.
- In certain places the nuclei of epithelial cells lie at various levels giving a stratified appearance. But in these cases all cells reach the basement membrane though all do not have a free surface. This type of epithelium is called pseudostratified and is characteristic of ducts or passages of respiratory and reproductive systems.

Surface of the epithelial cell

- Each epithelial cell has four surfaces.
    1. Basal surface rests upon the basement membrane,
    2. A free surface opposite to basal surface,
    3. lateral surfaces, with which it is in contact with the adjacent cells.
- *Basement membrane* is a condensation of the intercellular substance lying between the epithelial cell and the underlying connective tissue.

Attachment between cells

- In some locations the cells of epithelium are attached to each other by adhesions of the cell membranes of adjacent or opposing cells.
- At these points of adhesions, the membrane of each cell is thick and under EM fine fibrils are seen in the adjacent areas of cytoplasm. These thickened areas of adhesion are known as desmosomes with light microscope.
- The adhesion present in stratified epithelium give the appearance by fixatives between the adjacent borders the cells because of shrinkage caused by fixatives between the adjacent borders of cells except at the sites of adhesions) and hence they were called intercellular bridges under EM it has been observed at the sites of desmosomes there is thickening of opposing membranes and in the adjacent areas of cytoplasm fine fibrils are seen to converge at the desmosomes but there is no protoplasmic continuity between the cells.

Modification of cell surface

- The cytoplasm of cells at the free surface may show modifications.

- The cells of intestinal epithelium show a pronounced modification of free surface. They have a definite banded layer of uniform thickness known as the *striated border / brush border* in which are striations vertical to the surface. These striations have been found to be microvilli under EM. This is a particular adaptation for absorption.
- The cells of kidney tubules (proximal convoluted part) show *brush border .*
- The surface cells of epithelium lining respiratory passages and many cells of the epithelium lining uterine tubes show *motile cilia (kino-cilia);* parts of male reproductive tract have epithelial cell with *non-motile cilia (stereo cilia).*

Basement membrane (membrana propria)

- This is a sheet of variable thickness and is interposed between epithelium and subjacent connective tissue. It consists of a ground substance of the underlying connective tissue.
- Embedded in this condensed ground substance are delicate reticular fibres, which are continuous with those of underlying connective tissue Basement membranes in ordinary preparations are distinguishable in some locations (eg. trachea).
- In other locations beneath stratified squamous epithelium and columnar epithelium of the intestine it is not easily seen. Basement membrane serves for attachment of epithelium to the underlying connective tissue.
- Blood vessels with few exceptions, epithelia are avascular. Nutritive materials and oxygen enter by diffusion through cells and intercellular substance; Capillaries are present in the epithelium of the stria vascularis of internal ear.

CLASSIFICATION OF EPITHELIUM

Epithelia are classified on the basis of the number of cell layers and the shape of the cells in the surface layer.

Based on number of cell layers

- Simple epithelia: one layer of cells in the epithelium.
- Stratified epithelia: two or more layers of cells.

Based on Shape of cells

- Cells in the surface layer are, as a rule, described according to their height as squamous (scale- or plate-like), cuboidal or columnar.

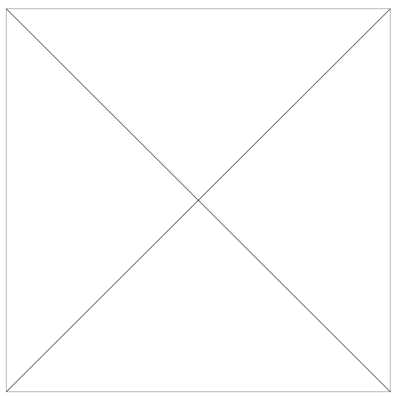
SIMPLE EPITHELIUM

- Here, only one layer of cells present on the basement membrane.

- It can be classifed as simple squamous, simple columnar and simple cuboidal type.

Simple squamous epithelia

- The simple epithlia is also called as pavemental epithelia.
- Consists of *flat scale like or plate like squamous cells* separated by narrow intercellular spaces.
- The *edges of the cells* are usually serrated but may be smooth.
- The cells rest on connective tissue and their free surface shows delicate, cuticular border.
- The nucleus situated in the centre of the cells is spherical or oviod causing a bulging of cytoplasm.
- On surface view the cells appear as delicate mosaic which can be demonstrated well by precipitation of silver in the intercellular spaces.
- In profile the cells are spindle shaped, thin at the ends and thicker in the centre where the nucleus is situated.

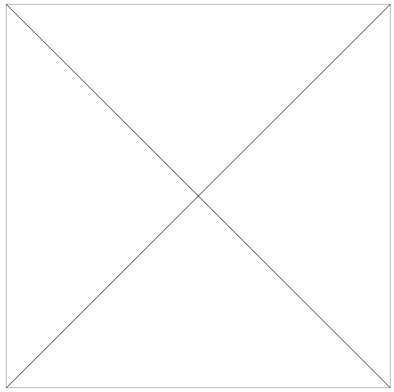


Distribution

- This epithelium lines the peritoneal, pleural and pericardial, cavities. Here it is called *mesothelium*.
- The mesothelium together with an underlying stratum of connective tissue, forms *serous membranes* viz. peritoneum, pleura and pericardium.
- It lines the heart and all blood vessels and lymph vessels; here it is called *endothelium***.** It also lines the membranous labyrinth of the internal ear, Bowman's capsule and tubules, alveoli of the lungs.

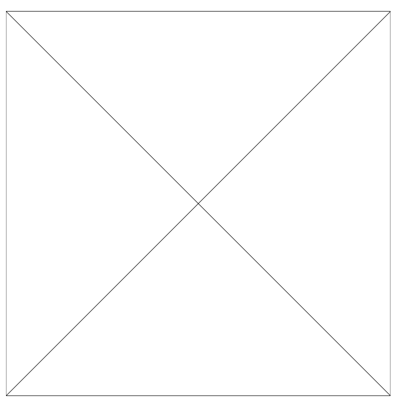
Simple cuboidal epithelia

- It consists of a single layer of more or less cubical cells, resting on a basement membrane.
- This is found in many parts of kidney tubules, thyroid gland acinar ducts of exocrine glands, mammary glands etc.



Simple columnar epithelium

- It consists of a single layer of tall prismatic cells resting on the basement membrane.
- The cells generally are wider at the free borders and narrow at the basal or attached ends and have oval nuclei, situated at the basal part of the cell.
- Pyramidal epithelium of many glands is a modification of the columnar epithelium.
- Simple columnar epithelium is found in the stomach, intestines interlobular and lobar ducts of many glands, in gall bladder, uterus, vas difference etc.
- The simple columnar epithelium of the small intestines shows certain special features. The free borders of cells show fine striations under EM which have been identified as *micro villi*.



Goblet cells

- They are the common variation of simple columnar epithelium found in the intestine and respiratory passages.
- They are unicellular mucous secreting glands.
- They become modified from the columnar cell by the deposition of mucous droplets.

- The cells swell up and the nucleus surrounded by a little cytoplasm is displaced by mucin. On further expansion, the cell membrane ruptures with escape of mucin.
- In ordinary H&E preparations mucin is unstained. The cell after rupture regenerates and the process is repeated.

Cilia

- The motile cytoplasmic processes present at the free surface columnar cells are called as cilia in certain locations.
- The length of cilia in different types of epithelium varies considerably.
- At the base of each cilium, in the superficial layer of protoplasm is a small thickening, the basal corpuscle, which stains back with iron haemotoxylin.
- The movement of the cilia consists of a rapid effective beat and a slow recovery stroke, always in one direction (usually towards the external opening of tube or passage which is lined by the ciliated epithelium). The ciliary movement occurs in regular waves.n some organs, the cells carry long non-motile cilia (stereo-cilia and these are supposed to help in elimination of secretion from the cells.

TRANSITIONAL EPITHELIA

- This epithelium is seen in the mucous membrane of the excretory passages of the urinary system.
- The cells are often divided into three groups: the *basal polyhedral cells, the intermediate pear shaped or pyriform cells* with their broad, end towards the free surface and flattened or umbrella like *surface squamous cells*.
- This epithelium accommodates itself to cover larger or small areas. Completely covering the small areas; cells are six or more layers. Covering a large area, the cells may be two or three layers only.
- The cells are held together by viscous cement which permits gliding over of cells on one another.

Click here to see Transitional Epithelium

PSEUDO STRATIFIED EPITHELIUM

- In this type of epithelium the *nuclei, lie at different levels* giving it a stratified appearance.
- All the cells reach the basement membrane but not all of them extend to the surface. Those reaching the surface are columnar with one or more processes extending to the basement membrane.
- Between these are ovoid or spindle shaped Basal cells, which also reach the basement membrane.

- This is type of epithelium is usually ciliated (motile or stereo cilia), the cilia being present on the free surface of the columnar cells.
- This epithelium occurs mainly in the lining passages of the respiratory and male reproductive systems.

Click here to see Pseudo stratified Epithelium

SPECIAL FEATURES OF EPITHELIA

Glandular epithelium

- It refers to the lining and secretary cells of the glandular organs, which are developed as down growths from the epithelial layer in the underlying connective tissue, followed by structural modification and differentiation.

Neuro-epithelium

- It denotes the specialized epithelial cells in certain locations, which are concerned in reception of sensory stimuli.

Mucous membrane (Mucosa)

- This lines all of the canals and cavities of body which connect with the exterior that is the line alimentary tract, the respiratory passages and the genitor-urinary tract.

- The essential parts of the mucous membrane are surface epithelium, basement membrane and a stratum of connective tissue called the lamina propria.
- The surface epithelium is of different types in the different systems and even in different parts of the same system.

General features

- Epithelia generally possess a remarkable capacity for repair and regeneration after injury.
- Certain epithelia, notably epidermis and intestinal epithelium, are continually recycled, with new cells being created by mitotic activity while old cells are sloughed off (from the surface of the epidermis or the tips of intestinal villi).

STRATIFIED EPITHELIA

- Epithelia are classified on the basis of the number of cell layers and the shape of the cells in the surface layer.
- If there is only one layer of cells in the epithelium, it is designated simple.
- If there are two or more layers of cells, it is termed stratified.
- Cells in the surface layer are, as a rule, described according to their height as squamous (scale- or plate-like), cuboidal or columnar.
- The cells are arranged in more than one layer is known as stratified epithlum

Stratified squamous epithelium

- It is the *main protective epithelium* of body and has several cell layers.
- The number of layers of the epithelium varies in different regions but shape and the arrangement of cells are characteristic.Two types of this epithelium are recognized
    - Keratinizing and
    - Non-keratinizing.
- Deepest layer consists of columnar cells resting on an indistinct basement membrane is called as *stratum cylindricum*.
- Above this the cells become polyhedral and are usually larger than the basal cells. As the free surface unit is approached the cells are more flattened and at the surface they become squamous. The deeper cells of the basal polyhedral layers (*stratum germinativum*) are young soft cells with large nuclei rich in chromatin and a finely granular cytoplasm. The intercellular bridges are prominent, giving the cell a prickly appearance (prickle cells) and hence this layer is called *stratum spinosum*. Mitosis seen in these layers.
- In the keratinizing type above the stratum germinativum there is *stratum granulosum* consisting of 2 - 5 rows of flattened; rhomboid cells with basophilic kerato hyalin granules in the cytoplasm.
- Above this is the *stratum lucidum* consisting of a few row of flattened cells devoid of any nuclei, appearing as a translucent homogenous highly refractive band, in

- which cell boundaries cannot be made out. The cytoplasm in these cells contains droplets of eleidin.
- Above the stratum lucidum is the most superficial layer the *stratum corneum*. The thickness of this varies in different locations. It is composed of dead scales with no nuclei and is formed of keratin.
- In the *non-keratinizing* type, stratum granulosum, stratum lucidum and stratum corneum are usually absent. The extent of the charges in the superficial cells varies with the location and the environment of the epithelium. The epidermis of the skin for instance, is subjected to phagus. Its surface cells are non-nucleated, scale-like and keratinized. The keratinized surface cells being flattened. The process of keratinization in epidermis is so important for bodily protection and is probably dependent on insufficient nutrition of the upper cell layers. The dead scale-like cells are constantly cast off to be replaced by cells from the deeper strata. In man this is slow and continuous process, in some of the lower vertebrates (snakes) there is periodic shedding of the whole superficial layer of the epidermis.

Distribution

- Stratified suqamous epithelium covers the entire body and the orifices of the cavities opening upon it.
- It lines the mucous membrane of the digestive tract from the mouth to the secretory portion of the stomach, and the anal canal, anterior surface of the cornea, bulbar conjuctiva, lacrimal canaliculi, vaginal vestibule, glans penis and elsewhere.

Stratified cuboidal epithelia

- This type of epithelium is comparatively rare.
- It the most superficial layer of cells are columnar
- They are located in larger excretory ducts of some glands, palpebral conjuctiva of the horse and dog.
  - The top cells are cuboidal.
  - They are seen in ducts of sweat glands, cells lining antrum of the ovarian follicles.

Stratified columnar epithelia

MODULE-3: CONNECTIVE TISSUE

Learning outcomes

At the end of this module the learner will be able to know about connective tissue and its types.

DEFINITION - CONNECTIVE TISSUE

- The various types of adult connective tissues in contrast to epithelium have relatively a few cells and a large amount of intercellular substance. But the proportion of these two elements shows variations.
- In some type, especially loose connective tissue, cells are quite numerous.
- In other types, they are few in number and tissue is composed almost entirely of closely packed fibres.
- The type and the nature of the substance in which they are embedded (ground substance) furnish the basis for the subdivision of adult connective tissue into three main groups of connective tissue proper, cartilage and bone.

CLASSIFICATION OF CONNECTIVE TISSUE

EMBRYONAL CONNECTIVE TISSUE

- There are two varieties
    - Mesechyme and
    - Mucous.
- Mesenchyme consists of a network of branching cells, in the meshes of which is a homogenous intercellular fluid. The processes of a cell appear to anastomose with those of other cells.
- As development progresses, wavy primitive fibres appear between branching cells and the fluid matrix becomes viscid due to formation of mucoproteins. This developmentally more nature tissue is mucous connective tissue which is widely distributed in the embryo.
- The primitive fibres later become collagenous. Elastic fibres appear later classical example of mucous connective tissue is umbilical cord and the term Wharton's jelly is applied to it in that location.

LOOSE CONNECTIVE TISSUE

- Loose or areolar connective tissue is very widely distributed in the body.
- It forms the superficial and of the deep fascia; forms part of the frame work (stroma) of most of the organs; or surrounds blood vessels and nerves and fills in any otherwise unoccupied spaces.
- Areolar tissues contain cells, fibres and ground substance.

Cells:

- Cells constantly present are:
    - Fibroblasts
    - Macrophages or histiocytes
    - Mast cells
    - Plasma cells
    - Wandering cells
    - Pigment cells
    - Fat cells
- Of these fibroblast and histiocytes are the most numerous.

Fibroblasts

- These cells are larger flat branching cells with extensive processes which may join the processes of other fibroblasts. The cell membrane is delicate and usually not seen. The nucleus is spherical or oval and in ordinary preparations is lightly stained. In section, the fibroblast nuclei are usually shrunken and stain deeply with basic dyes. It contains dusk like chromatin and one of two nucleoli. The cytoblasm is homogenous or finely granular and stains very lightly.
- Fibroblasts are present in all connective tissue such as tendon. They are responsible for formation of fibres. The name fibroblasts instead of fibrocytes indicate that after injury they are active and form new fibres. Fibrocytes on the other are inactive. Their cell bodies are less irregular and nucleus is condensed to a long cylinder or flattened oval. Chromatin is dense.

TOP

Histiocytes or Macrophages

- These cells are irregular cells with short processes. The nucleus is smaller and darkly staining than fibroblasts: cytoplasm coarsely granular and shows vacuoles. They are studied by vital staining. They are present in all fasciae and in the stroma of organs. They also occur in sinusoids of liver in lymphoid organs and in bone marrow. They show amoeboid movement and phagocytosis is pathological conditions.
- When activated, the histiocytes become larger and more rounded and the cytoplasm will be filled with granules of ingested material. They form part of the macrophage system or reticulo endothelial system.

TOP

Mast cells

- Occur in most loose connective tissue especially along the course of blood vessels. They are large oval or round cells with pale-staining nucleus and coarse cytoplasmic granules which stain with certain basic dyes. They resemble basophils of blood and contain an anticoagulant heparin, histamine and serotonin.

TOP

Plasma cells

- Plasma cells are comparatively rare in loose connective tissue, but are numerous in the alimentary mucous membrane and the great omentum and also in pathological conditions. They are smaller than macrophages of round or irregular shape, with basic staining homogenous cytoplasm. The nucleus is small and eccentrically placed. Large granules of chromatin radially arranged in a regular manner give a cart wheel appearance to the nucleus. There is a characteristic unstained or lightly stained area in the cytoplasm at the side of the nucleus, where the cytoplasm is more abundant. They are derived from lymphocyte like cells and are active in forming antibodies.

TOP

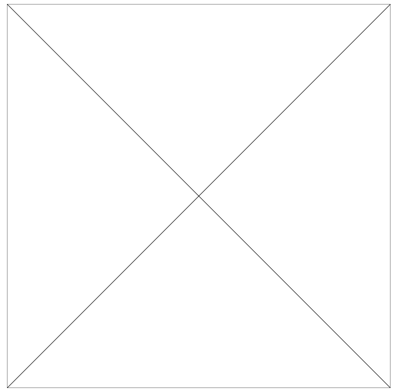
Wandering cells

- These cells are lymphocytes, eosinophils and neutrophils, migrated from blood.

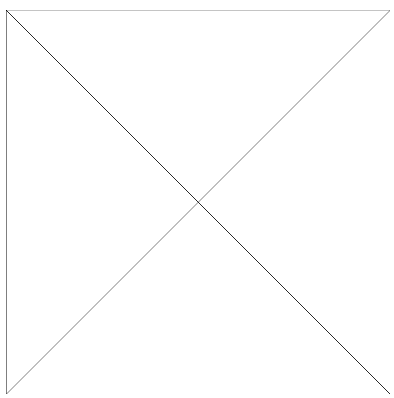
Three types of fibres are seen in adult connective tissue.

- White or collagenous fibres
- Elastic or yellow fibres
- Reticular fibres

- *White or collagenous fibres*
    - These vary in size and are really bundles of extremely fine fibrillae, which lie parallel to one another giving the fibre a longitudinally striated appearance and are united by a small amount of intercellular cement substance. Fibrillae do not branch. The fibres is usually wavy, soft and flexible. They are non-extensile. They stain with acid dyes. Chemically they contain an albuminous substance called collagen which on boiling yields gelatin. The fibres shrink slightly in water; swell enormously in dilute acids or alkalies. In the dilute acids or alkali the fibres break up into fibrils, become individual the inter-fibrillar cement substance is dissolved. Gastric juice rapidly digests the fibres, but alkaline trypsin has no effect on them. Collagen fibres are birefringent or aniostropic throughout their length.
- *Elastic or yellow fibres*
    - These are homogenous highly refractive fibres which are thinner than the white fibres. They branch and anastomose freely forming networks. Smaller fibres are round in cross section and larger are flat or polygonal. They are highly elastic. Chemically they contain elastin which does not yield gelatin and has a remarkable resistance to most agents. It is not affected by heat or cold water, by dilute acids or gastric juice. It is however rapidly dissolved by pancreatin. The elastic fibres are lightly stained by ordinary methods, but deeply stained by orcein and resorcin fuchsin.



- *Reticular fibres*
    - These are smaller branching fibres which form netlike supporting frame work or reticulum. They become black in silver impregnation methods. Hence they are also called argyrophilic fibres. In most areolar tissue these reticular fibres are few. In glandular organs and between musclefibres they are numerous. In lymphoid organs and in red bone marrow, the reticular fibres are associated with a special type of cells called reticular cells. Reticular fibres with reticular cells form a type of tissue called the reticular tissue. In other situation reticular fibres have the same relationship to fibroblasts as do collagenous or elastic fibres. Chemically though related to collagenous fibres the reticular fibres are not dissolved by pepsin and on boiling yield reticulin and not gelatin.



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Ground substance

- It is the background material within which all other connective tissue elements are embedded. It varies from a fluid-like to a gel like state. It is one of the two components of non-fibrillar intercellular substance. The other is the tissue fluid. In ordinary connective tissue, the ground substance consists mainly of water whose major role is to provide a route for communication and transport (by diffusion) between tissues. This water is stabilized by a complex of glycosaminoglycans (GAGs), proteoglycans , and glycoproteins , all of which comprise only a small fraction of the weight of the ground substance.

- Ground substance may be highly modified in the special forms of connective tissue.
    - In blood, the ground substance lacks stabilizing macromolecules. We call this free-flowing ground substance as plasma .
    - In skeletal tissue, the ground substance may become mineralized by deposition of calcium salts. We call this rigid ground substance as bone .
    - In cartilage, the ground substance is much more solid than in ordinary connective tissue but still retains more resiliency than bone.

TOP

Functions of areolar tissue

- It binds structures or holds them in position.
- It acts as padding and serves as a pathway for blood vessel and nerves. Nutrient substances to body cells and metabolites from the cells traverse connective tissue.
- Spread of localized infections is limited by connective tissue.

DENSE CONNECTIVE TISSUE

- Here fibres are closely packed to form sheets, cords or bands (e.g dermis, capsules of certain organs, aponeurosis, ligaments and tendon) based on the nature of arrangement of the fibres.
- They are classified into two groups
    - Irregularly arranged
    - Regularly arranged
- Dense irregularly arranged connective tissue occurs in the form of sheets. Main component a coarse collagenous tissue but elastic and reticular are also present.
- The fibres interlace to form tough feltwork. Fibroblasts and macrophages are present. (e.g dermis of the skin, periosteum, perichondrium and capsules of some organs).
- Dense regularly arranged connective tissue occurs in the form of cordlike or band like structures.
- Fibres are arranged parallel to one other (e.g tendons, ligaments and aponeurosis).
    - ***Tendons*** are composed almost only of white fibrous tissue. Fibres are densely packed in parallel bundles. Fibroblasts alone are present in small numbers. These are called tendon cells. The tendon cells are quadrangular and so highly flattened that in profile they appear as thin linear structures. They occur between tendon bundles around which they have extensions.
    - ***Aponeuroses*** have same structure as tendons but are broad sheets. Fibres run in superimposed layers those of one layer at an angle to adjacent layers. The layers may interweave.

- ***Ligaments*** are predominantly of white fibrous tissue but a few are composed entirely of elastic fibres. The yellow elastic ligaments are formed of parallel coursing yellow fibres, bound together by small amount of areolar tissue (e.g. ligamentum nuchae where elastic fibres are very large and ligaments flava).

SPECIAL CONNECTIVE TISSUE

Reticular tissue

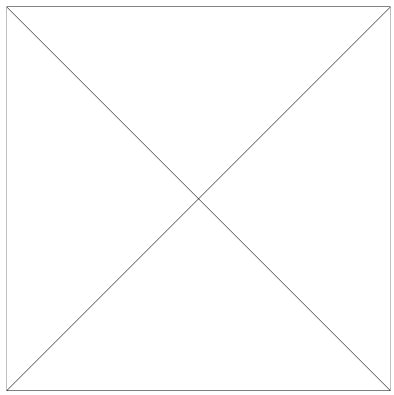
- It is composed of cells and reticular fibre network. The cells have stellate shape with processes which extend in all directions and joins those of wrapped by reticular fibres.
- The reticular tissue forms the frame work of organs like lymphatic glands; spleen, red marrow of bones. The reticular cells line the lymph sinuses in lymphatic glands or blood sinusoids in spleen, Liver Red marrow etc. These cells are actively phagocytic and form part of the Reticulo-endothelial system.
- It appears likely that the reticular cells may be of different types which cannot be distinguished by morphological means alone. Some of them have retained their embryonic or developmental tendencies and in red marrow give rise to erythrocytes and granulocytes in lymphoid tissue to lymphocytes etc and these primitive reticular cells as they are some times called are usually non-phagocytic.
- The reticular tissue forms the frame work of organs like lymphatic glands, spleen and red marrow of bones. The reticular cells line the lymph sinuses in lymphatic glands or blood sinusoids in spleen, liver red marrow etc. These cells are actively phagocytic and form part of the Reticulo-endothelial system.

TOP

Adipose tissue

- Fat is regarded as arising from specific cells (steatoblasts). Fat cells are found isolated or in groups in all areolar connective tissue but in which justifies the name adipose tissue. The largest deposits of fat are found in subcutaneous connective tissue (panniculus adiposus) in the kidney region in the mesenteries and mediastinum and in the cervical axillary and inguinal regions.
- Fat is different from other connective tissues, in that the cells and not the intercellular substance make up the bulk and determine the nature of the tissue. The large ovoid or spherical cells consist of peripheral cytoplasmic membrane enclosing a large fat droplet. The nucleus is flattened and surrounded by a small amount of cytoplasm and is usually found pressed against the cell wall.

- In sections, when the fat is dissolved out, the cells appear as empty rings or have a signet ring shape when the plane of section passes through the nucleus. This is so when they occur isolated or in small groups. But in denser masses due to pressure of adjacent calls they become polyhedral. Fat is usually arranged in groups or lobules, each lobule being separated from the other by areolar connective tissue. Delicate connective tissue passes between the cell and serves as bed for capillaries.
- Chemically fat contains esters of glycerol and certain fatty acids. It is not soluble in cold alcohol or water, but readily dissolves in xylol. That is why fat dissolves in ordinary preparations. But by special methods fat can be stained (e.g. black by Osmic acid by Sudan red III).



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Brown fat tissue

- This is different from the common or white fat tissue. In rats and other rodents, it is highly developed and forms yellowish, lobated masses in certain parts of the body - between the scapulae, on the neck, in the mediastinum, in the inguinal region and elsewhere.
- Microscopically, latter name was given because this tissue was believed to play a peculiar role during hibernation. The brown fat contains a pigment which gives the tissue its colour.
- The fat cells assemble in groups separated by this network of collagenous or reticular fibres and numerous capillaries. The microscopic structure suggests an endocrine gland. While the common fat tissue loses or accumulates neutral fat with changes in the nutritional condition of the animal, these factors do not seem to affect the brown fat tissue.

TOP

Pigmented connective tissue

- The cells of this tissue occur in the chorioid and iris of the eye and in the corium of dark skinned animals.
- The cytoplasm is filled to a varying degree with brown or black pigment which is usually melanin. They are specialized cells, called as Melanocytes, irregular in outline with cytoplasmic processes.

TOP

Blood and nerve supply of connective tissue

- Connective tissue received its blood supply from the vessels which pass through them and for which they form supporting bed. For dense connective tissue the supply is scanty.
- Nerves are numerous in connective tissue. Some of them terminate in the tissue itself, but other go to epithelium or muscle. Tendons, fibrous membranes and periarticular connective tissue have special nerve endings.

RETICULO-ENDOTHELIAL SYSTEM

- This name is given to the system more on physiological and pathological consideration than on anatomical structure.
- The cells of this system do not form true endothelium. All highly phagocytic cells of the body, except leucocytes belong to this system.
- The only certain method of identification of these cells is by injection of nontoxic inert particulate matter like the carbon particles or Indian ink into the living animal.
- Injection of trypan blue or lithium carmine into living animal is called vital or intra-vital staining.
- The macrophages engulf the particulate matter like carbon particles. After vital staining the cells containing the dye are found in the cells in loose connective tissue in the reticular tissue or in the blood sinuses of certain organs.
- In the connective tissue they correspond to the histocytes.
- Kupffer cells of liver, reticular cells of lymph nodes, spleen and bone-marrow, cells lining the sinusoids of spleen and microglia cell of the nervous system are examples of this system.

MODULE-4: EPITHELIUM - GLANDS

- Learning outcomes
- At the end of this module the learner will be able to know about glands and its classifications.

GLANDS

- Certain cells of the body in addition to carrying out some metabolic processes necessary for their own existence, also manufacture specific substance not for their own use, but to be extruded, from the cells and used elsewhere in the body – *secretion* (e.g. gastric juice) or discarded - *excretion* (e.g. urine). Such cells are known as gland cells or glandular epithelium cells are usually grouped into small units, enclosed and supported by a connective tissue framework.
- A gland may consist of a single cell, as for example, the goblet cell or the unicellular glands of invertebrates. Most glands of the body are composed of more than one cell (multicellular gland).

CLASSIFICATION OF GLANDS

- The glands of the body are classified as exocrine or endocrine.
- Exocrine glands have ducts which carry out the secretion to an epithelial surface, while endocrine glands are ductless and pour their secretion into the blood or lymph.

Exocrine gland

- The exocrine gland consists of a secretory portion and a duct.

- The secretory portion is arranged as a cluster of secretary cells known as a secretory unit, which has a central lumen, which opens into the first portion of the ductular system.
- The exocrine glands can be classified in several different ways based on the shape and form of the secretory unit, nature of secretion and mechanism of secretion.

Endocrine gland

- Certain glands are lacking in ducts and are termed endocrine glands.
- The endocrine glands secrete specific chemical substance called hormones which have specific effects on the other tissue or organs of the body *e.g., thyroid, parathyroid, pituitary etc***.**
- The secretions of these glands are conveyed directly into the blood stream.
- To facilitate this endocrine glands have numerous sinusoids forming an extensive network, surrounding the secretory cells, which are usually arranged in small groups, follicles or anatomizing cords of cells.

EXOCRINE GLANDS

- The exocrine gland consists of a secretory portion and a duct.
- The secretory portion is arranged as a cluster of secretary cells known as a secretory unit, which has a central lumen, which opens into the first portion of the ductular system.
- The exocrine glands can be classified in several different ways based on the shape and form of the secretory unit, nature of secretion and mechanism of secretion.

BASED ON THE SHAPE OF THE SECRETORY UNIT

- If the secretory units are tubular in shape it is a *tubular* gland. If secretory units are more rounded, then they are called *alveolar or acinar* glands.
- Glands which have characteristics of both these, or which have tubular portions with terminal alveoli, are called *tubuloalveolar* glands.

BASED ON THE DUCTULAR SYSTEM

- Glands are classified into Simple and compound glands in this view**.**
- The ductular system of a gland may consist of simple epithelial tube draining a secretory unit and opening at the epithelial surface or it may be in the form of an extensively branched system, the initial smallest ducts draining the secretory units, uniting to form larger ducts at various levels.

- Finally forming the main duct, which conveys the secretion from the gland to an epithelial surface. Based on the ductular system glands are classified as simple glands, which has an unbranched duct system, and compound glands which has a branched duct system.

Simple glands

- Simple tubular glands
    - The glands consist of simple tubular secretory unit which opens on the surface. All the cells may be secreting or only the deeply situated cells alone. In the later case the more superficial portion of the tubule serves merely as a duct. The more highly developed simple tubular glands consist of a mouth opening upon a surface, a neck usually somewhat constricted and a fundus or deep secretory portion of the gland.
    - Simple tubular glands are divided according to the structure of the fundus into
        - *Straight*
            - A Straight tubular gland is one in which the entire tubule runs in a straight unbranched course. e.g. glands of the large intestine.
        - *Coiled*
            - A coiled tubular gland is one in which the deeper portion of the tubule is coiled or convoluted. The sweat glands of the skin are the most typical examples.
        - *Branched tubular glands*
            - A branched tubular gland is a simple tubular gland in which the deeper portion of the tubule branches, the several branches being lined with secreting cells and opening into a superficial portion which serves as a duct e.g. fundic, pyloric and cardiac glands of the gastric mucous membrane.
- Simple alveolar glands
    - These are found in branched form, e.g., *Sebaceous and Meibomien* glands.
- Simple tubulo-alveolar or tubulo–acinar glands
    - These are found only in the branched form e.g. *Brunner's glands* of the duodenum.

Compound glands

These contain a large number of branching duct systems, which finally join to form a common or main duct, which coveys the secretion from the glands. Based on the nature of secreting units compound glands are classified into:

- Compound tubular glands
    - The terminal ends of the duct systems end in tubular secretary units, which are usually tortuous or coiled e.g. kidney, Testis.
- Compound alveolar glands

    - The terminal part of the duct system ends in alveoli with dilated sac-like lumen e.g. mammary gland.
- Compound tubulo-alveolar or (tubulo-acinar) glands
    - In these the secretary units are with terminal or lateral alveoli. E.g. parotid gland, pancreas etc.
    - Large amount of connective tissue present in a compound gland, which starting off from the capsule divides the gland into lobes by *interlobar* connective tissue septa. Each lobe is subdivided by connective tissues into lobules, which are usually microscopical in size called *interlobular* connective tissue septa. Each lobule is made up of a number of secreting units or acini, with the ducts and inter acinar connective tissue.

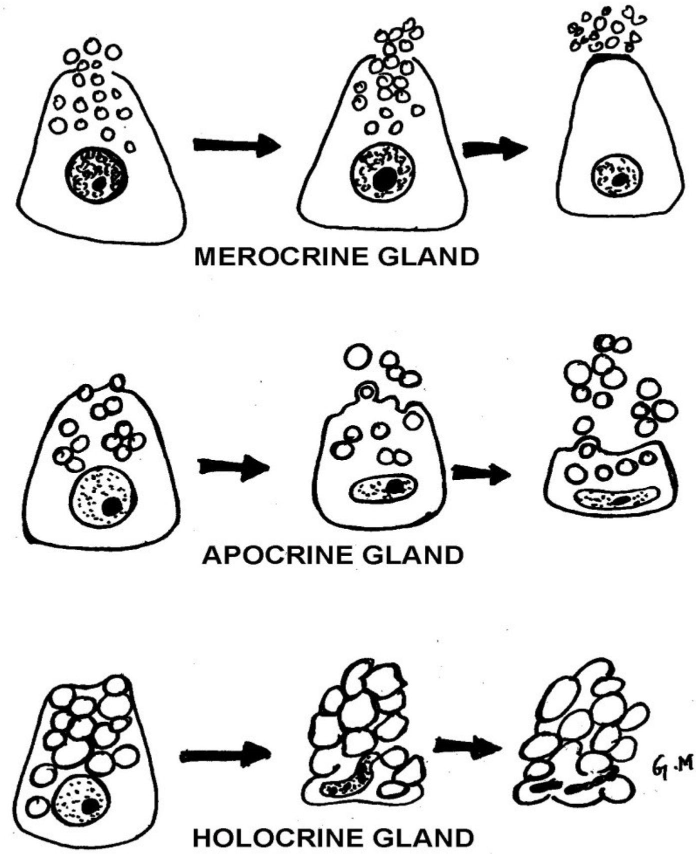
Parenchyma

- The secreting units may be tubular, alveolar or tubulo alveolar and are made of secretory cells. The acinar duct is the smallest duct continuous with the lumen of the acinus and is usually lined by flattened or cuboidal epithelium. The acinar ducts unite within the lobule to form intralobular ducts and several of this type unites to form an Interlobular duct, located in the connective tissue between the lobules. Interlobular and interlobar ducts are similarly formed, the latter uniting to form the main duct of the gland.
- Interlobular ducts are lined by columnar epithelium but have a thin connective tissue coat. As the duct increases in caliber the connective tissue coat also proportionately increases and the epithelium may become two layered columnar.

BASED ON THE MODE OF SECRETION

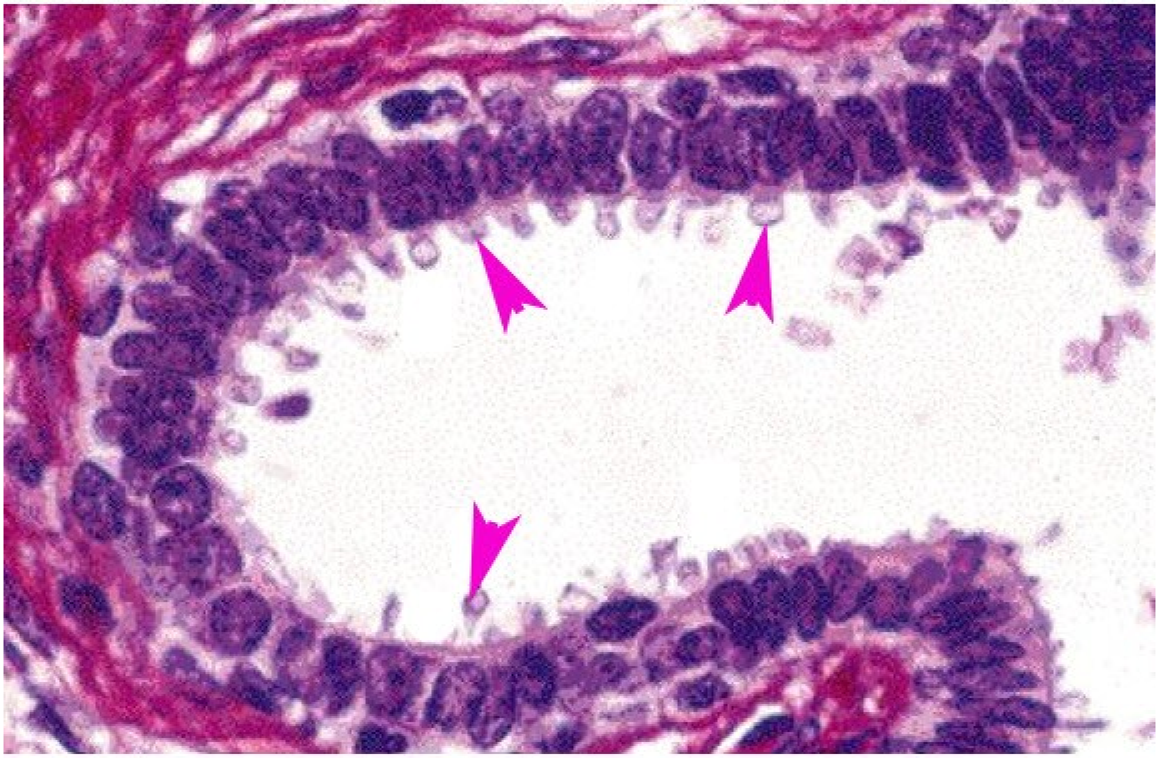
This classification is based on the manner in which the secretory cells of the glands elaborate their secretion. Based on this glands are classified into Holocrine, merocrine and apocrinegland.

CLASSIFICATION OF GLANDS BASED ON METHOD OF ELABORATION OF SECRETORY MATERIAL



- In ***holocrine*** glands, the secretory products are accumulated in the cytoplasm of a cell, which disintegrates fully and constitutes the secretion secreted e.g. sebaceous gland.
- ***Merocrine*** glands elaborate secretion without losing any part of the cell e.g. salivary glands.
- In ***Apocrine*** glands, a little or the cytoplasm along the free secretory or apical borders of the cells is lost e.g. mammary gland.

APOCRINE GLAND (Mammary gland)



The pink arrows point the apical part of the cells being removed during secretion

BASED ON THE NATURE OF SECRETION

Glands may be classified as cytogenous and non-cellular;

- ***Cytogenous gland*** produces living cells as their secretion. Eg. Testis, Ovary.
- ***Non-cellular glands*** are further classified into serous, mucous and mixed glands based on the consistency of their secretion

BASED ON THE CONSISTENCY OF THE SECRETION

- Based on the consistency of the secretion glands are classified into
    - **Serous**,
    - **Mucous** and
    - **Mixed** glands.
- Serous glands produce a whey-like serous secretion. Mucous gland produces a slightly more viscid fluid.
- The glands that secrete mucin, glycoprotein which when mixed with water become mucous are termed as mucous glands. Any gland that produces a mixture of serous and mucous secretions is called a mixed gland.

Serous secretory unit

- The nucleus of a serous secretory cell is usually rounded and lies towards the base of the cell.
- At the base of the cytoplasm contains secretory granules called *zymogen granules*.
- Cytoplasm and Zymogen granules stain with eosin (acidophilic).

Mucous Secretory unit

- The nuclei of the mucous secretory cells are flattened and located at the base of cells that contain them.
- There is less chromoideal substance. Above the level of the nucleus the cytoplasm contains mucin droplets, which impart a vacuolated appearance to the very light staining cytoplasm, since with ordinary staining techniques mucin is dissolved.
- Cytoplasm stains only lightly with haematoxylin.
- *Mixed glands* posses both mucous and serous secretory units.

ENDOCRINE GLANDS

- Certain glands are lacking in ducts and are termed endocrine glands.
- The endocrine glands secrete specific chemical substance called hormones which have specific effects on the other tissue or organs of the body *e.g., thyroid, parathyroid, pituitary etc***.**

- The secretions of these glands are conveyed directly into the blood stream.
- To facilitate this endocrine glands have numerous sinusoids forming an extensive network, surrounding the secretory cells, which are usually arranged in small groups, follicles or anatomizing cords of cells.

MODULE-5: CARTILAGE AND BONE

Learning outcomes

- At the end of this module the learner will be able to know about
    - cartilage and its types and
    - bone and its types.

CARTILAGE

- Cartilage consists of the cells termed as chondrocytes, matrix (ground substance) and fibres.
- The matrix is solid and has marked elastic properties. It withstands considerable pressure and tension.
- According to the nature and visibility of fibrillar elements, cartilage is subdivided into three varieties:
    - Hyaline
    - Elastic
    - Fibrous
- Of this hyaline cartilage is the most widely distributed type of cartilage.

HYALINE CARTILAGE

- This appears as a bluish-white translucent mass when fresh. It forms the articular cartilage of joints, the costal cartilages and cartilages of nose, larynx trachea and bronchi.
- In the foetus nearly the entire skeleton is first laid down as hyaline cartilage and later replaced by osseous tissue in the formation of bone. The tissue is organized into plate like masses which with the exception of articular cartilages, are invested by a fibrous membrane, the perichondrium.
- Each plate consists of cells and a homogenous matrix, the connective tissue fibrils being masked by ground substance. There is neither blood supply nor nerve supply for the cartilage.
- Cartilage cells (chondrocytes) are situated in smooth-walled spaces or lacunae. Each cell has a large central spherical nucleus with one or more nucleoli. The cytoplasm is finely granular and contains fat, glycogen and occasionally pigment.
- In life the cells fill up the lacunae, but after fixation in ordinary methods, fat and glycogen are dissolved and the shrunken cells are separated by spaces from the walls of the lacunae, give the cells a branched appearance.
- In the centre of the mass the cells are arranged in isogenous groups, each group representing the offspring of one parent cartilage cell. The cells are spherical or ovoid, flattened on adjacent sides, their long axes directed radially towards the surface of the plate, towards the periphery, cells become flattened loose their definite grouping until in the subperichondrial layers they appear as rows of narrow elongated cells with their long axes parallel to the surface. Cartilage here merges insensibly with the fibrous connective tissue of the perichondrium.

ELASTIC CARTILAGE

- In this, elastic fibres are present and embedded in the matrix. These fibres branch and run in all directions and anastomose to form a dense network.
- In the peripheral layers, the fibres are thin and the network wide meshed.
- In the deeper portions, they are thicker and more closely packed.
- Elastic cartilage is present in the external ear, the eustachian tube, the epiglottis and in a part of aretynoid cartilages.

WHITE FIBRO CARTILAGE

- This is a combination of dense collagenous fibres and cartilage cells. The cells are surrounded by capsules which in turn are surrounded by variable amounts of matrix.
- Frequently, the cells enclosed in capsules, lie in rows between which are dense wavy bundles of collagenous fibres.
- Fibrous cartilage occurs in intervertebral, discs, interarticular cartilage, the glenoid and cotyloid ligaments and the ligamentum teres of the femur.
- It is bound at certain attachment of the ligaments or tendons to bone.

GROUND SUBSTANCE

- It appears homogenous in fresh condition or in ordinary preparations.
- Only the walls of the lacunae stand out as mere refractive rings intensely staining with basic dyes. These rings are called ***capsules***.
- These are not of the nature of cell membranes but represent considerations of the matrix surrounding the cells.
- The ground substance or matrix masks the fine collagenous fibres, which are present in the apparently homogenous intercellular substance because both have the same refractive index.
- The ground substance is strongly metachromatic with toluidine blue and is slightly basophilic but the superichondrial layer is acidophilic.

PERICHONDRIUM

- Surface of cartilage is invested by a connective tissue membrane called perichondrium which consists of an inner chondrogenic and outer fibrous layer.
-

BONE

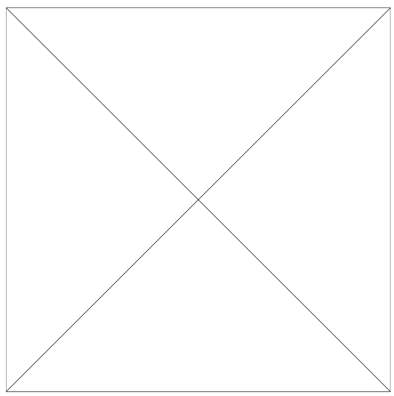
Bone or osseous tissue consists of cells, collagenous fibres, and an intercellular matrix of organic substances.

- The organic matrix is chiefly made up of osseo mucoid and in this matrix, collagen fibres are embedded and the fibrils form a major portion of the intercellular substance.
- The inorganic matter is composed of calcium phosphate, calcium carbonate and small amount of other minerals. The minerals are present in the form of crystals of hydroxyaptite embedded in the matrix and are arranged in a regular manner in relation to the collagen fibres.
- The bone cells or osteocytes are irregularly oval cells with fine cytoplasmic processes, a large oval nucleus and faintly basophilic cytoplasm. These cells occupy spaces called lacunae in the solid intercellular substance and numerous canaliculi radiate from the lacunae and are occupied by the cytoplasmic processes of osteocytes.
- The intercellular substances of bone are in the form of thin plates or lamellae between or within which are the lacunae and canaliculi occupied by osteocytes and their processes. The arrangement of these lamellae is different in compact and cancellated bones.
- Organisation of bone tissue:
    - Grossly two types of bone may be distinguished the spongy or cancellous and the dense or compact.
    - The spongy and compact varieties do not represent histologically distinct types of osseous tissues, but differ only in the degree of porosity. In the

spongy bone, the space is large and the bony matter reduced to a network of slender bars of bone.
  - In compact bone, the bony tissue is abundant and more densely packed. The histological character of the cells and intercellular substance are the same in both.
- In all bones, there is an outer layer of compact bone enclosing the cancellated bone and within the cancellated bone is the bulk of the bone, except in the diaphysis of long bones and certain flat bones of the skull.

COMPACT BONE

- This is composed of numerous systems of concentrically arranged bony lamellae, around a central canal, the Haversian canal, which run longitudinally and encloses blood vessels.
- Each concentric system is known as a Haversian system or Osteone.



- Haversian canals of adjacent systems are inter connected by transverse channels and volkmann's canals connect haversian canals with periosteal and endosteal surfaces.
- In a cross section of the bone, the Haversian canals are seen to be surrounded by a varying number (8 to 15) of concentric lamellae. These concentric lamellae and the central canal constitute a Haversian system or Osteone. In the periphery, the lamellae are not concentric but run parallel with the surface and form a relatively thin outer layer of the bone, the outer circumferential or general lamellae. Similarly arranged inner circumferential lamellae separate the Haversian systems from the marrow cavity.
- Finally, the intervals between the Haversian lamellae are occupied by more irregular layers of bone which constitute the intertitial lamellae. Adjacent lamellar systems are as a rule sharply delimited from each other by a dark staining thin layer of modified matrix (cement membrane, cement line).

CANCELLATED BONE

- This consists of a network of columns of lamellae enclosing spaces which contain bone marrow.
- There are no Haversian systems.

PERIOSTEUM AND ENDOSTEUM

- Periosteum is a fibrous membrane investing the bones except at their articular surfaces.
- It consists of two layers, the outer of which is composed of course fibrous connective tissue containing few cells but numerous blood vessels and nerves.
- The inner layer is more cellular and less vascular and contains many elastic fibres.
- In the growing bones, the inner layer of periosteum is osteogenic and in the adult, this layer is converted into a row of flattened cells. Periosteum serves as a supporting bed for blood vessels and nerves going to bone and for anchorage of tendons and ligaments.
- Some of the periosteal fibres pass into the bone, either obliquely or at right angles to the long axis of bone and are termed as perforating fibres of Sharpy.
- Endosteum lines the surface of the cavities within a bone (Haversian canals) and also the surfaces of trabeculae in the marrow cavity. The cells of endosteal layer are like those of the periosteum and rest on a thin layer of connective tissue.

BONE MARROW

This is a soft tissue which occupies the medullary cavity of the long bones and the space between trabeculae of spongy bone. It consists of a delicate reticular connective tissue in the meshes of which are many kinds of cells.

- Two varieties of marrow are seen, red and yellow.
    - *Red marrow:*
        - It is the only type found in foetal and young bones, but in the adult it is restricted to the vertebrae, sternum, ribs, cranial bones and the epiphyses of long bones. It is the chief blood forming organ of the adult body being the normal source of the red blood corpuscles and granular leucocytes.
    - *Yellow marrow:*
        - Consists of mainly fat cells which have gradually replaced the other marrow elements.

BLOOD VESSELS AND NERVES OF THE BONE

- Bone is richly supplied with blood vessels and nerves which pass into it form the periosteum.
- An artery, the medullary artery runs through the nutrient canal, through the nutrient foramen into the marrow cavity. In its course through compact bone, the

branches of the medullary artery communicate with the vessels of the Haversian canal.

- The medullary artery divides into ascending and descending branches to supply all part of marrow and terminates in a network of sinusoidal capillaries.
- Veins arising from these accompany the medullary artery and communicate with veins of the Haversian canals. Others enter the compact bone through Volkmann's canals and run in the Haversian canals.
- They enter marrow cavity and anastomose by branches with the capillaries of the medullary artery.
- Nerves enter through Volkman's canals and ramify in the Haversian canals and the marrow. Pacinian corpuscles occur in the periosteum, whereas osseous tissue is insensitive.

MODULE-6: BLOOD AND LYMPH

Learning outcomes

- At the end of this module the learner will be able to know about
  - blood,
  - lymph and
  - red marrow.

BLOOD AND LYMPH

- Blood is the connective tissue consisting of free cells and a fluid intercellular substance or plasma.
- The structural elements of Mammalian blood include *red blood corpuscles (erythrocytes), white blood corpuscles (leucocytes) and blood platelets*.

ERYTHROCYTES (RED BLOOD CORPUSCLES)

- They are highly differentiated and specialized for the function of transporting oxygen. In the lower vertebrates, the erythrocyte is nucleated but in mammals, it loses it nucleus, Golgi apparatus, mitochondria and centroiles before entering blood stream.
- The erythrocytes are acidophilic biconcave discs and round in all mammals except in camel and llama where they are elliptical. (Birds, reptiles and fishes have elliptical nucleated erythrocytes). On surface view, the erythrocyte is circular in outline and the central depression appears as a lighter area depending on the focus.
- Histologically, the erythrocytes appear entirely homogenous. The covering is a delicate plasma membrane formed by a condensation of the lipo-protein complex of the corpuscular substance. The contents of the corpuscle are present as a relatively fluid colloidal mixture.

- Chemically the erythrocyte consists of a protein and lipoid colloidal complex, of which the most important element is hemoglobin. ***Hemoglobin*** is the pigment which gives the red colour to the erythrocytes.
- The average diameter of the erythrocyte is as follows in microns: *Elephant 9.0; man 7.3; rabbit 6.5; cow 6.1; cat 6.0; horse 5.7; sheep 5.0; goat 3.7; musk ox 2.5.*
- Number (in millions per cubic m.m.) *Goat 17.3, Sheep 11.5, cat 7.2, Horse 7, Dog 6.1, Ox 6, Man 5; Guinea pig 5; Rabbit 4.6, Chicken 2.9.*
- The number, the size and shape of the erythrocytes are correlated to the metabolic activity of the different animal groups. High metabolic activity is correlated with small size and circular shape and large number of cells conversely, lower metabolic rate is correlated with larger size and small number of cells.

LEUCOCYTES (WHITE BLOOD CORPUSCLES)

- These are nucleated, (true cells) and may be divided into ***non-granular*** *(agranulocytes)* and ***granular*** *(granulocytes)* varieties.
- The cytoplasm of granular leucocytes shows numerous granules. In many, these granules are fine and slightly refractive but in others they are coarse and highly refractive.
- Total number of leucocytes in thousand Per cubic mm.

Chicken	19.8

Cat	17.2
Swine	14.9
Goat and guinea pig	12
Dog	11.3
Sheep	9.2
Horse	9
Man	9
Ox	8
Rabbit	8

Granulocytes

- These are divided into three classes according to the nature of the staining reaction of the granules present as neutrophils, eosinophils and basophils.
- *Neutrophils*
    - They are large cells 8 to 12 microns in size. The nucleus shows 3 to 5 lobes connected by fine stands and is in the form of 2 or horse shoe. Granules are neutrophilic as they have affinity towards the neutral stain of the Romanowsky compound and take a light purple stain. In the rabbit, guinea pig and chicken they take acid stain. In different species, based on staining reaction, these cells are also called heterophils.
    - They are highly phagocytic and show great amoeboid motility. After the migration from blood stream, the neutrophils phagocytose bacteria or other small particles. They have been cells that engulf larger particles. The neutrophils also elaborate powerful proteolytic enzymes which may act within the cell as in the digestion of phagocytosed bodies liberated and act outside the cell body.
    - Chemotactically attracted by devitalized tissue bacteria or other foreign bodies the cells reach these places by amoeboid movement and they liberate the proteolytic enzymes either by secretion or most commonly by disintegration and rupture of the leucocytes themselves. These cells form the so called pus corpuscles.
    - Number of neutrophils in percentage of total number of leucocytes. In man, dog cat, horse and pig, the neutrophils are in majority. Whereas in ruminants, chicken and laboratory rodent, the lymphocytes are in majority.

Dog	74
Man	72
Cat	59
Horse	58
Swine	53

Guinea pig and rabbit	40
Goat	35
Ox	30
Chicken	24.4
Sheep	24

- *Eosinophils*
  - These are larger than neutrophils and the size is about 10 to 14 microns. It contains spherical and highly refractive granules which stain with eosin and other acid dyes. The nucleus generally has only two lobes. The granules are especially large in horse. They show amoeboid movement but are not actively phagocytic. Their number is greatly increased in allergic states, bronchial asthma, skin diseases and parasitic infestations.
  - Number of eosinophils in percentage of total number of leucocytes.

Ox	10
Guinea pig	8
Horse	7
Goat	5.8
Cat	5
Sheep	4
Swine	4
Dog	2
Chicken	1.9
Rabbit	1.5

- *Basophils*
  - These are rare in adult blood being only 0.5 percent of leucocytes except in the chicken (3 percent). Their size is 8 to 10 microns. The nucleus is large irregularly polymorphous. The coarse granules are basophilic, intermediate in size between eosinophil and neutrophil types and are soluble in water. They resemble the mast cells of connective tissue.

Non granular leucocytes or agranulocytes

- These include the lymphocytes which are small about the size of erythrocytes, and a group of largest cells, the monocytes which have more cytoplasm and a more indented nucleus.
- *Lymphocytes*
  - The size of the small lymphocyte varies from 6 to microns majority being 7 to 8 microns. The nucleus is large and stains intensely. The basophilic

cytoplasm forms a narrow rim around the nucleus. The large lymphocytes measures from 10 to 12 microns. The larger lymphocytes also have a deeply stained spherical nucleus and a basophilic cytoplasm, but there is greater proportion of cytoplasm than in the small lymphocyte. The basophilia of the cytoplasm in both is due to diffuse distribution of free ribosome or RNA granules.

- The lymphocytes migrate through walls of capillaries into the connective tissue where they are believed to perform a number of functions. They are believed to act as precursors of monocytes and macrophages in the connective tissue. Following a primary antigenic stimulation, the lymphocytes give rise to a line of cells which differentiate into plasma cells, which produce the specific antibodies. They probably have a detoxifying action and are concerned in protection against foreign substance including response against grafts of foreign tissue.
- Number of lymphocytes in percentage of the total number of leucocytes.

Sheep	68
Chicken	62
Goat	57
Rabbit	55
Ox	52
Guinea pig	45
Swine	38
Horse	28
Man and dog	20

- *Monocytes*
    - These are large cells, size varying from 12 to 15 microns, but they may occasionally be up to 20 microns. The nucleus is ovoid, kidney or horse-shoe shaped and eccentrically placed. It stains less intensely than lymphocytes. Cytoplasm is basophilic and abundant. They migrate through the capillary wall into the surrounding connective tissue, become actively phagocytic and transform into macrophages, indistinguishable from the macrophages present in the connective tissue. They serve to combat certain types of bacterial infection like tuberculosis.
    - Number of monocytes in percentage of total number of leucocytes.

Chicken	9.4
Ox	7
Guinea pig	6
Horse	5
Man	5
Swine	4
Sheep	3

Rabbit and cat	2.5
Goat	2.2

Blood platelets

- They are colorless about 3 microns biconvex discs but appear spindle shaped when seen sideways.
- They have no nucleus. They show a central granular mass which stains deeply with basic stains called the chromatomere and a peripheral hyaline lightly stained zone called the hyalomere.
- In mammals they are not cells but are only fragments of cells derived from the giant cells in red marrow.
- Birds and other lower vertebrates have true thrombocytes which are nucleated and have basophilic cytoplasm.
- The platelets play an important role in coagulation of blood.

LYMPH

- Lymph consists of a fluid, in which various corpuscular elements are suspended. Red blood corpuscles and platelets are absent.
- The chief cellular elements are lymphocytes with few granulocytes.

RED MARROW (MYELOID TISSUE)

- It is composed of stroma of reticular cells and fibres with free cells located in the meshwork. The stroma also shows varying number of fat cells. Majority of free cells in bone marrow are the developmental stages of the granulocytes and a few lymphocytes, monocytes and plasma cells. Sinusoids are numerous and form anastomosing networks.

Haemocytoblasts

- They are large cells up to 15 microns in size. The nucleus is large and rounded and the cytoplasm is deeply basophilic. They constitute normally 0.3 to 0.5 percent of the cells of marrow.

Erythroblasts

These are the precursors of erythrocytes and undergo a series of divisions and transformation before the erythrocytes is formed. The important stages in erythrocyte formation are;

- *Proerythroblasts or Basophilic erythroblast*
    - These are large round cells with spherical nucleus containing angular particles or chromatin and the cytoplasm is homogenous and is intensely basophilic.

- *Polychromatophilic erythroblasts*
    - These arise by mitotic division of proerythroblasts. There is an increase in the haemoglobin in successive stages so that erythroblasts at successive stages show less of basophilia and more of acidophilia. Hence these cells are called poly-chromatophilic erythroblasts. Chromatin becomes more regularly arranged. The cells are smaller than proerythroblasts and larger than normoblasts.
- *Normoblasts*
    - These are derived from polychromatophilic erythroblasts after a number of divisions. The cytoplasm has more haemoglobin and stains like erythrocytes. The cells are slightly larger than erythrocytes. Their nucleus is smaller and dense in chromatin and stain intensely. The normoblasts extrude their nuclei to become erythrocytes. The youngest erythrocyte shows a delicate reticulum and so it is called reticulocyte. The reticulum disappears before reticulocytes leave the marrow.
- *Erythrocyte*

Myelocytes

- These differentiate from myeloblasts. These constitute 12 percent of the marrow cells. These cells show an increase in the granules and increase in the density of chromatin of the nuleus. The earliest myelocytes are known as Promyelocytes. They are large cells with rounded or oval nucleus and basophilic cytoplasm. The cytoplasm contains a few granules of one of the specific types (neutrophilic or acidophilic) but because of the few granules promyelocytes are not classified into three groups. The promyelocytes proliferate and differentiate into myelocytes proper. The cells become smaller in size show an increase in the number of granules, decrease in the basophilia of cytoplasm and increase in the density of the chromatin of the nucleus.
- Neutrophilic, esoinophilic and basophilic myelocytes are distinguished. The myelocytes after a number of generations, differentiate into metamyelocytes. They have an indented or kidney shaped nucleus and the cytoplasm showing numerous specific granules of each type. The metamyelocytes differentiate into mature leucocytes, which enter the blood stream.

Megakaryocyte

- These are also called as giant cells and are large (30-100 microns) rounded cells but the cytoplasm may show irregular processes. The nucleus consists of many lobes connected by short stalks. Processes of cytoplasm of their cell extend through the walls of sinusoids and by constriction and segmentation.

MODULE-7: MUSCLE TISSUE

Learning outcomes

- At the end of this module the learner will be able to know about
    - muscle and its types and
    - regeneration of muscle.

MUSCLE

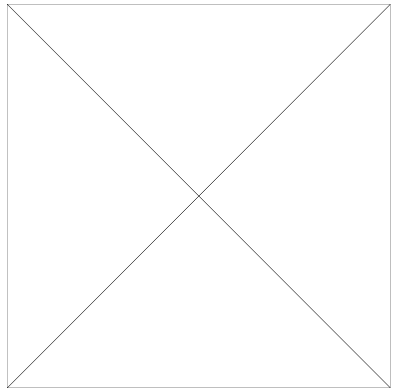
- Three types of muscle viz., ***smooth, skeletal*** and ***cardiac*** are distinguishable histologically.
    - Smooth or non-striated muscle lacks the cross striations seen in other two muscles. The smooth muscle is involuntary, being especially associated with viscera which are not under the voluntary control.
    - Skeletal muscle is striated and voluntary making up the bulky muscles of the body.
    - Cardiac or heart muscle is striated but involuntary.

SMOOTH MUSCLE

- Consists of fusiform or spindle shaped cell 15 to 500 microns in length with abundant cytoplasm in whose central thickest position the nucleus lies.
- The nucleus is oval elongated or rod-shaped. The nuclei of contracted muscle cells usually have a folded outline.
- The cytoplasm contains the usual organoids and appears more or less homogenous in routine sections. By treatment with dilute nitric acid, longitudinally arranged myofibrils can be made out.
- The cytoplasm in routine preparations takes the eosin stain. A plasma membrane, similar to those in other cells is present.
- As a rule the cells are gathered into dense sheets or bands, but they may occur as isolated units scattered among the connective fibres in a tissue like the dartos tunic of the scrotum.
- Within the bands the cells are parallel to each other but are packed together so that the narrower position of one lies against the wider portions of its neighbors.
- Delicate reticular and elastic fibres surround individual cells in a bundle. Between larger bundles there is collagenous tissue.
- The smooth muscle cells increase in the pregnant uterus where the length may exceed half m.m. (500 microns).
- Smooth muscle is not richly supplied with blood vessels. Capillaries are seen in between groups of cells. There are nerve endings in smooth muscle but motor termination for every cell is not seen.
- The contraction of smooth muscle is slow and sustained, in contrast to the skeletal muscle which contracts rapidly.
- Smooth muscle is found in the wall of the alimentary canal from the stomach to anus, gall bladders, trachea bronchial tree, ureter, bladder, prostate and Cowper's glands; oviduct; uterus; vagina; blood vessels and larger lymphatic, spleen and lymph nodes.
- Smooth muscle occurs in skin in connection with hair follicles. In the eye, it is found in the Iris and ciliary body.

SKELETAL MUSCLE

- The independent units of skeletal muscle are called as muscle fibres. The fibres have many nuclei and are larger than most cells. Fibres are grouped together into bundles of fasciculi. Larger muscles are composed of many fasciculi.
- The skeletal muscle fibres are elongated and cylindrical and 1.5 cm in length and 10-15 microns in diameter. The thickness varies with species, individual stage of nutrition, age, size and especially functions of muscle. With growth or exercise the size increases.
- Surrounding the fibre is a covering or sheath called Sarcolemma. This sheath is elastic, transparent, homogenous and difficult to see except when broken in the fresh preparations. It can be seen in stained longitudinal sections. Inside the sarcolemma, are the nuclei and a cross striated substance composed principally of myofibrils. Surrounding fibrillae is sarcoplasm which corresponds to cytoplasm of other cells. The skeletal muscle fibre has many nuclei, several hundred appearing within a fibre of average size. The nuclei are directly under the sarcolemma. The nuclei are flattened and oval. They show a loose network of chromatin.
- The skeletal muscle fibre shows a characteristic striated appearance due to regular alternation of dark and light stripes or striations across. They are produced by alternating light and dark segments of longitudinally arranged elements, by myofibrillae. The latter are 1.2 microns in diameter. They are visible within the fibres of teased fresh muscle as well as in fixed preparations. Similar segment of adjacent fibrillae are placed side by side in an intact fibre to form characteristic cross striations seen in the fibre as a whole.
- In a cross section of a fibre the cut ends of myofibrils are visible as definite areas with individual size and shape. They are separated from each other by narrow spaces which represent the sarcoplasm. In routine preparations the fibrils appear to be arranged in irregular groups known as Cohanheimsfields.
- In the cross striations of the fibrillae the dark band is called the A or Q band (anisotropic). The light band is designated I or J band (isotropic). Each of these bands is bisected by a narrow line, that in the 1 band stains deeply and is designated ‘Z” line and the line bisecting the A (q) band is pale deeply and is called H zone. The Z line is also called Krause’s membrane. The portion of a fibril between the two successive ‘Z’ line is called a sarcomere. In the relaxed condition, the sarcomere is to 3 microns.



- Each myofibril is made up of thin, thread like elements myofilaments. Two types of myofilaments have been observed. One is thick and extends from one end of the A band to the other. These are myosin filaments. The thin filaments from either side of the 'Z' line extend across the adjacent I band into the 'A' band as far as the 'H' zone. These are made up of the actin and tropomyosin. Thus the cross striations seen with the light microscope are related to the distribution of myofilaments which can be seen only under electron microscope.
- Sarcoplasm fills in the spaces between myofibrils is clear cytoplasmic ground substance. It contains Golgi apparatus, mitochondria, endoplasmic reticulum and has few ribosomes. It also contains glycogen and fat droplets. Fibres rich in sarcoplasma, appear darker with the naked eye or low magnifications. These are called dark fibres or red fibres. Those poor in sacroplasm are light fibres. Both kinds are intermingled in the muscles of mammals.

Changes during contraction

- During contraction the fibre as a whole becomes shorter and broader, when it contracts. Each sarcomere also becomes are stimulated to contract by about 50 per cent. The H zone of A band usually disappears at the same time.
- The total length of A band remains constant usually during contraction and relaxation.
- It is believed that during contraction the thin actin filaments slide over the thick myosin filaments, the actin filaments being more or less pulled into the "A" band or that the actin filaments fold or coil up during contraction.
- During contraction an acto-myosin complex is formed.

Muscle tendon attachment

- At the ends of a skeletal muscle the fibres are attached securely either to tendon, periosteum pr some fibrous connective tissue structure.
- Muscle fibrillae end abruptly and are not continuous with those of tendon or other connective tissue structure. But the connective tissue of muscle (see below) is continuous with the connective tissue of the tendon or other connective tissue structures to which muscles are attached.

Connective tissue of muscle

- Surrounding each muscle fibre is a network of fine reticular fibres the endomysium. Groups of muscles fibres are surrounded by collagenous connective tissue called perimysium. Thus a dozen or more muscle fibres are completely surrounded by perimysium to form fasiculi or muscle.
- Fasciculi are in turn bound into larger and larger orders of bundles by epimysium and the entire muscle has its outer investment the deep fascia of gross anatomy.
- Endomysium, perimysium and epimysium are continuous with one another in the order mentioned blood vessels and nerves ramify through the connective tissue.

Blood and nerve supply

- The larger branches of arteries penetrate the muscle by following laminae of perimysium.
- The arterioles penetrate the fasciculi capillary supply is very rich.
- Every skeletal muscle fibre receives at least one motor nerve ending from different nerves.
- The sensory or afferent fibres are associated with specialized endings called neuromuscular spindles (Refer Nervous tissue).

CARDIAC MUSCLE

- Myocardium or heart muscle is composed of an interlacing network of muscle fibres (cells). The muscle net is irregularly and incompletely divided into bundles and laminae which wind about the heart in the form of spirals. The fibres within a bundle are mostly parallel but the bundles themselves course in different directions so that a section of myocardium shows fibres cut in longitudinal, transverse and oblique planes.
- The muscle substance is composed of fibres or cells which show cross striations like skeletal muscle and are 9 to 20 microns in diameter, connected with each other by anastomosing branches. The myofibrils resemble that of skeletal muscle but the cross striations are closer together and not very distinct. These fibrillae are thicker and more closely packed together at the periphery of the fibre but may be so fine and sparse in the centre that there appears to be an axial core of sarcoplasm.
- In cross section the arrangement of cut ends of fibrillae frequently suggests short parallel bands or the spokes of a wheel Nuclei are in the interior near the central axis. They are oval and quite large. There is an accumulation of sacroplasm around the nucleus which contains mitochondria, fat droplets etc. A sarcolemma or plasmalemma is presented similar to that of the skeletal muscle.
- Cardiac muscle also shows intensely staining transverse bands, at certain levels and these are known as intercalated discs. These are 0.5 to 1 micron thick that is less than a cross striation or sarcomere. They are strongly refractile in fresh muscle, but deeply stained in fixed material. They run in a straight line across but

frequently are irregular or broken into “step formations”. They are the cell membranes of adjacent cells meeting each other at cell junctions.

Connective tissue of cardiac muscle :

- A network of reticular fibres and fine collagenous fibres surrounds each muscle fibre.
- It corresponds to endomysium of skeletal muscle. Between the bundles of muscle fibres there are coarser collagenous fibres and elastic fibres. These regions corrspond to perimysium of skeletal muscle.

Blood vessels and nerve supply

- An extensive plexus of blood and lymph capillaries is found in the connective network surrounding each muscle fibre.
- Branches of sympathetic and parasympathetic (vagus) nerves terminate in fine free endings on the muscle fibres.

Conducting system

- Some of the cardiac muscle fibres are modified to form the impulse conducting system, whose function is to regulate successive a contractions of atria and ventricles. It extends from the right atrium into the ventricles and is known as the atrio-ventricular bundle of his. The AV bundle and its branches consist of modified cardiac muscle fibres called purkinje fibres.
- They are distinguished form cardiac muscle fibres by
    - the reduced number of myofibril which are restricted to the periphery of the fibre ,
    - greater amount of sarcoplasm ,
    - more rounded nuclei, which occur in groups of two or more innermost of the cells.

REGENERATION OF MUSCLE

- With slight injury the smooth and skeletal muscle fibres may proliferate but a larger defect of the muscular tissue is made good only by a connective tissue scar.
- The cardiac muscle has little regenerative capacity and healing is by formation of scar tissue.

MODULE-8: NERVOUS TISSUE

Learning outcomes

- At the end of this module the learner will be able to know about
    - axon or axis cylinder,
    - neurolemma or sheath of schwann,

- medullated or myelinated nerve fibres,
- amyelinated or non-myelinated nerve fibres,
- connective tissue of peripheral nerve,
- blood supply of nerve fibres,
- physiological properties of the nerve fibre,
- nerve terminations,
- effectors and
- visceral efferent fibres.

NERVOUS TISSUE

- The nervous tissue is specialized to receive stimuli from the environment to transform them into nerve impulses and to transmit them to the nerve centers, from where appropriate response is transmitted to another organ or part of the body which reacts to the response of the original stimulus.
- Nucleus is pale staining and vesicular but the nuclear membrane stains dark with haematoxylin- chromatin is fine and dispersed. Nucleolus is single larger very prominent and may be basophilic or acidophilic. In sympathetic ganglia, the mitochondria, golgi apparatus chromophil substance or Nissl bodies and neurofibrils.
- The neurofibrillae are fine cytoplasmic fibrils which form bundles are interlace in the cell body but are parallel in axon and dendrites, demonstrable by special techniques Neuroplasm is the undifferentiated part of the cytoplasm which surrounds and separates the neurofibrillae. It is also called inter fibrillar substance.
- The chromophil substance also called as ***Nissl bodies*** are characteristic of nerve cell. The cell body they form irregular clumps or granules in the nueroplasm between the bundles of neurofibrils. They are basophilic. They are seen in the dendrites also but not in axons and axon hillocks and larger in motor neurons.
- E.M. studies reveal that Nissl bodies are composed of dense network of rough surfaced endoplasmic retriculum with RNA granule on the outer surface of the double membranes. Their presence indicates high metabolic activity in synthesizing neuro transmitter proteins, essential for replenishment of cytoplasmic material in the axon. Following repeated stimulation during degeneration and regeneration after an injury to an axon or in other pathological conditions. Nissl material undergoes an apparent reduction or disappearance (chromatolysis).
- Nerve cells may also show some inclusions or pigments under certain conditions. Two kinds of pigments are seen lipofuchsin and melanin. Lipofuchsin is yellowish or brown insoluble in usual fat solvents and appear in the form of granules dispersed throughout the cell. This pigment is not present in this newborn but appears in increasing amounts with advancing age.
- Melanin appears in the form of dark brown granules in nerve cells of the factory bulb, in the floor of IV ventricle, in the substantia nigra of midbrain etc. Its significance is not known.

- Dendrites appear as unmodified extensions of cell body. These branch repeatedly and terminate near the cell body to produce terminal arborization (telodentria). They contain neurofibrillae, nissl bodies and neuroplasm, like the cell body.

AXON OR AXIS CYLINDER

- The single axon arises from a special part of the periphery of cell body called axon hillock. This area is devoid of nissl bodies and golgi apparatus.
- Length of axon varies from a fraction of a millimeter to several feet.
- Branches arise at right angles form axons and are called collaterals axon is made up of fibrillae embedded.
- In axioplasm and covered by a membrane axolemma.
- Nerves fibres are formed by the axon and its sheaths.
- All peripheral nerve fibres consist of the axon covered with a thin protoplasmic sheath called neurolemma or sheath of schwann.
- Another sheath myelin or medullary sheath seen in some nerve fibres is next to the axis cylinder and nuerolemma. These latter fibres showing myelin sheath are called myelinated or medullated nerve fibres.
- Those without myelin sheath are amyelinated or non medullated nerve fibres.

NEUROLEMMA OR SHEATH OF SCHWANN

- This is a thin tube like membranes or sheath, containing a nucleus surrounded by cytoplasm and is also known as ***schwann's cell***.
- The neurolemma forms sheath of the axon in all peripheral nerves and inside the central nervous system there is no neurolemma but the nerve fibres have a neurolemma and axon known as myelin or medually sheath.
- In those nerve fibres where there is no myelin sheath, neurolemma closely invests the axon.

MEDULLATED OR MYELINATED NERVE FIBRES

- The medullated nerve fibres of the peripheral nervous system consist of the axon, myelin or medullary sheath and neurolemma. In the central nervous system, instead of the neurolemma, there is an irregular covering made of glial cells.
- Myelin forming the myelin sheath is glistening while when fresh, but with osmic acid fixation becomes grey or blacks in ordinary preparations the myelin is dissolved by fat solvents and in its place a clear space is left. This space is bridged by fine trabeculae- neurokeratin network.
- Myelin sheath is not continuous but interrupted at intervals or 80 to 600 microns by constrictions called the nodes of Ranvier.
- Myelin sheath is absent where the fibre branches and also at the beginning and at termination of the fibre.
- In certain preparations, the myelin between the node of Ranvier is broken up by oblique clefts or fissures extending from the surface called clefts of Schemidt-

Lantermann and the segments between them are the Schemidt Lantermann segments.

- At the nodes of Ranvier the neurolemma sheath dips into come in contact with the axon.

AMYELINATED OR NON-MYELINATED NERVE FIBRES

- Sometimes called fibres of Remak. There is no medullary or myelin sheath Axis cylinder is very slender and the thin neurolemma sheath contains scattered nuclei of Schewann cells.
- There are no nodes of Ranvier, up to a dozen or more of these nerve fibres are enclosed by the cytoplasm of the same sheath of Schwann cells.
- Majority of the axons of automatic ganglia and the processes of many of the smaller cerebrospinal ganglia have no myelin sheath.
- In the CNS there are many non-myelinated nerve fibres (without neurolemma).

CONNECTIVE TISSUE OF PERIPHERAL NERVE

- A cross section of a peripheral nerve shows that it is surrounded by a sheath of loose connective tissue called epineurium inside this wrapping several bundles of nerve fibres are seen and each of these is surrounded by a dense connective tissue sheath called perineurium. Inside these bundles are the nerve fibres.
- Each nerve fibre is surrounded by a tube of delicate connective tissue fibrils. These tubes are endoneurial tubes or sheath of Henle. Endoneurium is adherent to neurolemma.
- Each bundle of nerve fibres surrounded by perineurium is called a fascicle.

BLOOD SUPPLY OF NERVE FIBRES

- Nerves are profusely supplied by blood vessels.
- There are inter-fascicular, perineurial, intra-fascicular arteries and arterioles.
- Endoneurium contains a capillary network.

PHYSIOLOGICAL PROPERTIES OF NERVE FIBRE

- The nerve fibre is essentially a highly irritable conductor. Along it the dynamic nervous excitation propagates in waves, faster in large than in small axons.
- During the conduction of excitation the activity of one portion of the axon, serves as a stimulate activating the next portion, and so on. As the nerve fibres become active it changes in its electric potential, the outside of each active portion becoming negative relative to resting portion.
- Muscle action currents the flow of impulse between active and resting regions. Conduction of nervous impulse is influenced by the permeability of axon membrane, permitting g sodium ions to enter the axon and potassium ions to migrate from it.

- Nerve fibres can be classified into three types A B and C according to the speed of conduction.
- The 'A' fibres, with high velocity of conduction have a large diameter, a thick myelin sheath and long internodes.
- The B fibres are small myelinated fibres with relatively short internodes. The 'C' fibres with the lowest conduction rate, have little or on myelin.

NERVE TERMINATIONS

- Axons which form peripheral fibres terminate in some peripheral structure to which or from which they convey nerve impulses.
- Efferent fibres terminate in tissues which are excited into activity by the nerve impulses somatic efferent fibres in voluntary striated muscle and visceral efferent in smooth muscle or secretory epithelium. These are called effector organs.

- Afferent fibres end freely in tissues or in specially organized structures which in either case they receive stimuli which cause them to carry nervous impulses to the CNS. These nerve endings are receptors.

EFFECTORS: MOTOR END PLATE

Motor end plate (Somatic efferent fibres)

- Nerve fibre outer perimysium and branch to pass to individual muscle fibres where they end in structures called motor end plate.
- At the end plate region the myelin is lost and endoneurium becomes continuous with endomysium of muscle fibre.
- The axon devoid of its sheath divides to fine terminations which are in close contact with the sarcolemma.
- The nerve ending does not penetrate into sarcolemma.
- Beneath the end plate region, there is an increase in the number of muscle nuclei in a region known as the sole of motor plate.

VISCERAL EFFERENT FIBRES

- These are myelinated fibres terminating in cardiac muscle, smooth muscle of viscera, blood vessels, hairs and glands.
- The nerve fibres form plexuses around the muscle bundles. From these plexuses fine fibres pass to individual muscle fibre.
- In glandular epithelium, the nerve fibres from plexus beneath the basement membrane through which fibres pass to end in free nerve endings on gland cells.

MODULE-9: RECEPTORS, GANGLIA AND NEUROGLIA

Learning outcomes

- At the end of this module the learner will be able to know about
  - receptors,
  - muscle spindles (Neuromuscular spindles),
  - muscle tendon spindle (Organ of Golgi),
  - the synapse,
  - ganglia,
  - neuroglia and
  - repair and regeneration of adult tissues.

RECEPTORS

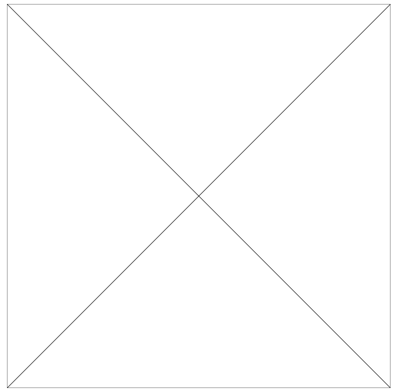
- These are of many kinds those concerned with general bodily sensibility or somaesthetic sensibility, touch, pressure, heat, cold, paid, temperature, position, movement), and those which form organs of special senses (smell, sight, taste, hearing and head position and movement).
- They may also be classified as ***exteroceptors,*** the receptors, affected by external stimuli (touch light, pressure cutaneous pain and temperature, smell sight and hearing) ***proprioceptors,*** those affected by stimuli arising within the body wall, especially those of movement and posture and ***visceroceptors,*** those affected by stimuli arising within the Viscera. All receptors, depending upon their terminal arborizations, come under two classes: ***Free*** *or* ***encapsulated***.

Free or Nonencapsulated endings

- These are found practically in all epithelia in connective tissue, in muscle and serous membranes.
- Here the fibres after losing their myelin form a subepithelial plexus from which the axons or their branches between cells and end in knob like terminal swellings.

Encapsulated endings

- They include end-bulbs, Meissner's corpuscles, pacinian corpuscles, muscle spindles and muscle tendon spindles.



- These are all characterized by a capsule of more or less flattened connective tissue cells, which enclose the terminations of the axon.

End bulbs (Krause's end bulbs)

- Spherical or oval in shape consists of a thick lamellated capsule of connective tissue cells and fibres surrounding a central cavity or inner bulb. Within this end bulb, the naked axons of onr or more mylinated fibres and either simply or in the form of skeins.
- End bulbs are found in lips, man of tongue, cheeks, soft palate, epiglottis, nasal cavities lower end of rectum peritoneum and other serous membranes tendons ligaments, connective tissue of nerve trunks, synovial membranes of certain joints, glands penis and clitoris. These are receptors for cold.

Meissner's corpuscles or tactile corpuscles

- Occur in hairless portion of skin and especially most numerous in finger tips, palms of hands and sales of feet.
- They lie within the connective tissue of dermal papillae. They are oval compose of flattened horizontally arranged connective tissue cells and lamellae surrounded by connective tissue capsule. One myelinated fibre is distributed to each corpuscle.
- After losing the myelin the naked axons pass into the corpuscle branch, and pursue a spiral course among the connective tissue elements. These corpuscles are concerned with the sense of discriminative touch.

Pacinian corpuscles

- These are laminated elliptical structures. They are large and visible to naked eye. Each corpuscle is formed of a large number of concentric lamellae of connective tissue fibres, lined by a single layer of connective tissue cells.
- The spaces between the lamellae filled with the fluid or semi-fluid substance. There is an inner bulb in the centre. Each corpuscle is supplied with a single

myelinated naked axon extends through the centre of the inner bulb and ends in a knob like expansion.

- Fine capillary networks are seen within the lamellae but they do not enter the inner bulb, pacinian corpuscles are found in deeper subcutaneous connective tissue of hand and foot peritoneum, pancreas, mesentery penis, clitoris, urethra nipple, mammary gland in connective tissue in the vicinity of tendons, ligaments, joints.
- They are stimulated by deep or heavy pressure.

MUSCLE SPINDLES (NEUROMUSCULAR SPINDLES)

- In voluntary muscle, sensory nerves end in end bulbs and muscle spindles. The muscle spindles, is a cylindrical elongated structure within which are one or several muscle fibres, connective tissue blood vessels and myelinated nerve fibres.
- The whole is enclosed in a connective tissue capsule, which is pierced, at various points by one or more nerve fibres.
- The thicker myelinated sensory fibres lose their myelin, as they branch repeatedly within the spindle.
- The axons terminate in close opposition to the sarcolemma of the enclosed muscle fibres.
- The muscle fibres of the muscle spindle are thinner, richer in sarcoplasm and have more nuclei.

MUSCLE TENDON SPINDLE (ORGAN OF GOLGI)

- Found at the junction of muscle and tendon spindle shaped composed of tendon bundles covered by a connective tissue capsule.
- Into this enter one or several afferent nerve fibres which terminate in arborization around bundles.
- Muscle spindles and muscle tendon spindles are proprioceptors of position and movement receiving stimuli due to constant or varying tensions of voluntary muscle and their attached tendons.

THE SYNAPSE

The relations between two neurons are of the nature of contact rather than complete structural continuity. This junction of two neurons is called a ***synapse***.The synapse may be defined as a point of contact of the cell membrane (plasma membrane) of an axon terminal with the cell membrane of another neuron. The synapse may be between the axon termination of one neuron and the cell body of another ***(axo-somatic synapse)*** or it may be between the axon terminals and the dendrites of another neuron *(**axo-dendritic synapse**)*. In the CNS, interwoven telodendria of Axon and dentrite arborization forms a dense feltwork of fibres which termed ***neuropli***.

- The axon terminals of a single axon may from synapses with both the body and dendrites of another neuron. Various methods of contact occur among which are;
    - by ***neuropodia*** or terminal boutons,
    - by ***gemmules***,
    - by parallel opposition.
- In the first method the axon terminals end in small bulb like expansions or neuropodium consists of neurofibrillae. Loops embedded in perifibrillar substance, some times there are simply small neurofibrillar rings. In the gemmule type of synapsis axon processes running at right angles to the dendrites of another neuron appear to come in contact with their gemmules.
- In the third type the axon terminal comes into length wise opposition with the dendrite cell body or in some cases, the amyelinated portion of the axon of the receiving neuron. It is obvious that one axon may carry impulses to a number of neurons and that each neuron may receive impulses from the axons of a number of other neurons.

GANGLIA

- Ganglia consist of aggregations of neurons situated outside the central nervous system. Each ganglion is surrounded by a connective tissue capsule which is continuous with the epineurium and perineurium of the peripheral nerve.
- Connective trabeculae extend from the capsule into the ganglion to form a framework. Within the ganglion the nerve cells are separated into irregular groups by strands of connective tissue and by bundles of nerve fibres.
- Each ganglion cell is enveloped by a double layer. The outer part of capsule is composed of flat fibroblasts and connective tissue fibre which are continuous with the endoneurium of the associated nerve fibre.
- The inner part consists of a layer fusiform of satellite cells or ***amphicytes***, which derived from the same source as the ganglion cells themselves.
    - *Cranial and spinal ganglia*
        - They are made up of pseudo-unipolar or 'T' bipolar neurons with prominent nucleolus. Chromophil substance may either be scattered throughout the cytoplasm as diffuse granules or it may form rather small finely granular.
        - Nissl bodies which are concentrically arranged around the nucleus. Most of these cells have one Principal myelinated process which at some distance from the cell body, divides into a peripheral nerve and a central branch which enters the CNS as a sensory root fibre.
    - *Autonomic ganglia*
        - The majority of the sympathetic and parasympathetic ganglia have a connective tissue framework and multipolar neurons with numerous nerve fibre. The cell bodies vary in size from 20 to 45 microns.
        - The nucleolus is relatively large and vesicular round or oval and has one or more well defined nucleoli. The nucleus is often eccentrically situated. Binucleated neurons are not uncommon and multi nucliated neurons have also been seen.

    - Chromophil substance or ***Nissl bodies*** may be distributed uniformly throughout the cytoplasm or may be confined to the perinuclear zone or to peripheral cytoplasm.
- In large ganglia, stellate cells are present. The dendrites either terminate within the capsule or pass through capsule to form intercellular plexus of fibres depending on their length.
- Often two ganglion cells share a single capsule in smaller terminal ganglia such as those in the intestinal wall, many of the ganglion cells lack capsule parasympathetic ganglion cells are found in almost all visceral structures.

NEUROGLIA

- This is the interstitial tissue of the nervous system. In the brain and spinal cord the connective tissue is limited to the enveloping membranes the meninges and a slight amount accompanies the blood vessels. The supportive framework the interstitial tissue is formed by a special group of cells and fibres called ***neuroglia***.
- In ordinary preparations of CNS many nuclei are seen which belong neither to nerve cell nor vascular tissue. These nuclei which do not possess nucleoli belong to Neuroglia cells. The neuroglia (often simply termed glia) may be divided into the following classes.
  - Astroglia or Astrocytes,
  - Oligodendroglia,
  - Microglia or mesoglia and
  - Ependyma.
- Except microglia all of the above are of ectoderm origin.
- Special and often difficult methods should be employed to study details neuroglia. What are described below will not be seen in ordinary preparations.
- *Astrocytes*
  - These are stellate cells with many processes. They are of two varieties ;
    - ***Protoplasmic astrocytes***, of numerous processes which extend from the cell body in all directions and branch frequently. The nucleus is oval and has scan chromatin and has no nucleolus. Small granules present in the cytoplasm of cell body and processes are called ***Gliosomes***. They are found principally in the great matter of brain and spinal cord. They partly envelop the neuron bodies to form satellite cells. One or more of the processes of these astrocytes have peculiar terminal expansions called foot plates or perivascular feet which are applied walls of capillaries or small blood vessels.
    - The ***fibrous astrocytes*** differ from the protoplasmic astrocytes having fewer processes. But these are most straight and longer. They possess gliosomes and coursing through their cytoplasm are fit straight, unbranched fibres the neuroglia fibres. The fibrous astrocytes have ***perivascular feet*** and are found chiefly in the white matter.
- *Oligodendroglia*

    - These are smaller than astrocytes. Their processes are few smaller and more delicate. They have no perivascular feet but their cell body may be applied to surface of a capillary as perivascular satellite.
    - They are present both in grey and white matter. In grey matter they form perinueuronal satellite to the neuron bodies. In white matter they lie in row between myelinated nerve fibres to form an investment around the myelin. They are known as ***inter-fascicular glia***. Their relation to myelin sheath in CNS is similar to that of Schwann cells myelinated fibres in PNS.
- *Microglia*
    - These are small cells with deeply staining small nuclei often elongated or irregular shape they resemble fibroblast nuclei.
    - They have neither gliosomes nor fibres. They are found both in the grey and white matter but a less in numbers in the latter.
    - They form in the grey matter perineuronal satellite and although they never have perivascular feet they form perivascular satellites.
- *Ependyma*
    - In ordinary preparations appears to consist of closely packed elongated nuclei lining the central canal of spinal cord and ventricles of brain. Their long axes are perpendicular to the cavity and they present the appearance of columnar epithelium.
    - Their process ramifies more or less deeply in the wall to the neural tube. They show neuroglia fibres and are to the regarded as neuroglial cell. They may have in certain places, cilia which protrude into the neural cavity.

REPAIR AND REGENERATION OF ADULT TISSUES

- *Epithelium:* In contrast to the more highly differentiated tissues like the nerve cells and skeletal muscle fibres epithelium has a capacity for cell division and repair if the injury is not very extensive.
- *Connective tissue proper* has the greatest powers for regenerations and repair and is the tissue involved in the healing process of wounds and the regenerating tissue is known as granulation tissue is known as granulation tissue. Regeneration of cartilage is a slow process and possibly does not occur at all in many instances. Osseous tissue has powers of regeneration and repair.
- *Smooth muscle* has limited powers of regeneration that of skeletal muscle is restricted, while the regenerative capacity of adult heart muscle is very slight.
- In *nervous tissue* in the adult, when nerve cell body dies, there will be no regeneration or replacement by mitotic division of existing cells. But when the cell body is intact the nerve fibre or axon alone is injured distal to the injury there is degeneration leading to complete break down and disappearance of the portion of the nerve fibre including its terminal arborization (**Wallerian or secondary degeneration**). But proximal to the injury, after certain initial degenerative processes, regeneration occurs leading to a new growth from the injured end. Changes in the nerve cell body (e.g) Chromatolysis also occur and fibre

regeneration occurs only if the cell body survives, it depends also on the type of neuron, nature and location of the site of injury etc.

MODULE-10: SPECIAL HISTOLOGY

Learning outcomes

- At the end of this module the learner will be able to know about
    - circulatory system,
    - blood vascular system,
    - capillaries,
    - arteries,
    - veins and
    - lymph vascular system.

CIRCULATORY SYSTEM

- The circulatory apparatus consists of a ***cardio vascular system*** and ***lymphatic system***.
- Cardiovascular system consists of
    - A central propelling organ- the *heart*
    - A series of efferent tubes - the *arteries*, which by branching constantly increase in number and decrease in caliber and which serve to carry the blood form heart to the tissues,
    - Minute anastamosing tubules - the *capillaries* into which the arteries empty and through the walls of which the interchange of elements between blood and the other tissue takes place,
    - A system of converging tubes (the efferent tubes) - the *veins* which receive blood form the capillaries, unite to form large vessels as they approach the heart; and serve for draining the blood from that organ.
- The lymphatic system consists of lymphatic glands or nodes and lymphatic capillaries and various sized lymphatic vessels, which ultimately drain into two main trunks, the *thoracic duct* and *right lymphatic duct*.

BLOOD VASCULAR SYSTEM

- The entire system the heart, arteries, veins, capillaries has a common lining, which consists of a single layer of cells forming the ***endothelium***.
- In the capillaries this single layer of cells forms the entire wall.
- In the heart, arteries and veins the endothelium is invested with accessory coat of muscle and connective tissue.

CAPILLARIES

- These are delicate tubes whose average diameter is about 7 to 9 microns. Capillaries branch extensively without change in caliber and these branches anastomose to form extensive networks whose meshes vary in size and shape in different tissues and organs. The greater the metabolic activity of the tissue, the denser is the capillary network.
- The wall of a capillary consists of a single layer of flattened endothelial cells *(simple squamous epithelium)* separated by narrow intercellular spaces, which are filled with a little intercellular cement. On surface view the cells appear as a delicate mosaic, which can be demonstrated by precipitation of silver in the intercellular clefts. The cell borders are usually serrated or wavy.
- Cells are arranged with their long axes parallel with the long axis of the tube. In capillaries of small caliber the cells are very narrow and their ends pointed. In wider capillaries cell are oval with blunt ends. Cytoplasm is clear or finely granular and nucleus is central and elongated. Cells are thicker in the region of the nucleus.
- In fixed preparation, there is pronounced bulging of nuclei into the lumen, due to shrinking of cytoplasm. Two endothelial cells and occasionally even one sufficient to form the circumference of a small capillary. For the larger ones, 3 to 5 cells are required.
- That part of a capillary, which is nearest to the arteriole, is called an *arterial capillary* and that part nearest the venule is called a *venous capillary* but these designations are based on topography and function.
- The sinusoids or sinusoidal capillaries of liver and other organs are larger, (25-30 microns). Lining cells have processes, which extend into the lumen of the sinusoids. The connective tissue which usually surrounds capillaries is so greatly reduced in amount in sinusoids that the lining cells of the latter are closely applied to the parenchyma of the organs, being separated form the latter by a fine network or reticular fibres. Lining cells of sinusoids, consists of phagocytic and non-phagocytic cells the former belonging to the reticulo-endothelial system.
- The capillary walls furnish the membrane for diffusion, filtration and osmosis of fluids to and from the blood stream. The passage of fluid through the walls of the capillary is partially dependent on the blood pressure within the capillaries and on the colloid osmotic pressure of the blood. Recent play a significant role in increasing capillary permeability.

ARTERIES

The wall of an artery is composed of three tunics or coats which are

- *Innermost coat* - the *Tunica intima* consisting of endothelium continuous with that of capillaries,
- *The middle coat* - *Tunica media* consisting mainly of smooth muscle with varying amounts of elastic and collagenous tissue and
- *The outer coat* - *Tunica adventitia or externa* composed of loose connective tissue.
    - The structure of these coats varies according to the artery and it is convenient to distinguish

- small arteries or arterioles,
- medium-sized arteries and
- large elastic arteries.

Small Arteries (Arterioles)

- The three coats are distinguishable as an endothelial intima, a muscular media and an adventitia of connective tissue. An internal elastic membrane is present and seen easily in arterioles of 40 microns diameter and upward. This marks the boundary between the tunica intima and media. The tunica media is made up of smooth muscle fibres circularly arranged formed of one or two layers only in arterioles and gradually increasing in thickness, as the caliber of the vessel increases.
- The Tunica externa is made up of flattened fibroblasts and longitudinally arranged collagenous fibres and as the caliber of the vessel increases elastic and reticular fibres are also present. These vessels serve more for distribution of blood to various capillary beds and to control blood pressure.

Medium sized (Muscular) **arteries**

- These include all named arteries excepting very large ones. The walls of these vessels are very thick due to large amount of muscular tissue in the media. These are called muscular arteries. They are also called *'distributing'* arteries because they distribute blood to all organs and regulate the supply according to functional needs. These Tunica intima exhibits three definite layers endothelium, intermediate layer and internal elastic membrane. The intermediate layer consists of delicate elastic and collagenous fibrils and a few fibroblasts.
- The *internal elastic membrane* is a thick fenestrated band. It marks the boundary between the intima and media owing to the large amount of muscle in their walls. The postmortem contraction of arteries throws the elastic membrane into longitudinal folds hence in transverse sections it has the appearance of a corrugated or wavy band. The media is the thickest coat and has layers of circularly disposed muscle fibres. There circularly disposed elastic nets in the media.
- The adventitia consists of a thick layer of connective tissue containing collagenous and elastic fibres disposed off longitudinally. Between the adventitia and the media is a very well defined external elastic membrane. The outer layer of adventitia blends gradually with the surrounding connective tissue when attaches the artery to other structures.

Larger arteries (Elastic arteries)

- Also called *conducting arteries* because they conduct blood from the heart to the muscular arteries. The wall is relatively thin for the size of the vessels. The chief representative of this type is the aorta. The T. intima is made up of endothelium and endothelial cells are short and polygonal. The deeper portion of intima is

made up of coarse collagenous fibres; some longitudinally oriented smooth muscle fibres and longitudinally arranged elastic fibres.
- The elastic membrane is usually split into two or more lamellae, which merge with other similar membranes, both in the media, and hence it is difficult to identify it. The muscle tissue is relatively reduced in amount. The adventitia is very thin and is composed of connective tissue mostly of collagenous fibres arranged in longitudinal spirals.

VEINS

- The caliber of veins is as a rule much larger but the walls are thinner than arteries due to a great reduction of the muscular and elastic elements.
- The collagenous connective tissue is present in much larger amount and constitutes the bulk of the wall. The three coats are present but their boundaries are often indistinct. The whole wall is flabbier and tends to collapse when not filled with blood.
- The histological structure of the veins varies greatly and the variations are not always related to the size of the vessels but depend on local mechanical conditions. The structure may be quite different in veins of same caliber and even in different portions of the same vein.

Small veins or venules

- These are endothelial tubes. Tunica intima surrounded by collagenous fibres and fibroblasts, with a few isolated, circularly disposed, plain muscle fibres forming the Tunica media.
- As the caliber of the vessel increases, circular smooth muscle fibres forms a continuous layer and may also become many layered, the individual layers being separated by loose connective tissue.
- The Tunica adventitia is relatively thick and is made up mostly of longitudinally disposed collagen fibres

Medium sized veins

- These include all the named veins and their immediate branches excepting the main trunks.
- The Tunica media is composed of circularly arranged plain muscle fibres and collagen fibres.
- The media is thickest in the veins of the limbs and is very thin in the views of the head and abdomen.
- The Tunica adventitia is well developed and forms bulk of the wall. It consists of collagenous and elastic tissues.

Large veins

- The Tunica intima is made up of endothelium.

- The Tunica media is usually thin with the reduction in circularly arranged smooth muscle fibres.
- Tunica adventitia is very thick and among collagenous and elastic fibres, there is dense arrangement of longitudinal bundles of plain muscle.

Valves

- Veins over 2 m.m. in diameter are provided with valves at intervals. These are *semilunar flaps*, which project into the lumen, their free margin being projected towards the heart.
- These are derived from the intima and consist of loose connective tissue covered by a single layer of endothelium.

LYMPH VASCULAR SYSTEM

- Besides the blood vessels, the body contains a collateral system of channels, lined by endothelium which collect the tissue fluid and return into the blood stream.
- The fluid in these vessels is lymph. Unlike blood, the lymph circulates in one direction only, from the periphery towards the heart.
- The lymphatic capillaries starts blindly from the tissue collect the lymph and freely anastomose along their course and lymph passes through one or more lymph nodes in the course of lymph vessels before entering into the blood stream.

Lymph capillaries

- These are like blood capillaries but are larger.
- Lymphatic capillaries are present in most tissues and organs except the central nervous system, bone narrow, eyeball, internal ear and foetal placenta.

Lymph vessels

- These are like veins in structure but their walls are thinner than veins of corresponding caliber.
- They contain numerous valves, which are directed in the direction of lymph flow.

MODULE-11: DIGESTIVE SYSTEM - SALIVARY GLANDS AND TONGUE

Learning outcomes

- At the end of this module the learner will be able to know about
    - salivary glands,
    - tongue and
    - taste bud.

DIGESTIVE SYSTEM

- The digestive system consists of the alimentary tract and other associated structures like the tongue, teeth, salivary gland, liver and pancreas.

SALIVARY GLANDS

- The Salivary glands may be classified on the basis of their secretion and the epithelium of their end-pieces as serous, mucous and mixed glands.
- Of the three pairs of salivary glands in mammals, the parotid glands is the serous type, the mandibular and sublingual glands are of the mixed type.
- The salivary glands are true compound tubuloalveolar glands, consisting of large and small lobules.
- The glands are enveloped by a connective tissue capsule, which sends trabeculae into the interior of the organ to form interlobar, interlobular connective tissue framework.

Serous gland

- Pyramidal cells resting on a basement membrane and enclosing a narrow lumen line the serous alveoli.
- The cell boundaries are indistinct. Secretory capillaries extend between the cells and communicate with the narrow lumen of the alveolus (intercellular secretory canaliculi).
- Continuation of these from the so-called intracellular secretory canaliculi, which are infoldings of the cell membrane.
- The spherical nucleus lies in the proximal half of the cells but not against the wall.
- The serous cells show inclusions of strongly refractive secretory zymogen granules which vary in number and arrangement in the cytoplasm which is generally acidophilic.
- Between the secreting cells and the basement membrane is a layer of flat, star shaped *myoepithelial cells*.
- These are joined to each other by their cytoplasmic processes to form a basket like shell around the secretory cells. Therefore they are called *basket cells*. These are believed to assist in the discharge of secretion into the ducts by their contraction.

Ducts

- The alveoli open into narrow acinar ducts lined by cuboidal epithelium. In salivary glands, the acinar ducts are also called as intercalated ducts.
- Within the lobule, the acinar ducts unite to form Interalobular ducts, which are lined by simple columnar epithelium, with intensely eosionophilic cells, which show basal striations.
- These are believed to posses a secretory function (secretion of calcium salts) and these ducts are also referred as striated tubules or salivary ducts.

- A thin connective tissue layer, containing collagen and elastic fibres and few muscle cells, surrounds the simple columnar epithelium resting on a basement membrane.
- The interlobular ducts are also lined by simple columnar epithelium, but the cells do not show striations.
- The larger ducts show a two layered columnar epithelium and the terminal portions show stratified columnar epithelium, which changes to the stratified squamous type at the openings of the ducts.
- There is gradual increase in the connective tissue layer as the ducts become two layered. In certain instances, like parotid gland of ruminants, mast cells are found around the salivary ducts.

Mucous gland

- Pyramidal or polygonal cells resting on a basement membrane line the mucous alveoli.
- The cell boundaries are distinct and the nucleus is flattened lies against the base of the cell and stains deeply.
- Secretory capillaries are absent. With haematoxylin and eosin staining, the cytoplasm of the mucous cells stains blue.
- When full of secretion, mucous cells are often markedly distended and occupied, except for a narrow strip of basal cytoplasm by mucinogen droplets, demonstrable only by special methods.
- They may be stained with mucin stains (e.g. mucicarmine). The pressure of the contents flattens mucous cell and nucleus is pushed against the basal wall.
- At the base of the mucous alveolus, a crescent shaped groups of serous cells, referred to as the *demilunes* or *crescents of gianuzzi*. These may have direct access to the lumen of the alveolus or may communicate with it by means of intercellular secretory canaliculi, which pass between the mucous cells.
- In addition to the true demilunes there are also groups of non-secreting mucous cells called *Stohr's crescents*. These lack secretory capillaries.
- The mixed glands either have separate serous alveoli or the same alveolus may contain both mucous and serous cells singly or in groups.
- In the second case, secretory unit is usually elongated and the serous cells usually occupy the terminal blind end of the alveolus, with mucous cells nearer the exit

.

TONGUE

- This organ consists essentially of a lining of stratified squamous epithelium and striated muscle, arranged in a number of layers. The connective tissue attaches the tough mucous membrane of the tongue to the muscular mass.

- The epithelium of the tongue is thickest and has the heaviest stratum corneum on the dorsal surface. The tongue bears various papillae, which are named for their characteristic gross morphology.
- The *papillae* are macroscopic projections formed with a central core of connective tissue and a covering layer of stratified squamous epithelium.
- The tissue core may give rise to small microscopic papillae (commonly referred to as papillary bodies) over which the epithelium is moulded. According to the shape, the (macroscopic) papillae of the tongue are divided into various types.
    - Filliform,
    - Fungiform,
    - Cirucumvallate (present in all animals) and
    - Foliate (present in horse, donkey, rabbit).

Filliform papillae

- The filliform papillae consist of a connective tissue core derived from the lamina propria and an epithelial covering characterized by a heavy stratum corneum.
- The papillae are usually slender and pointed. In most species the papillary core does not extend above the level of the glossal epithelium.
- The visible projection is made up entirely of epithelium.
- Large conical papillae, whose core projects beyond the surface of the tongue, occur in all domestic mammals except the horse and donkey.

Fungiform papillae

- These are relatively few in number and interspersed among the filiform palpillae.
- They have rounder and broader summits and narrow attached ends.
- The connective tissue core is rich in nerves and characterized by papillary body, have relatively less cornified epithelium containing taste buds.
- Taste buds may or may not be present.

Circumvallate papillae

- These are very few in number and are arranged in 'V' shaped row nearer the posterior part of the tongue. They resemble fungiform papillae but are much larger and are surrounded by a cleft *(moat)* lined with epithelium. They project above the lingual epithelium only slightly or not at all.
- Their connective tissue core bears microscopic papillae and is rich in nerves and lymphocytes. The epithelial surface facing the moat contains many taste buds.
- Deeper to that papillae lie groups of serous glands called Van Ebner's glands whose excretory ducts open into the moat at various levels.

Foliate papillae

- These are present only in some animals and each consists of a series of parallel connective tissue leaves, rich in nerves and bearing secondary papillae that project into the covering stratified squamous epithelium.

- Gustatory furrows separate them from each other.
- The epithelium covering the sides of the leaves bears taste buds.
- Deeper to the papillae lie serous glands whose ducts empty into the gustatory furrows.

TASTE BUDS

- These are microscopic structures found in the epithelium of the fungiform, foliate and circumvallate papillae of the tongue; they are also found widely separated in the soft palate; epiglottis and the free edge of the vocal folds.
- They are ellipsoid bodies embedded in an upright position in the epithelium of the mucous membrane. The taste bud is made up of *supporting or sustentacular cells* and *neuroepithelial cells*.
- The peripheral supporting cells form the outer layer of the taste bud. These are curved narrow cells with an ellipsoid nucleus, which surrounds the central supporting cells which are shorter and straighter than the peripheral ones and rounded off on the distal end.
- In some species the taste buds also contain basal supporting cells. These lie deep to the other supporting cells and are connected to them by means of processes.
- The neuroepithelial cells lie among the supporting cells. These are slender cells thickened slightly in the region of the nucleus and resemble the central supporting cells. Each is characterized externally by a fine hair-like process called *taste hair* which projects through a minute opening in the epithelium called the *taste pore*. The inner end of the cells tapers to a fine process, which may be single or branched.
- The sensory nerve fibre which convey gustatory impulses end within the taste buds in a network of varicose fibres called intragemmal fibres.
- The terminations of the intragemmal fibres end directly on the cells. Some of the termination also end between the cells (inter gemmal fibres). Dissolved substances stimulate the sensory cells.
- The lingual glands are situated partly below the mucous membrane, partly in the inter-muscular tissue, and are especially abundant on the root, on the margins and near the circumvallate papillae.
- Those in the region of circumvallate papillae are the serous *glands of Van Ebner*. The remaining glands are all mucous glands.

SPECIES DIFFERENCE

- *Filiform Papillae:* In ruminants the connective tissue core gives rise to several small secondary papillae, whereas the epithelial coat is raised into a single cornified one. In the horse, donkey and pig, the papillary core is an enlarged similar to papilla, from the top of which a cornified thread projects above the epithelial surface. In carnivores, the connective tissue core extends above the surface epithelium and bear papillae of unequal sizes.
- *Fungiform papillae:* Taste buds are very few in the Ox and horse. They are numerous in sheep, goat, pig etc.

- *Cirvumvallate papillae:* These bear numerous taste buds in pigs, and dogs and less so in cats. In the horse and pig, the taste buds are present over the entire papillary wall of the moat and are restricted to the bottom only in carnivores.
- *Foliate papillae:* Are absent in ruminants, rudimentary without taste buds in cats but are present in the horse, dog and rabbit.
- *Taste buds:* Those in the horse are melon-shaped and in Ox and Sheep they are Ovoid. In pigs, they are spindle-shaped and may extend into the tunica propria in the dog. They are more or less spherical in the cat and they are poorly defined.
- *Lingual glands:* Mixed glands are present in the margin of the tongue in the horse, in the root of the tongue in Ox and horse.
- In the horse, there is a fibrous cord in the middorsal region of the tongue located between the muscles. It is composed of fibrous and elastic tissue interspersed with fibrous and hyaline cartilage, fat and some striated muscle fibres, lingual muscles are inserted to it.
- In the dog there is ***Lyssa***, a collagenous sheath enveloping adipose tissue.

MODULE-12: DIGESTIVE SYSTEM - DIGESTIVE TUBE AND OESOPHAGUS

Learning outcomes

- At the end of this module the learner will be able to know about
  - digestive tube and
  - oesophagus.

DIGESTIVE TUBE

The digestive tube is lined internally by a continuous mucous membrane, which begins at the mouth and ends at the anus. Beginning with the oesophagus, the alimentary canal has a wall made up of four layers or tunics, which have some common general, features and specific regional characteristics. The four coats are from within outwards.

- Mucous membrane
- Submucosa
- Muscularis
- Serosa

Mucous Membrane

- This consists of three layers
  - Epithelium,
  - Lamina propria and
  - Muscularis mucosa.
- *Epithelium*
  - The type of epithelium varies in relation to the function of that part of the tube, it lines. In some parts, it is primarily protective, in other places it is

secretory and in some other places it is absorptive in function. It is of the stratified squamous type in oesophagus, rumen, reticulum and omasum of the ruminant stomach and simple columnar from stomach to large intestine and the anus being again lined by stratified squamous epithelium.

- *Lamina Propria*
  - This is a layer of loose connective tissue over which lies the epithelium. It is made up of fine interlacing fibres and contains fibroblasts and macrophages. It is frequently infiltrated with lymphocytes and plasma cells. From the stomach to large intestine, simple tubular glands are found in the lamina propria, isolated lymph nodules referred to as *Solitary glands* may also be present. In the small intestine minute projections, with a core of lamina propria covered by epithelium called *villi* are formed.
- *Muscularis mucosae*
  - It is a thin layer of plain muscle fibre and when present separates the lamina propria from the submucosa. It may be arranged in two layers, longitudinal and circular, but the two layers are not always clearly recognizable. It consists of only isolated bundles of plain muscle fibres in the oesophagus except near its termination, but is distinct from stomach onwards. It is absent in rumen and reticulum.

Submucosa

- It consists of loose connective tissue and connects the mucous membrane to muscularis.
- Glands may be present in this layer as in oesophagus and duodenum and in ileum dense aggregations of lymphoid tissue called *Peyer's patches* are present.

Tunica Muscularis

- The muscular coat consists of the layers of plain muscle fibres – outer longitudinal and inner circular layers.
- In the oesophagus it is made up of voluntary muscle, except near its termination in some species.

Tunica Serosa

- This consists of *mesothelium* (simple squamous epithelium with an underlying layer of loose connective tissue) which is adherent to the deeper muscular coat.
- Since these are reflections of the serous membranes lining the body cavities (pleura of thoracic cavity and peritoneum of abdominal and pelvic cavities), no serous membrane will be covering organs not contained in these cavity (oesophagus in the cervical region) and a fibrous coat of loose connective tissue will replace the serosa.

OESOPHAGUS

- The wall of oesophagus consists of a mucous membrane lined by stratified squamous epithelium and a muscular coat, which in the cervical region is covered by a loose fibrous adventitia. In the thoracic region, the latter is replaced by a serous membrane.

Mucosa

- It is lined by stratified squamous epithelium and is thrown into longitudinal folds.
- The lamina propria is made up of closely woven collagenous fibres with some elastic fibres interspersed in it.
- Its well-developed papillary body is overlaid by superficially cornified, stratified squamous epithelium.
- The musclaris mucosae is made up of longitudinal smooth muscle fibres, which may consist of a part of few muscle fibres, only in the initial part in some species.

Submucosa

- It is composed of loose network of coarse collagenous fibres, which permit formation of longitudinal folds.
- Mucous glands occur in the submucosa and they are made up of typical mucous alveoli with short ducts, which pass through the submucosa and muscularis mucosae and open between the two adjacent connective tissue papillae.
- The initial portions of the duct are lined by cuboidal epithelium but this change to a stratified epithelium in the lamina propria. The development of the submucosal glands varies in different parts of the oesophagus and also in different species.

Tunica muscularis

- It is made up of striated muscle with some smooth muscle at the caudal end.
- It consists of two layers, which course spirally at the beginning and become distinctly an inner and outer longitudinal layer gradually.

Tunica fibrosa

- This is composed of loose connective tissue which binds the oesophagus to the surrounding structures in the cervical region.
- In the thoracic region there is serosa, covering the muscular coat.

Bloods vessels and nerves

- Vascular trunks run longitudinally in submucosa. The branches ramify and form capillary networks in layers.
- Nerve cells occur in plexuses located in submucosa and between the main layers of tunica muscularis.

Species differences

- The muscularis mucosae is complete in man but in ruminants, solipeds and cat it consists at first only of isolated bundles.
- In the dog and pig it is entirely lacking in the initial portion in the caudal half, muscle bundles made their appearance but form a continuous layer only in the vicinity of the stomach.
- The submucosal glands are present only in the pharyangeo-oesophageal junction in the horse, ruminants and cat.
- In the dog, the glands form a continuous stratum up to the stomach and in pigs the glands extend to about middle of the oesophagus. In the pig numerous lymph nodules are present adjacent to the glands.

MODULE-13: DIGESTIVE SYSTEM - STOMACH

Learning outcomes

- At the end of this module the learner will be able to know about
    - stomach,
    - forestomach of ruminant and
    - glandular stomach.

STOMACH

- The wall of the stomach consists of a mucosa, submucosa, muscularis and serosa tunics.
- The true gastric mucosa is characterized by the presence of gastric glands.
- Only the stomach of man and carnivores are lined by gastric mucosa exclusively.
- In solipeds and swine the oesophageal portion of the stomach bears a cutaneous mucosa (stratified squamous epithelium).
- Ruminants have a stomach consisting of four compartments, three nonglandular diverticula comprising the fore stomach and a true glandular stomach.
- The forestomach consists of three compartments,
    - Rumen,
    - Reticulum and
    - Omasum.

FORESTOMACH OF RUMINANT

(Rumen, Reticulum, Omasum)

- The wall of the fore stomach consists of a non-glandular mucous membrane, a two-layered muscular tunic, and a serosa.

Rumen

- The mucosa forms large tongue shaped or conical papillae. The mucosa has neither gland nor lymph nodules.

- The stratified squamous epithelium is of the cornifying type and the stratum corneum forms relatively thick layer on the summits of the papillae.
- The stratum granulosum and stratum lucidum are more or less continuous.
- Cells of the of stratum lucidum often swells up to become nucleated vesicles, with a cornified wall and non-stailnable cytoplasm.
- The lamina propria consists of a dense filtered of fine collagenous and many elastic fibres. Muscularis mucosa is absent.
- Submucosa is loose and blends with the lamina propria without any line of demarcation.
- Tunica muscularis has two layers – an outer longitudinal and inner circular (of plain muscle).
- The serosa bridges the ruminal grooves, where the subserous connective tissue is thick with fat, nerves and blood vessels.

TOP

Reticulum

- Macroscopically the mucous membrane forms permanent folds enclosing 4 or 6 sided spaces or cells.
- Smaller folds subdivide the cells. These folds bear microscopic papillae on their sides.
- The folds and the papillae have a central core of connective tissue and are lined by stratified squamous cornified type of epithelium.
- A dense layer of stratum corneum covers the tip of the papillae and the folds.
- In very large fold a band of smooth muscle fibres occurs running in the same direction as the fold itself.
- Muscularis mucosae are otherwise absent. The two layers of muscular tunic (of plain muscle) follow an oblique course and cross at right angles. A tunica serosa is present.

TOP

Omasum

- The mucosa forms numerous folds or Omasal laminae of different sizes. These folds or laminae are studded with numerous papillae.
- Each lamina includes the entire mucosa, muscularis mucosae and submucosa.
- The mucous membrane is lined by stratified squamous epithelium and dense capillary nets are found under the epithelium.
- The muscularis mucosae are distinct and extend into the folds and may occasionally send fibres into the papillae on the laminae.
- The larger folds are composed of tissue, which resembles mucous connective tissue.
- The muscular coat consists of two layers of plain muscle – an outer thin longitudinal layer and inner thick circular layer.
- From the inner layer, bundles extend into the folds so that the large folds show on section, epithelium on both sides deeper to which lies the muscularis mucosae on each side.
- A thin stratum of submucosa separate the muscularis mucosae on each side form the central band of muscular layer derived form the inner circular layer of muscularis.
- At the free edge of the folds the central layer of muscle fibres fuses with the marginal thickening of muscularis mucosae. A serosa is present.

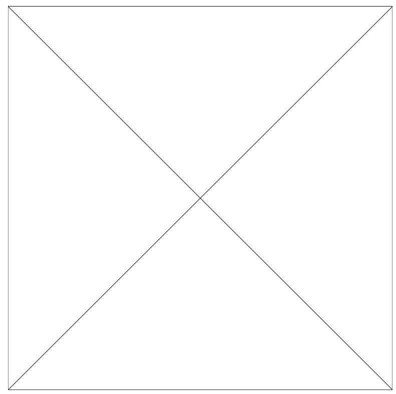
GLANDULAR STOMACH

- The wall of the stomach is composed of a mucosa, submucosa, muscularis and serosa.
- Tunica mucosa consists of
  - Surface epithelium,
  - The glandular lamina propria,
  - Muscularis mucosae

Mucosa

- Surface epithelium
  - It begins abruptly at the jagged border of stratified squamous epithelium of the oesophageal mucosa. It consists of a single layer of high columnar cells. The oval nucleus lies in the basal part of the cell.
  - No distinct striated border can be seen with light microscope. The surface epithelium is continued into depression in the gastric mucosa - the gastric pits, bottom of which show shorter and broader cells. The glands open into the bottoms of gastric pits, which correspond to ducts.
- Lamina propria
  - Contains gastric glands supported by delicate connective tissue framework. The connective tissue contains fibroblasts and histiocytes and there is diffuse infiltration with lymphocytes. There is less connective tissue between the glands than between the pits. The gastric glands are simple branched tubular glands. Several of them open into one gastric pit. These glands are of three types:
    - fundic,
    - pyloric and
    - cardiac glands
  - *Fundic glands*
    - They are distributed through the greater part of gastric mucosa. Each gland consists of a body or main part, which ends below in a blind and dilated extremity (the fundus) and is continued upwards into a constricted portion, the neck, which opens into the bottom of a gastric pit. The body of the gland contains two kinds of cells- Chief and parietal.
    - *Chief cells*
      - These are cuboidal or pyramidal and contain coarse secretory (zymogen) granules. In H and E preparations the cytoplasm of chief cells stain blue. Nuclei are spheroid and are at the basal end, Chief cells secrete *pepsin*.
    - *Parietal cells*
      - These are larger than chief cells, and are oval or polygonal; the finely granular cytoplasm stains deeply with acid dyes (eosin). Nucleus is spherical and centrally located in the cell. These cells lie outside the Chief cells or between them. They maintain connection with the lumen by intercellular canaliculi, which extend between the chief cells. Intracellular canaliculi are also present. The parietal cells/ oxyntic cells secrete *hydrochloric acid*.
      - The neck of the gland is made up of mucous cells, which may be interspersed among parietal cells. They are cuboidal with oval nuclei situated at the base of the cell. The cytoplasm stains light blue in ordinary preparations. These cells secrete mucous, it is

            believed that the mucous secreted by these cells contains the *intrinsic factor*, which enhances the absorption of *extrinsic factor* (Vitamin B12) necessary for haemopoiesis.
        - *Argentaffin cells or (Chromaffin cells)*
            - These cells show fine cytoplasmic granules, staining black by silver impregnation technique may occur as isolated cells between the basement membrane and chief cells. They are said to contain, serotonin, a vasoconstrictor substance, which stimulates the contraction of plain muscle.



    - *Pyloric glands*
        - These are coiled tubular glands. In sections mostly transverse and oblique sections of the tubule are seen. The ducts of the glands are longer but the body is shorter and the cells of the body resemble mucous cells.
        - The glands secrete mainly mucous. Between the cells of the gland, narrow eosinophilic *Stohr's cells* are often found. The gastric pits or ducts are longer (or deeper) and are lined by eosinophilic columnar cells.
    - *Cardiac glands*
        - They occur at the transition zone, between esophagus and stomach in simple stomached animals. In horse, it is restricted to the narrow zone close to the Margoplicatus junction. In ruminants, cardiac glands are located close to the omaso-abomasal junction. These are highly branched and coiled, tubular glands.
        - The ducts are very long i.e., the pits are very deep. The body has a relatively wide lumen and lined by clear pyramidal or cubodial cells with a basally located nucleus. They secrete mucous and these glands pass over gradual transition into typical gastric glands.

TOP

- Muscularis mucosae
    - Plain muscle fibres interwoven or stratified forming a thin layer fibres extend into the lamina propria.

TOP

Submucosa

- This is made up loose connective tissue.

Tunica Serosa

- The serous coat consists of a layer of loose connective tissue which is covered by mesothelium.

Species differences

- The anterior oesophageal region of the stomach in horse is lined by a cornified stratified squamous epithelium. Behind this there is fundic gland area and then pyloric gland area. Between the oesophageal region and fundic area, there is a narrow cardiac area.
- The abomasum of ruminant consists of cardiac, fundic and posterior pyloric gland areas.
- In the carnivores there is a fundic and pyloric area. Near the cardia there is a narrow zone of cardiac gland area.
- A lamina subglandularis intervenes between muscularis mucosae and the blind ends of the glands. In old animals, it becomes stratified into an inner stratum granulosum rich in cells and an outer stratum compactum consisting of network of dense, hyaline collagenous substance.

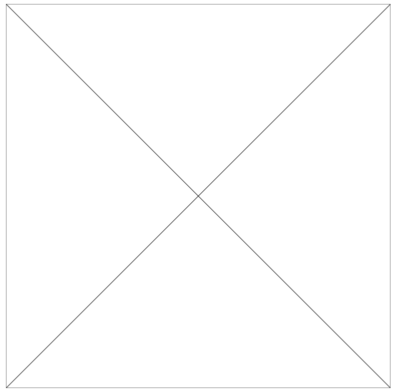
MODULE-14: DIGESTIVE SYSTEM - INTESTINES

Learning outcomes

- At the end of this module the learner will be able to know about
    - small and large intestine,
    - blood vessels to stomach and intestine,
    - nerves to stomach and intestine and
    - lymphatics to stomach and intestine.

SMALL INTESTINE

- Intestine consists to two parts - small and large.
- The small intestine is divisible into three portions, - *duodenum, jejunum* and *ileum*, which gradually pass into one another. Their general structure is similar although each division has certain distinctive features.
- The intestinal wall consists of a mucosa, submucosa, muscularis and a serosa.



Tunica mucosa

- This may be divided into the following layers:
        - Epithelium
        - Lamina propria, which has glands and in the small intestines forms villi;
        - Muscularis mucosae
    - Epithelium
        - Surface epithelium is *simple columnar* with goblet cells distributed among the columnar cells. Columnar cells are narrow and high and reach their greatest height on the villi. Nucleus is oval and is situated in the lower half of the cell. The cytoplasm is finely granular and usually acidophilic. These cells shown striated free border, which appear under light microscope as fine striations in the cytoplasm.
        - EM studies revealed that the striated free border is actually made up of fine closely packed cytoplasmic filaments or processes, which are now referred to as ***microvilli.*** The microvilli are considered as an adaptation of cell surface for better absorption of digested food material from the intestine.
        - Scattered among the columnar cells are mucous secreting goblet cells. They vary in appearance according to the amount of secretion they contain. The cell at the beginning contains a small amount of mucin near its apical border. As secretion increases the mucous gradually displaces the cytoplasm and the nucleus is flattened pushed the nucleus towards the base of the cell.
        - The distended cell has the appearance of goblet and the cytoplasm stains faintly basophilic or not at all but can be stained intensely by special mucin stains. The secretion is discharged through the free surface (apocrine) and goblet cells go through cycles of secretory activity.
    - Lamina propria
        - It has a supporting framework of reticular tissue with elastic fibres and delicate collagenous fibres. There is diffuse infiltration with numerous lymphocytes and in certain places isolated lymph nodules known as *solitary glands* may be found in the lamina propria. In the small intestine, projections of lamina propria covered by surface epithelium called *villi* occur throughout. Both in small and large intestines, the lamina propria contains simple tubular glands, called *crypts of lieberkuhn* or *intestinal glands*.
        - *Intestinal Villi*

        - These structures serve to increase the intestinal surface area available for absorption. They are narrow and elongated projections, measuring on the average of 0.5-1mm in length and 0.2 mm in width. In the center of each villus occur a tubular lymph space known as a *lacteal* and is lined by endothelium. The reticular spongy stroma of villi contains leucocytes, fat droplets, capillaries, elastic fibres and bundles of smooth muscle fibres. These muscle fibres originate from muscularis mucosae.
    - *Intestinal glands or Crypts of Lieberkuhn*
        - These are simple tubular glands found in the lamina propria. They open between the villi and extend to the lamina propria as far as the muscularis mucosae. They are surrounded by reticular fibres and consist of glandular epithelium resting on a thin basement membrane. The epithelium is made-up of columnar cells as the surface epithelium with which it is continuous but the cells of gland are shorter and their striated border becomes less distinct until they finally disappear, in the deeper portions of the gland. Goblet cells are more abundant in the deeper portions than in the surface epithelium.
        - In the small intestine the gland fundus contains the specialized granular cells of *Paneth*. These are serozymogenic having the characteristic striated chromophilic material in the basal region and large refractile acidophilic granules apically. They show activity during digestion. It is believed that these cells may be producing some digestive enzymes but the exact functional significance is not known.
        - *Enterochromaffin* or *argentaffin cells* also occur among the crypts of the intestinal glands. They occur usually singly and contain specific granules in the basal part of the cell, which are stained by silver and chromium salts. They contain serotonin but their exact functional significance is not known.
- Muscularis *mucosae:* consist of smooth muscle fibres, which are in two layers perpendicular to one another. They may interweave.

TOP

Submucosa

- Consists of loose connective tissue and elastic fibre nets. In contains large blood vessels, lymphatics and nerve plexus in the submucosa.

Tunica muscularis

- This is well developed, made up of plain muscle fibres and consists of thinner outer longitudinal layer and thicker inner circular layer. The two layers are connected by inter-muscular connective tissue.

TOP

Species differences

- In the Ox and pig, numerous renal pyramids are present with the formation of minor and major calyces. In the horse, sheep and dog the apices of the pyramids do not appear separate and the inner part of medulla forms the renal crest (results of fusion of papillae in the embryo), which shows numerous openings the area cribrosa.
- The renal crest projects into the renal pelvis the dilated origin ureter. No minor and major calyces are formed. In the cat the cells in the proximal convoluted tubules contain many fat droplets and a similar condition is also terminal portions of the tubule in the dog.
- The Excretory Passages are renal calyces pelvis, ureter, urinary bladder and urethra.
- From the renal papillae urine passes into the renal pelvis of the renal pelvis of the kidney, hence it flows through the ureter into the urinary bladder and leaves the body by way of urethra.

TOP

Regional differences in small intestine

- *Duodenal Mucosa:* The villi are broad spatula shaped and thin. In the epithelium, columnar cells preponderate over goblet cells. Submucosa - Branched tubuloalveolar glands are found in the connective tissue known as *Brunner' glands* or *Duodenal glands*.
- These glands are lined by low columnar cells, which resemble pyloric gland. The nucleus is flattened and is located at the base of the cell and the cytoplasm is faintly basophilic. These glands secrete mucous and the ducts, which are lined by columnar cells, open between the villi or into the crypt of Lieberkuhn.

LARGE INTESTINE

- The large Intestine consists of caecum, colon and rectum and the general structure of these parts are similar.
- The structure of large intestine resembles that of the small intestine except for the following differences.

Mucosa

- There are no villi. Intestinal glands or crypts of Lieberkuhn are present throughout and they are longer and straighter. The surface epithelium consists of tall columnar cells but the Goblet cells far exceed in number than the columnar cells. The crypts of Lieberkuhn also contain numerous goblet cells and towards the distal portions of the intestine the crypts appear to be lined entirely by goblet cells.

- The mucous membrane of the rectum is usually thrown into a number of longitudinal folds. At the anus, the simple columnar epithelium is replaced by stratified squamous epithelium, which becomes continuous with the epidermis beyond the anal orifice.
- The *submucosa* and *muscularis* do not present any special features. The *serous coat* is absent in the terminal portion of the rectum and is replaced by a fibrous coat.

Species difference

- The large intestine of man, solipeds and pigs, possess flat bands of longitudinal muscle known as taeniae. (For details about the number and extent of these bands in the horse, refer splanchnology).
- In the dog and pig at recto-anal junction, tubulo-alveolar anal glands are present. In pigs, it produces a mucous secretion and in dogs it produces a fatty secretion.
- In the dog, *circumanal glands* occur at the site where anal mucosa becomes continuous with the skin. These consists of a sebaceous portion, which opens through a patent duct into an adjacent hair-follicle and a non-sebaceous portion, which exhibits no evidence of any secretory activity.
- Lateral and ventral to the anus in carnivores are the *anal sacs*. The wall of anal sac is covered by stratified squamous epithelium. In the loose subepithelial layer are apocrine tubular glands in the dog and in the cat, sebaceous glands are present in addition. The excretory ducts of anal sacs also contain tubular and sebaceous glands.

BLOOD VESSELS TO STOMACH AND INTESTINE

- The arteries reach the gastro-intestinal trunk through the mesentery or omentum, gives off small branches to serosa and pass through the muscular coats to submucosa where they form an extensive plexus of large vessels called *Heller's plexus*. From this plexus, one set of branches passes outward to supply the muscular coats and another set passes inward to the mucous membrane.
- Short branches supply the muscularis mucosae, while long branches enter the lamina propria and form periglandular capillary networks. In the small intestine, each villus receives one small artery, which passes to the summit of the villus gives off a network of capillaries, which lie immediately under the epithelium. Veins correspond to the arterial branches.
- The capillary network from the mucous membrane and muscular coats are drained by veins, which form a submucous venous plexus where large veins are formed. They accompany the arteries into the mesentery.

NERVES TO STOMACH AND INTESTINE

- The nerve supply is from the autonomic nervous system and consists of non-medullated sympathetic fibres and medullated preganglionic parasympathetic fibres. They reach the intestinal wall through the mesentery and form a *myenteric plexus* or *plexus of Auerbach* in the inter-muscular connective tissue, in association with the ganglion cells of the parasympathetic system.
- From the plexus, fine branches are given off to the muscular coat. Fibres form this plexus also pass to the submucosa, where they form a submucosal plexus from which fine branches are distributed to the muscularis mucosae and glands of the mucous membrane.

LYMPHATICS TO STOMACH AND INTESTINE

- Lymph capillaries begin as blind tubules in the lamina propria in the stomach and as the lacteal in the small intestine, which occupies the center of the long axis of each villus.
- These small lymph capillaries form a plexus in deeper part of the lamina propria, from which large vessels arises.
- Pass through the muscularis mucosae and forms a submucous plexus. There is a third plexus, found in the inter-muscular connective tissue.
- Large vessels arise form the submucous plexus pass through the inner muscular coat and serosa, to enter the mesentery accompanying the arteries and veins.

MODULE-15: DIGESTIVE SYSTEM - LIVER, GALL BLADDER AND PANCREAS

Learning outcomes

- At the end of this module the learner will be able to know about
    - liver,
    - gall bladder and
    - pancreas.

LIVER

- The liver is the largest gland in the body and is an important metabolic organ of many functions.
- It has also an exocrine function, the secretion of bile, which is conveyed to the intestine by a system of ducts.
- The organ is invested with a connective tissue sheath called the *Glisson's capsule* most of which is covered by peritoneal serous membrane.
- From the connective tissue sheath fibrous bands or septa arises and enter into the substance of the gland and divide the gland into numerous hexagonal or polygonal units, the hepatic lobules. These connective tissue septa from the capsule are collectively termed as the Glisson's capsule and the interlobular columns of connective tissue convey blood vessels and ducts and are also referred to as the *portal canals*.

- The interlobular connective tissue in all domestic animals and men, except in the pig and camel. In the liver of pig and camel, the lobular is very well seen, as each hexagonal or polygonal lobule is distinctly circumscribed by connective tissue.
- At the hilus of the liver, the Glisson's capsule forms a sheath for the hepatic artery and portal vein which enter the liver and the hepatic duct which comes out of the liver.
- The branches of these structures are conveyed by the interlobular connective tissue septa or portal canal and these three (i.e. interlobular branches of hepatic artery, portal vein and hepatic duct) are fanned at the periphery of the lobules together, forming the *portal triad*.

Hepatic lobule

- Each lobule consists of
    - A central vein,
    - Cords or laminae of hepatic cells, radiating away from the central vein,
    - Hepatic sinusoids, which converge from the periphery toward the central vein and
    - Bile canaliculi or capillaries, formed between the opposing surfaces of hepatic cells representing the initial portions of bile ducts.

- Hepatic cells
    - In sections they appear as cords of cells radiating away from the central vein. The cells are arranged in regular laminae or plates extending radially form the central vein to the periphery. The plates are one cell thick and curved. They anastomose by interlaminar bridges and between them are broad, irregular spaces-lacunae, containing sinusoids.
    - Liver cells (hepatocytes) are polyhedral in shape and have a large round nucleus, which is vesicular and show a few chromatin and one or more prominent nucleoli, cytoplasm presents a variable appearance, depending upon the functional status. Glycogen and fat are both dissolved in the usual preparations. Some cells have two nuclei.

TOP

- Hepatic Sinusoids
    - The plates of liver cells are separated form one another by the sinusoids. These are irregular tortuous blood spaces, which pursue a radial course in the lobule and connect the ends of the interlobular portal veins with the intralobular central

veins. They also receive blood form the branches of hepatic artery. They fill all the interlaminar space and anastomose irregularly.

- The sinusoids are lined by irregularly alternating cells of two different kinds. One of these has small dark nucleus. Its cytoplasm extends as a thin film along the sinusoid. The other lining cells are larger and have processes, which appear to extend from one wall to other of the sinusoid or extend into the sinusoid. These have large oval vesicular nuclei and prominent nucleolus. These are referred to as stellate *cells of Kupffer*. They are phagocytic cells and form a part of the reticulo endothelial system.
- There is potential space between the Kupffer cells lining the sinusoid and hepatic cells. It is called as *space of Disse*, which is traversed by a reticular fibre network. It is considered by some workers that lymph might pass through these spaces to the lymphatic vessels in the portal canal, as within the lobule no lymphatic capillaries are present.
- The hepatic artery entering at the hilus divides into branches to supply the capsule of Liver. Some enter the portal canals and by divisions interlobular arteries which supply capillaries to interlobular connective tissue and then become continuous with the intralobular capillaries of portal vein.
- Some of these may open directly into the sinusoids. Portal vein like the hepatic artery enters the hilus and divides into number of branches, which pass the portal canals as the interlobular veins. Branches of interlobular veins enter the periphery of the hepatic lobules and break into a brush of capillaries. These intralobular capillaries anastomose to form a sinusoidal network.
- The hepatic sinusoids between the laminae of hepatic cells. These sinusoids converge towards the center of the lobule where they unite to form the central vein. The central vein is the efferent vessels from the lobule. Several central vein join to form a sublobular vein.
- Sublobular veins are found in the interlobular connective tissue between the opposed faces of lobules. Several sublobular veins join to form a collecting vein, which in turn join to form hepatic veins which pursue independent of the portal venous system and open in the posterior vena cava.

TOP

- Bile Canaliculi and ducts
  - Between the opposing faces of hepatic cells are minute channels, the bile canaliculi. In sections they appear as fine round openings between the two opposed hepatic cells. They are like the intercellular secretory capillaries of other glands; and fine tubules. They are formed by indentations or grooves on the opposing faces of two or three adjacent cells.
  - The bile capillaries form continuous networks within the liver plates and interlaminar bridges. Because they are always enclosed between adjacent cells, they are as far removed as possible from sinusoids. The hepatic cells therefore have two different physiological surfaces through which they discharge their products.
  - On the surface of the lobules the bile capillaries pass by the canal of herring into the lobular bile duct. The canals of Herring are lined by cuboidal epithelium. The interlobular ducts are lined by columnar epithelium. The interlobular bile ducts unite to form the hepatic duct which leaves the liver at the hilus. The large ducts are lined by high columnar epithelium and have a connective tissue coat.

GALL BLADDER

- It is a diverticulum of the hepatic duct developmentally to store bile It is absent in horse, elephant, rat and pigeon.
- Duct of gall bladder is called *cystic duct*, which unites with hepatic duct and forms the *bile duct*.
- Structure
    - Similar to large bile ducts. The wall consists of the following layers.
        - Mucosa consisting of a surface epithelium and lamina propria,
        - A layer of smooth muscle;
        - A perimuscular connective tissue and
        - A serous layer.
    - Mucosa is thrown into folds. Epithelium consists of *tall columnar* (which has goblet cell in the Ox.)
- The lamina propria contains lymph nodules and glands. The carnivores have few glands while ruminants have many mucous and serous glands.
- The muscular layer consists of smooth muscle running in different directions, circular and oblique, with the circular predominating, in some place regular inner circular and outer longitudinal layers can be seen.
- The *perimuscular connective tissue* layer is usually thick and outside this is the subserous layer of connective tissue containing blood vessels and nerves. On its free surface it is not attached to the liver, it is covered by serosa (Peritoneum).

PANCREAS

- It is a dual gland, which consists of an *exocrine portion* that secretes certain digestive juices and *endocrine* portion that secretes hormones. Both these functions of pancreas are carried out by distinctly different groups of cells. It is compound tubuloalveolar gland.
- The pancreas is covered by a thin layer of loose connective tissue (which does not form a distinct capsule) from which septa pass into the gland, subdividing into many lobes. The acini are all of the serous type and are lined by pyramidal cells resting on a basement membrane.
- The pyramidal secretory cells are arranged in a single layer. They resemble serous acini but are distinguished by the presence of two zones. The inner zone is coarsely granular, while the outer (basal) zone appears almost homogenous or may show fine radial striations. The spheroid nucleus lies in outer basal zone but in such a manner as to project into the inner zone. The nucleus contains one or two prominent acidophilic nucleoli.
- The acini open into the acinar or intercalated ducts, which are fairly long and are lined by cuboidal epithelium and have all the characteristics of intercalated ducts. It should be noted that in pancreas all the ducts within the lobule (inter-calated and intralobular) are lined by cuboidal epithelium only and there are no striated ducts. The interlobular ducts are lined by simple columnar epithelium and there is a connective coat, the thickness of which is directly proportional to the size of the duct.

- The cuboidal cells of the intercalated ducts sometimes extend into the lumen of the acinus as a projection and these extensions appear in sections as one or more small cell appearing within the lumen and lying in contact with apical ends of acinar cells. These are called the *centro-acinar cells of Langerhans*. These differ form secreting acinar cells in having lightly stained clear cytoplasm, devoid of secretory granules or basophilic substance.

Islets of Langerhans

- The endocrine part of pancreas consists of cellular aggregations interspersed irregularly among the acini. These cell groups are called islets of Langerhans. Tthey have no functional communications with the duct system of the gland and their secretions are poured directly into the blood stream.
- In ordinary hematoxylin eosin preparations they appear as lightly stained cell groups, between the deeply stained acini. The size of the islets and their number vary in different portions of the gland and also in the different animals.
- In routine preparation all the cells in the islets appear to be similar, but by special staining techniques different types have been identified. Three types are commonly recognized
    - A or alpha cell
    - B or beta cell and
    - D or delta cell.
- By Mallory azan technique - Alpha cells shows bright red granules, Beta cells shows brown to orange granules and Delta cells shows blue granules in the cytoplasm. 'A' cell contains fine granules and cell membranes are distinct. 'B' cells contain coarse granules and cell membranes are indistinct.
- With chrome-haematoxylin-phloxine method of staining-A cells show red granules and B cell show blue granules. The relative number of A and B cells constitute 20, 75 and 5 percent. In the dog B and D cells produce insulin and A cells are produce glucagon which has an antagonistic action to that of insulin. The D cells produce somatostatin.
- Pancreatic juice contains several proteolytic enzymes *(trypsinogen),* Lipase *(steapsin)* and are important for normal digestive processes. The endocrine secretion, Insulin plays an important role in carbohydrate metabolism.

MODULE-16: URINARY SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about
    - kidneys,
    - renal pelvis and calyces,
    - ureter,
    - urinary bladder and
    - blood vessels.

URINARY SYSTEM

- The urinary system consists of the glandular organs, the kidneys and the excretory passages, the ureter, the urinary bladder and the urethra.

KIDNEYS

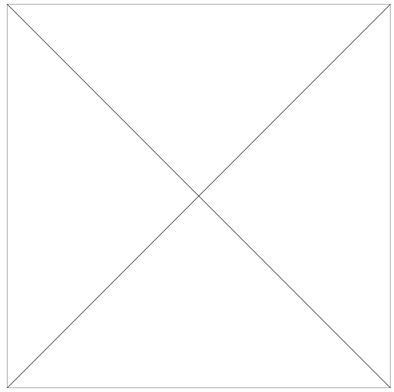
- The kidneys are compound tubular concerned with excretion of urine. It consists of excretory or uriniferous tubules, which produce urine, conducting tubules, which convey urine form the kidney to the renal pelvis, and blood vessels. The kidneys are embedded in fat and each kidney is covered by a capsule of dense collagenous fibres and a elastic fibres.
- The glandular part consists of peripheral cortex and an inner Medulla. The Medulla is in the form of renal pyramids whose bases are in contact with the cortex and apices form the *renal papillae*. The glandular part surrounds a cavity adjacent to the hilus called the *renal sinus* in which lies the *renal pelvis*, the dilated origin of ureter.
- The renal pelvis divides into primary divisions or Major calyces, which in turn divide into minor calyces. Each minor calyx receives a renal paila and the tip of the papilla shows small openings called the *area cribrosa*.
- The cortex forms the outer zone but cortical tissue also projects down into the medulla between the bases of the renal pyramids as the *renal columns of Bertini*.
- The cortical region is subdivided into a *pars convoluta* or cortical labyrinth containing convoluted tubules and glomeruli and a *pars radiata* or medullary rays, which are columns of straight tubules, which radiate out ward from the medulla.
- The parenchyma of the kidney consists of uriniferous tubules and related blood vessels and collecting tubules between which are a scanty amount of interstitial tissue.
- The structural and functional unit of the uriniferous tubule is called a *nephron*. Each nephron begins as a spherical expansion known as Bowman's capsule, which encloses a tuft of capillaries – the *glomerulus*. The Bowman's capsule and the glomerulus together form the *Renal or Malphigian co*rpuscle. These are distributed in the pars convoluta of the cortex.
- Apart from the Bowmans' capsule the nephron consists of the following segments;
    - Proximal convoluted tubule - a highly tortuous tube in the cortical labyrinth, which passes down into the medulla as,
    - the Descending limb of Henle which extends for varying distances into the medulla and then forms,
    - the loop of Henle after which it passes up into the cortex as,
    - the Ascending limb of Henle. This reaches the renal corpuscle of its nephron, attaches itself to its vascular pole and is then continued as the ,
    - Distal convoluted tubule in the cortical labyrinth. Here ends the nephron or secretory segment of the renal tubule and opens into arched collecting tubule in the cortical labyrinth. These arched collecting tubules open into

straight collecting tubules, located in the pars radiata of the cortex, which pass down the medulla and reach the apex of the renal pyramid and form the papillary ducts of Bellini, which open through the area cribrosa of renal papilla into a minor calyx.

STRUCTURE OF THE PARTS OF A NEPHRON

Renal corpuscle

- The glomerulus consists of a number of separate capillaries connecting an afferent arteriole with an efferent arteriole. These vessels are usually closer together where they enter and leave the glomerulus and this end is known as the *vascular pole* of the renal corpuscle.
- The endothelial cells of the glomerular capillaries are extremely thin and the cytoplasm is fenestrated. The endothelium rests on a basement membrane, which fuses with the basement membrane of the visceral layer of Bowman’s capsule, which closely invests the glomerulus.
- The Bowman’s capsule consists of two layers of epithelium, a visceral layer closely investing the glomerulus and a parietal layer made up of simple squamous epithelium. Between the two layers of capsule is a space where provisional urine, first formed as glomerular filtrate collects.
- The visceral layer of the capsule is made up of cells whose nuclei project into the capsular space and their cytoplasm shows numerous foot-like processes, which are in contact with the basement membrane. Hence these cells are termed as *podocytes*. The arrangement of podocytes with the fenestrated endothelium of glomerular capillaries, leave only the basement membranes as the barrier between the blood in the capillaries and capsular space.
- The afferent arterioles of the glomerulus show special features. It lacks a distinct tunica adventitia and there is no internal elastic membrane. In the tunica media instead of plain muscle are *myoepithelioid* cells having pale staining afibrillar cytoplasm. These cells exhibit granules demonstrable by special techniques. These are referred to as the *Juxta-Glomerular cells or apparatus (JG cells).*
- It is now established that these JG cells secrete a substance known as *Renin,* which acts on *hypertensinogen* in the blood to form *hypertensin (angiotensin),* which produces vaso-constriction of blood vessels and increases blood pressure.



Neck of the tubule

- Here the epithelium is of the cuboidal variety.
- It is a very short segment with a diameter of 34 microns.

Proximal convoluted tubules (PCT)

- It is the longer and broadest portion of the renal tubule arising as a continuation of the neck.
- In the pars convoluta goes towards the surface of the cortex runs a tortuous course and then enters medullary ray to pass down into the medulla runs straight course (termed as the straight or medullary) segment of PCT to be continued by the descending limb of Henle.
- The diameter of PCT is about 45-60 microns and is lined by high *pyramidal cells* with granular cytoplasm and spherical nucleus located in the basal part. The lateral margins of the cells interdigitate so that cell boundaries are indistinct. The apices of the cells show a *brush border* (stereo-cilla), which is indistinct in ordinary preparations.

Descending limb of Henle

- (Thin segment of loop of Henle). It is the continuation of the medullary segment of PCT and extends down into the medulla for varying distances. The extent of the thin segment and length of the loop varies greatly in different tubules.
- The diameter varies form 10-17 microns. It is lined by flattened squamous cells with bulging nuclei (resembling a capillary) with a faint staining cytoplasm. The nuclei of the opposite sides alternate.
- *Loop of Henle:* It is present in the medulla and may show the structure of descending or ascending segments.

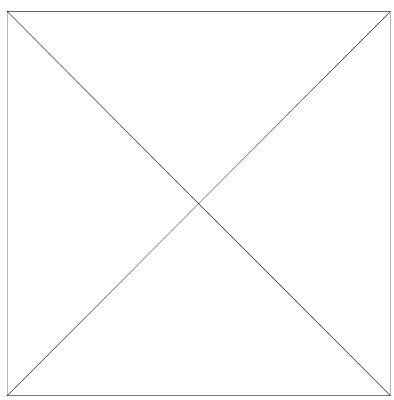
Ascending limb of Henle (ALH)

- (thick segments of Henle's loop) is 25-40 microns in diameter. From the medulla, it passes up to the cortex (in pars radiata), reaches the renal corpuscle of its nephron, attaches itself to the vascular pole and is then continued as the distal convoluted tubule.

- The ALH is lined by cuboidal cells with granular cytoplasm and spherical nuclei. Cell outlines are distinct.

Distal convoluted tubule (DCT)

- It is present in pars convoluta of the cortex and begins at the vascular pole of the Renal corpuscle and after passing a winding course becomes continuous with an arched collecting tubule (in the pars convoluta itself). It is much less convoluted than the PCT and the diameter varies form 35-53 microns.
- It is lined by cuboidal cells with granular cytoplasm stains intensely than the cells of PCT. The cell borders are fairly distinct and they do not show a brush border. In cross sections cells are more numerous, nuclei are placed close and lumen is wider than that of the PCT.
- At the Vascular pole of the Renal corpuscle, the wall of the DCT is in close contact with afferent arteriole with JG cells. This wall of the tubule shows numerous nuclei close together and the cells are also taller and this zone of the tubule is referred as Macula Densa.
- Between it and the glomerulus proper in the concavity between the efferent and afferent arterioles is a collection of small with pale nuclei. This group of cells is referred to as polkissen. The functional significance of Macula Densa and polkissen is not clear.
- This DCT terminates the nephron or secretory segment of the renal tubule.



Arched collecting tubule

- 22.60 microns in diameter. It starts form the periphery of the medullary ray and reached the apex of pyramid. The diameter progressively increases.
- The epithelium is cuboidal gradually increasing in height with clear lightly stained cytoplasm and deeply stained nuclei with definite cell out lines.

Papillary ducts of Bellini

- Diameter 200-300 microns. Columnar cells with clear basophilic cytoplasm line these.
- Near termination at the renal papilla the epithelium become two layered and it may become transitional as the duct opens into a minor calyx.

BLOOD VESSELS

- The branches of renal artery at the hilus extend radialy between the pyramids as the inter lobar arteries. At the cortico-medullary junction they bend sharply and form short arches, the *arcuate or arciform arteries*.
- The arcuate arteries give a number of interlobular arteries, which ascend vertically through the cortical labyrinth towards the surface. From these interlobular arteries small branches enter the glomeruli as the afferent vessel. The presence of JG cells in the afferent glomerular arteriole has been described with the structure (Renal Corpuscle).
- The efferent glomerular arteriole after leaving the corpuscle divides into a system of capillaries - the *peritubular plexus* that form a dense network around the tubules of the cortex. The arterial supply to the medulla is furnished by efferent glomerular vessels of those renal corpuscles, which lie close, the medulla. These vessels, the arteriolae rectae spurlae pursue a straight course into the medulla and give rise to capillary nets, which extends to the apex of the pyramids.
- The blood from the cortex is collected into small venules, which unite beneath the capsule to form stellate veins. From these arise interlobular veins, which receive small veins in the cortex and open into arcuate veins. Straight veins form the medulla open directly into arcuate veins. From the arcuate veins large interlobular veins pass between the medullary pyramids to form the renal vein.

EXCRETION OF URINE

The kindneys perform their functions by;

- *Filtration* of blood plasma in the glomeruli,
- Selective *reabsorption* by the tubules of substances which the body needed to retain,
- Active *excretion* by the tubules of certain substances to be added to the urine and
- *Exchange* of Hydrogen ions and formation of ammonia as a part of the process of acid base regulation.

SPECIES DIFFERENCES

- In the Ox and pig, numerous renal pyramids are present with the formation of minor and major calyces. In the horse, sheep and dog the apices of the pyramids do not appear separate and the inner part of medulla forms the renal crest (results of fusion of papillae in the embryo), which shows numerous openings the area cribrosa.

- The renal crest projects into the renal pelvis the dilated origin ureter. No minor and major calyces are formed. In the cat the cells in the proximal convoluted tubules contain many fat droplets and a similar condition is also terminal portions of the tubule in the dog.
- The excretory passages are renal calyces, pelvis, ureter, urinary bladder and urethra.
- From the renal papillae urine passes into the renal pelvis of the renal pelvis of the kidney, hence it flows through the ureter into the urinary bladder and leaves the body by way of urethra.

RENAL PELVIS AND CALYCES

- These are lined by transitional epithelium resting on loose connective tissue proper. The mucularis consists of two ill-defined layers of plain muscle and sphincter-like arrangement of the circular layer is found in each minor calyx at the base of each papilla and at the beginning of the ureter. A connective tissue coat containing fat cells, large blood vessels and nerves covers the muscular coat.
- *In the horse:* Goblet cells occur in the epithelium and tubulo-alveolar mucous gland in the lamina propria of the renal pelvis. A distinct submucosa is present in the horse and the ox.

URETER

- It has connective tissue coat externally.
- The muscular coat consists of an outer circular and an inner longitudinal layer of plain muscle fibres.
- In the lower third there is an additional external longitudinal layer.
- The mucous membrane is thrown into folds and is lined by transitional epithelium.

URINARY BLADDER

- The anterior part of the bladder is covered by serous membrane.
- The muscular coat is very thick and consists of three layers, an outer longitudinal, middle circular and inner longitudinal layers made up of plain muscle.
- The mucous membrane is lined by transitional epithelium, which is thick when the bladder contracted and thin when distended with urine.
- In the distended condition, the cells are thin, flattened and stretched parallel to the wall resemble narrow spindle.
- There is no distinct submucosa. The deeper layers of propria have a looser arrangement and so help to form thick folds.

BLOOD VESSELS

- In addition to capillary nets in the muscular coat and propria a rich capillary plexus is seen immediately under the epithelium.

- Capillaries also enter the epithelium.
- In the bladder there is a submucosa separated form propria, by bundles of plain muscle running longitudinally.

Note: The Urethra will be described with the genital organs.

MODULE-17: INTEGUMENTARY SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about
    - skin,
    - hair,
    - skin gland,
    - blood vessels and nerves.

SKIN

- The function of skin is to protect the body and to serve as an organ of heat regulation, excretion and sensation. It consists of an epithelial part - *epidermis* and a connective tissue part - the *dermis* and other structures, such as hair follicles, sebaceous glands, sweats gland etc. The hair, the horny portion of the hoof, nails or claws, on the digits, the horns of cattle, etc., are also derived from the skin, by special modification and development.
- The skin or cutis is divided into the epithelial epidermis and the connective tissue corium of dermis. The underlying loose *subcutis* attaches the skin to the subjacent organs. The thickness of the skin varies considerably in different parts of the body. The relative proportions of epidermis and dermis also vary. Hair follicles are generally present but there are some non-hairy regions and the epidermis show considerable thickening in these regions.

Epidermis

- This is a stratified squamous epithelium covered by a stratum corneum and rests on the papillae of dermis.
- The free surface may be smooth or show elevation caused by underlying papillae.
- Epidermis consists of two main layers - a deep layer stratum germinativum or stratium Malphigi and a superficial horny layer.
- The deep layer is subdivided into two and superficial into three. So starting from the corium one can distinguish the following layers:
- *Stratum Cylindricum:* consists of a layer of columnar cells resting on a thin basement membrane.
- *Stratum spinosum:* composed of polygonal cells arranged in a number of layers. The cells show spherical nuclei and basophilic cytoplasm. They are arranged more transversely, towards the surface. In routine preparation examined under light microscope fine processes may be seen extending between the cells. These

were referred to as “intercellular bridges” and since the cell showed spines or processes projecting form their surfaces, they were called “Prickle Cells”. EM studies have shown that these intercellular bridges are artifacts. The membranes of the cells normally in close apposition but tend to pull apart except at the region of desmosomes due to the shrinkage caused by technical procedures.

- Numerous mitotic figures may be seen in this layer and both stratum cylindricum and spinosum form the stratum germinativum.

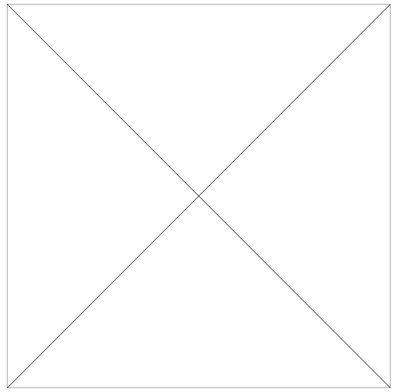
- *Stratum granulosum:* consists of a few layers of flattened rhomboid cells. These cells show first signs of cornification in the form of basophilic granules of *Keratohyalin* which increase in size and number toward surface and lend a granular appearance to this layer. With increase of granules, nucleus disintegrates and becomes pale.
- *Stratum lucidum:* is a shiny acidophilic layer of homogeneous appearnce. Here the Keratohyalin granules have liquefied to form eleidin, which is uniformly distributed throughout the many layers of cell. The cells show neither nucleus nor cell boundaries.
- *Stratum* Corneum: Consists of many layers of flat elongated cornified cells. The material forming the cells is keratin or true horny substance. Nucleus is absent. The superficial cells are dried horny plates, which are constantly shed off. New ones from the deeper layers replace the cells thus lost. The superficial layer, which is constantly desquamated, is known as *stratum disjunctum*.

Corium or Dermis

- The dermis varies in thickness and is composed of dense irregularly arranged connective tissue. It contains the connective tissue fibres, fibroblasts and histiocytes. It can be divided into a superficial or subepithelial papillary payer and a deeper reticular layer, though the two layers blend without any distinct line of demarcation.
  - *Papillary layer:* This is just below the epidermis and there is a dense interweaving of fine collagenous bundles. This layer bears on its surface contain papillary bodies, over which the epithelium is moulded. These papillae may contain capillary loops or sensory nerve endings of tactile sense. (Tactile or Meissner's corpuscles). Between the bases of papillae, three may be down growths as inter-papillary pegs of epithelium.
  - *Stratum reticulare:* The reticular layer is deeper and thicker, not sharply marked off from papillary layer. These are characterized by a network of coarse collagenous and elastic fibres. The fibres form an extensive feltwork with rhomboid meshes, the direction of fibres being parallel to the surface of the skin. The elastic fibres form basket-like capsular condensations around hair-bulbs, sweat and sebaceous glands.

Subcutis or Hypodermis

- Consists of loose collagenous tissue which contain many elastic fibres cross with each other to form a meshwork. Smaller bundles subdivide the meshes.
- A homogeneous adhesive ground substance converts the fibre nets into thin membranes. The degree to which skin can be displaced or folded depends on the development of subcutis i,e., the thickness, length, extensibility of fibre bundles.
- The spaces of subcutis are filled with adipose tissue forms a flat cushion *(panniculus adiposus)* which in well conditioned animals extends to the deeply placed cutaneous muscles. There is no clear demarcation between corium and subcutis.



Regional differnce

- The epidermis is considerably thicker in the palm, sole and volar surfaces of digits and all layers are distinct.
- The stratum corneum is very thick and forms as major part. In these regions the hair follicles are absent.
- Tactile corpuscles are numerous in the dermal papillae in the skin, at the tip of fingers and palm.
- In other region, the epidermis is thinner. All the layers are reduced and stratum corneum and stratum germinativum are constantly present, the stratum granulosum and lucidum being indistinct or totally absent.
- In the dermis the papillae are not prominent and are less numerous. Most of the area of the skin over the body contains hair follicles.
- The colour of the skin is primarily dependent upon the presence of *melanin pigment* in the epidermal cells. Certain patches of skin are especially rich in pigment (nipples, axilla, circumanal region, scrotum, labia majora), while practically no pigment is present in some regions (palm, sole).
- Melanin is formed in specialized cells known as *melanocytes*. These are found in the basal layers of stratum germinativum. The cell bodies of melanocytes appear clear, free of granules located among the basophilic epidermal cells in routine preparations. The processes of melanocytes are demonstrable only by special techniques, extend between the epidermal cells.
- The melanin granules as they are formed are pushed to the periphery and hence the processes of melanocytes will contain pigment but the cell body appears relatively clear. From the processes of melanocytes, the pigment is distributed to the epidermal cells. In white races the pigment granules occur only in the deepest cell layers and in coloured races, the pigment is distributed in more layers, throughout the stratum germinativum.
- Melanocytes stain black on treatment with Dioxy phenylalanine *(Dopa reaction)* and this reaction is attributed to the presence of the enzyme tyrosinase in the cytoplasm of melanocytes. The formation of melanin is stimulated by ultraviolet radiation.

- In the coloured races, pigmented connective tissue cells containing melanin, called dermal chromatophores may also occur in the dermis, close to the epithelium.

HAIRS

- The hairs are flexible, horny threads developed form the epidermis. They are placed in deep narrow epidermal pits, which traverse the dermis to varying depths, and usually extend into the subcutaneous tissue. Each hair consists of a *shaft* which projects above the surface and a *root* embedded within the skin.
- At the root presents a knob-like expansion, the hair-bulb, which is in close association on its under surface with a conical elevation of connective tissue (form dermis) known as the papilla of the hair. Enclosing the hair root is the hair follicle ;which consists of an epidermal and dermal parts.

Structure of hair

- The hair is composed entirely of epithelial cells, which are arranged in three definite layers.
  - Medulla
  - Cortex
  - Cuticle.
- *Medulla*
  - It forms the central axis of hair and consists of two or three layers of cells which vary in appearance in different parts of the hair. In the root, cells are cuboidal with rounded nuclei.
  - In the shaft the cells are cornified and shrunken and the nuclei are rudimentary or absent. The intercellular spaces are usually filled with air.
  - The medulla is absent from the finer, shorter hairs (lanugo) and is also absent in the hairs of scalp. If often does not extend the whole length of the hair.
- *Cortex*
  - Makes up the main bulk of the hair and consists of the several layers of cells.
  - In the root, it is composed of cuboidal cells with nuclei of normal appearance, in the lower part. At higher levels the cells become progressively flattened and in the shaft the cells become cornified, elongated and shrunken with degenerated nuclei.
  - In coloured hair, pigment granules are found in and between the cells. Air accumulating in the intercellular spaces also modifies the hair colour.
- *Cuticle*
  - It is exceedingly thin and is composed of a single layer of clear cells.
  - In the deeper part of the root, the cuticular cells are nucleated but in the upper part of the root and on the shaft, the cuticular cells are clear, scale like and non-nucleated.
  - The cells overlap giving the surface of the hair a serrated appearance.

HAIR FOLLICLE

- The follicle consists of the inner and outer epithelial root sheaths derived form the epidermis and connective tissue sheaths derived form dermis.
- The *inner epithelial root sheath*
    - cuticle of root sheath similar to the cuticle of hair and lies against it.
    - Huxley's layer consisting of several rows of elongated cells, the cytoplasm containing eleidin-like granules.
    - Henley' layer-a row of flattened clear cells.
- The *outer epithelial root sheath* is a direct continuation of stratum germinativum to which it corresponds is structure.
    - The connective tissue sheath is derived from dermis and consists of three layers. An inner layer of Vitreous membrane, a homogenous, narrow hyaline band, a middle layer of connective tissue fibres arranged circularly and an outer layer of loosely arranged collagenous fibres, running longitudinally.
    - All these different layers can be clearly seen only in the deeper portions of the root, a little above the bulb but below at the level of the bulb and above in the upper part of the root and shaft the different layers cannot be clearly demarcated.
    - The Hair bulb is not organized into layers but constituted a matrix of growing multiplying cells, which superficially become transferred into the horny cells of the hair and inner root sheath. It is in the form of bulbous thickening which surrounds the dermal papilla. Laterally, cells of the bulb become continuous with the outer root sheath.
    - The papilla of the hair is similar to other papillae and consists of delicate elastic and collagenous fires, cellular elements and capillary loops.

Muscles of the hair follicle

- The *errectores pilorum,* the errectors of the hair are oblique bands of smooth muscle fibres, which arise in the subepithelial tissue and are inserted to the connective tissue sheath of the hair follicle about middle of the follicle. The muscle usually arches around the sebaceous glands, which fill the angel between the muscle and hair. The muscle is poorly developed in certain regions like axilla, face etc. and are absent in eyelashes etc.
- The contraction of the muscle caused the hair to become more vertical to the surface and a small depression appears in the skin at the place where the muscle is attached. This gives rise to the so called "*goose flesh*".

Color of hair

- It is due to the presence of pigment granules found in and between the cells of the cortex of the hair.

- Presence of air also modifies the colour to a certain extent and hair in which pigment has faded and the medulla has become filled with air appears silver white.

SKIN GLANDS

Sebaceous glands

- These are associated with hair follicles and open into neck of hair follicle. In certain places of the body they occur independent of hair (e.g. glans penis, prepuce, labia vulvae, anus, external ear canal and tarsal glands of eyelids). Sebaceous glands are simple or branched alveolar, holocrine glands.
- The alveolus has a basement membrane and is filed with epithelial cells. Of these, the one nearest periphery is smaller and cuboidal and the central ones are bigger and polygonal.
- The fatty secretion (sebum) in the cytoplasm of cells is dissolved in ordinary preparations leaving honeycombed appearance. Ducts are lined by stratified squamous epithelium.

Sweat glands

- Two kinds of these are seen,
  - Merocrine and
  - Apocrine.
- The secretory portion of merocrine glands is a tubule rolled into a ball and lined by cuboidal epithelium (coiled tubular glands). The tubule has a basement membrane. The duct has a double layer of cuboidal cells with condensed, retractile borders.
- The secretory portion is located in dermis and duct passes between the dermal papillae to open, at the free surface of epidermis, at the sweat pore (Visible as minute pit to the naked eye).
- In the epidermis, the duct has no wall of pit to the naked eye). In the epidermis, the duct has no wall of its own but passes as spiral tunnel through the epithelium.
- The secretory portions of apocrine glands are very wide. They are also coiled tubular glands. Cytoplasm of the cell is basophilic, finely granular and contains fat droplets and pigment.
- The apical portion of cells detached into the lumen during secretion. The cells after discharge of secretion are lined with flattened nucleus.
- Ducts open into hair follicles above the sebaceous glands. There is one apocrine gland per hair follicle. The secretion is fatty.

BLOOD VESSELS AND NERVES

- From the larger arteries of the subcutaneous tissue, branches pass into the reticular layer of dermis, where they form networks.

- From this network, branches pass into the papillary, layer where they form second network. From this the papillae, hair follicles, sebaceous glands etc., are supplied.
- The primary plexuses supplies sweat gland, fat lobules etc.
- The venous capillaries form similar plexuses in the papillary layer, in the reticular layer and finally in the subcutaneous tissue, form where veins arise and accompany the arteries.
- The nerves to the skin are mainly sensory and sympathetic efferent supply to sweat glands errectores pilorum and plain muscle in the walls of blood vessels.
- The sensory nerves end in Pacinian corpuscles in the subcutaneous tissue, in tactile corpuscles of Meissner in the dermal papillae and free nerve endings among the epithelial cells in the epiedermis, pacinian corpuscles are receptors for pressure sense.
- Meissner's corpuscles for tactile or discriminatory touch and free nerve endings for pain.

SPECIES DIFFERENCE

- The thickness of the skin varies with age, sex species and body region. The Ox has the thickest skin and sheep has the thinnest skin. It is thickest on the back and on the extensor surfaces of limbs than on the belly and flexor surfaces. The skin is very thick on the tail of the horse, on the dewlap of the Ox and on the ventral aspect of the neck of the pig.
- The wattles of the goat are appendages consisting of skin and subcutis. They include a striated muscle, a bar of elastic cartilage, vessels and nerves.
- The tip of the nose, foot pads and all muco-cutaneous junctions in all animals are devoid of hair. The hair root are set vertically in sheep and obliquely in all other animals. The medulla of the hair is lacking in the wool, hairs of ungulates and the hair of human scalp.
- The hairs are evenly distributed in horse and ox and occur in groups in dog, cat and pig. There is usually three hairs in a group. Of which, one is the main hair and is larger than the other two. In carnivores, each of these three hairs is surrounded by six to twelve wool hairs, the follicles of which branch off form the follicle of the main hair and thus a whole bundle of hairs may project form a common follicular opening.
- In tactile or sinus hairs, the connective tissue sheath is well developed and a blood sinus lined by endothelium occurs between the outer and inner layers of dermal sheath. They are present in the lips, nostrils and eyes.
- Coarse hairs of great length occur in the mane of horse and the tail of the horse and ox.
- *Sebaceous glands* are large in the horse and dog while those of the pig are rudimentary. In ungulates two to six sebaceous glands empty into one follicle. Sebaceous glands are largest at muco-cutaneous junctions but are absent from footpad, hooves, claws, the planum naso labiale and teats of Ox and planum nasale of sheep, goats and carnivores.
- *Sweat glands**:*** In man the merocrine glands are distributed over the entire skin surface while the apocrine glands are restricted to a few areas such as axilla, in

domestic animal. The apocrine glands make up the majority of tubular skin glands, in sheep, pig, cat and horse the secretory tubule is wound up (glomiform) whereas in the Ox, goat and dog, it is serpentine. In the cat, the glands are poorly developed and are present only in a few body areas (oral region, anus, lower jaw, foot pads).

- The epidermis shows a high degree of specialization in forming the hooves, claws and horns in the different domestic animals.

MODULE-18: RESPIRATORY SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about
    - trachea,
    - lungs,
    - conducting and respiratory division.

RESPIRATORY SYSTEM

- This system serves mainly for intake of oxygen and elimination of carbon dioxide.
- It may be divided into conducting and respiratory portions.
- The former are air-conducting tubes which connect external air with that portion of lungs where exchange of gases takes place.
- The tubes are hollow and comprise nose, pharynx, larynx, trachea, bronchi of various size.
- The branch divides within the lung to smaller and smaller branches, the smallest division finally ending in alveoli, where exactly the exchange of gases takes place.

TRACHEA

- Trachea is thin walled, rigid tube continuing with larynx and terminates in two chief bronchi.
- The following layers are recognized:
    - Mucosa
    - Submucosa
    - A layer of fibroelastic membrane with hyaline cartilage rings and
    - Adventitia
- *Mucosa*
    - It is lined by pseudostratified ciliated columnar epithelium with numerous Goblet cells between the ciliated columnar cells.
    - The basement membrane is distinct.
    - The lamina propria contains numerous elastic fibres and a fibro-elastic membrane may be formed in the deeper zone, separating the lamina propria form the submusosa.
- *Submucosa*

- It consists of loose connective tissue and contains, mixed or mucous glands.
- The framework of trachea consists of series of regularly arranged C-shaped rings of hyaline cartilage. The open segment of C is dorsal and between the free cartilage, smooth muscle bundles (trachealis) are present. Most of the muscle fibres are arranged transversely. A fibroelastic membrane, which blends with the perichondrium extends between the adjacent cartilages and also between the open ends of the cartilaginous rings enclosing the smooth muscle bundles. **This fibro elastic membrane is called the tracheal annular ligament.**
- The adventitia has collagenous and elastic tissue with adipose tissue and contains blood vessels and nerves.

- Species differences
  - In the horse, ruminant and pig, the smooth muscle fibres lie inside the ends of rings of cartilage, but in the dog and cat they lie outside the ring. In man, it connects the two ends.

LUNGS

- The lungs are paired organs located in the thoracic cavity.
- The surface of each lung is covered by a serous membrane (pleura).
- Each lung is divided into a number of lobes and pleura, dips into interlobar fissures tissue and covers interlobar surfaces. Each lobe is sub-divided by interlobular tissue into lobules.
- Each lobule is pyramidal with apex towards the hilus and base towards serous membrane Lobulations are visible as polygonal areas on the surface of lungs.
- The lobulation is not so distinct in many animals, because there is less of interlobular connective tissue.
- The septa of interstitial tissue contain, bronchi, vessels and nerves.
- Each lobule contains the respiratory structures arising from a terminal bronchiole.

CONDUCTING DIVISION

- Trachea divides into two chief bronchi one for each lung, entering at the hilus, the bronchus divides into smaller bronchi which gives rise to several orders of bronchioles.
- The general structure consists of a mucosa, muscularis, a fibro-elastic membrane which encloses a cartilage and loose collagenous peribronchial layer.
- Gradual changes in structure occur, as the main bronchus, divides into smaller bronchi, several order of bronchioles till the segment called terminal bronchiole is reached.
- These changes consist of the following.
  - The mucosa is lined by pseudo-stratified columnar cilated epithelium, in the larger bronchi.

- The epithelium gradually decreases in height and the goblet cells become fewer.
- The epithelium becomes simple columnar ciliated with no goblet cells in the terminal bronchiole.
- The glands in the submucosa progressively decrease and finally disappear.
- There is a relative increase of smooth muscle till the terminal bronchiole.
- The hyaline cartilage does not occur in the form of rings as in trachea but as isolated plates in bronchi, which also disappear, in bronchioles.

Bronchi

- *Mucosa:* Pseudostratified columnar ciliated epithelium with numerous goblet cells. In submucosa mucous glands are present. Plain muscle lies inner to cartilage plates and forms a continuous cuticular layer (unlike in the trachea). Hyaline cartilage occurs only in the form of isolated plates.
- *Bronchioles* (small unit) Mucosa simple columnar ciliated epithelium with Goblet cells. No glands occur in the submucosa. Smooth muscle forms a continuous cirular layer. Cartilage plates are absent.
- *Terminal Bronchioles:* The mucosa is lined by simple columnar ciliated epithelium. No goblet cells are present and no glands occur below the mucosa. A relatively thicker smooth muscle is present, in the wall but cartilage is absent. The terminal bronchiole divides into two or more respiratory bronchioles.

RESPIRATORY DIVISION

- From the respiratory bronchioles onwards, the structures contain alveoli in their walls and serve both as conducting and respiratory passages. The epithelium is initially simple cuboidal but become flattened or squamous later. No Goblet cells or glands occur in any part. The respiratory structures consist;
    - Respiratory bronchiole,
    - Alveolar duct,
    - Alveolar Sac,
    - Alveoli.

Respiratory bronchiole

- These bear alveoli in their walls and between the alveoli, the wall is lined by simple cuboidal epithelium, which may be ciliated in the initial portion.
- Smooth muscle and elastic fibres are present, though they do not form a thick layer as in terminal bronchiole.
- They are arranged in a spiral direction forming a loose elastic and contractile network.
- The respiratory bronchioles branch into alveolar ducts.

Alveolar ducts

- These are long and branch repeatedly. Their walls are formed by alveoli, without intervening patches of cuboidal epithelium.
- Smooth muscle bundles are present and are concentrated around the openings of alveoli.
- There is no separate epithelium other than that of the alveoli which consists of flattened or exceedingly thin squamous cells. The alveolar ducts open into a variable number of alveolar sacs.

Alveoli

- These are cup-shaped structures, through the wall of which interchange of gases between the blood and air takes place. An alveolus may open into the lumen of respiratory bronchiole, or alveolar duct or alveolar sac.
- Between adjacent alveoli, an inter alveolar septum is formed. The wall of an alveolus contains a network of fine elastic and reticular fibres and in the meshes of this network is a rich plexus of capillaries. The lumen of the alveolus is lined by simple squamous epithelium made up of very thin attenuated cells.
- The cells shows such a thin layer of cytoplasm that except at the region of the nucleus, no outlines can be made out in routine preparation under light microscope.
- EM studies have shown that this epithelium rests on a basement membrane wherever a capillary lies close to the alveolar wall, the basement membrane of the capillary endothelium and that of the alveolar epithelium fuse together. This arrangement results in a minimum of tissue intervening between air in the alveolus and blood in the capillary, thus facilitating gaseous exchange between the two.
- In the alveolar wall, in addition to the lining epithelial cells and endothelial cells of the capillary, connective tissue cells often referred to as septal cells are present. These correspond to macrophages and have the potency to become actively phagocytic in function.

Blood vessels

- The Capillary nets described above are derived from intralobular arteries which are branches of pulmonary artery (functional blood) and which go along with the terminal bronchiole.
- The interlobular arteries (nutrient arteries) are branches of bronchial artery and supply bronchial wall and interstitial tissue.
- The satellite veins are pulmonary and bronchial veins respectively.

MODULE-19: MALE REPRODUCTIVE SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about
    - testis,

- epididymus,
- vas deferens,
- accesory genital glands,
- urethra and
- penis.

MALE GENITAL SYSTEM

- Consists of the testis, epididymis, vas deferens, penis and accessory genital glands.

TESTIS

(Seminiferous tubles)

- Testis produces *Spermatozoa* (when the gland becomes mature and functional), and *male sex hormone*.
- The testis is a ***cytogenous gland*** i.e. it produces living germ cells. The testes are compound tubular glands.
- The gland is enveloped by a capsule of dense fibrous tissue, the *tunica albuginea* and serous layer, which is visceral layer of *tunica vaginalis* outside it. The capsule is rich in blood vessels.
- The capsule projects as thickening into the gland as mediastinum testis at its posterior edge and extends through its long axis from this mediastinum radiate septa - Septula testis towards the capsule dividing the gland parenchyma into a number of pyramidal or cone-shaped lobuli testis, whose apices converge towards the mediastinum testis.
- Each lobule is occupied by the terminal portions of seminiferous tubules. One to three of these occupy a lobule. They have an extremely tortuous course, rarely branch and are called *convoluted seminiferous tubules*.
- Sperms are formed in the convoluted tubule. The seminiferous tubule is 80-90cm. long and 100-200 microns thick with lumina of varying sizes. They start blindly at the periphery continue as tubuli contorti and run towards the mediastinum testis. At the mediastinum testis they become straight - the tubuli recti and then form a system of irregular, anastomosing structure with cavernous spaces, the rete testis.
- At the upper part of posterior edge 6 to 20 *efferent ductules* arise from the rete testis and emerge on the surface of testis. Through many convolutions they form vascular cones, whose apices point towards the mediastinum. The vascular cones form the head of the epididymis. They fuse to form a single ductus epididymis. This duct is highly coiled and forms the body and tail of epididymis.
- The duct gradually becomes straight to continue as ductus deferens. Tubuli recti, rete testis, epididymis and ductus deferens forms the excretory portion of the gland.

Seminiferous tubules

- Wall of the convoluted Seminiferous tubule is composed of lamellar collagenous connective tissue containing elastic fibres and condenses into a thin basement membrane.
- The seminiferous epithelium consists of two kinds of cells - *spermatogenic cells* and *sertoli cells*.

- Spermatogenic cells through proliferation and transformation produce sperms. They have indistinct boundaries and are not seen distinctly.
- *Sertoli cells*
  - These are tall, irregularly columnar cells and placed perpendicular to the basement membrane to which they are attached.
  - They have a distal ragged edge and project into the lumen of the tubule.
  - Basal portion contains a light staining vesicular oval nucleus. The cytoplasm shows a loose reticular structure.
  - The spermatogenic cell at certain stages of development embeds themselves into the cytoplasm of sertoli cells.
- *Spermatogenic cells*
  - These occur in 3 to 7 layers and include several generations of cells produced by division. The mother cells Spermatogonia make up the basal layer and by division give rise to many generations of spermatogonia.
  - These by growth, form Spermatocytes which occupy a few layers. Each primary spermatocyte soon divides to form two minute spermatids and make up the remaining layers. Spermatids become attached to the cytoplasm of sertoli cells.
  - Spermatogonia have dark staining spheroid nuclei and are round Primary spermatocytes also have round, dark staining spheroid nuclei. The secondary spermatocytes are smaller than the primary spermatocytes and almost immediately divide into two spermatids.
  - The nucleus of the spermatocytes will present a variable appearance, as the cells will be found in various stage of division. The division of primary spermatocyte is by meiosis or reduction division.
  - Each *primary spermatocyte* gives rise to two secondary spermatocytes by reduction or maturation division. Each secondary spermatocyte receives only half the number of chromosomes (haploid number) present in the primary spermatocyte.
  - Each *secondary spermatocyte* divides into two spermatids. The spermatids are small cells about half the size of secondary spermatocyte and have a round darkly staining nucleus.
  - Spermatids do not divide but by transformation form the specialized cells the Spermatozoa.
  - The tubuli recti and rete testis are lined by cuboidal or squamous epithelium. These receive the sperm produced by seminiferous epithelium.
  - The interstitial tissue i.e. the thin collagenous tissue between the tubules contains vessels, nerves and interstitial cells of Leydig. These cells are polyhedral. Nuclei are and spherical with a distinct nucleolus. Their cytoplasm stains light, due to dissolution of lipoid granules and droplets in ordinary preparations. They secrete testosterone or male hormone.
  - In undeveloped testis only spematagoina are present. Only with onset of sexual maturity several layers of sepermatogenic cells are seen.

EPIDIDYMUS

- Epididymis is a highly convoluted tube to form a solid body so that in section the tube is cut several times.
- The duct is enveloped by collagenous tunic, which contains circular smooth muscle.
- The duct has a wide lumen and the mucosa has no folds.

- The epithelium is pseudostratified columnar ciliated and consists of two types of cell-tall columnar cells with *sterocilia* and small angular basal cells which do not reach the surface.
- Columnar cells show elongated nuclei at different levels and contain secretory granules.
- Basal cells contain lipids and so in ordinary preparations stain light.
- The lumen shows clumps of spermatozoa.

VAS DEFERENS

- Ductus deferens or Vas deferens has a mucosa, muscularis and fibrosa.
- The mucosa form longitudinal folds and is lined by pseudostratified columnar cells similar to that of ductus epididymis. But the cells are low and stereocilia shows variable distribution, absent form some cells and present in others.
- Lamina propria is rich in elastic tissue.
- Muscularis is the thickest coat and shows three layers - inner longitudinal, middle circular and outer longitudinal.
- The inner muscular layer is thin. The middle circular layer is the thickest and in the stallion, bull and carnivores the fibres of the three layers are interwoven so that the layers are less distinct.
- Outer fibrous coat shows blood vessels and nerves.

ACCESORY GENITAL GLANDS

- These open into the urethra and include *seminal vesicles, prostate and bulbourethral or cowper's glands*.

Seminal vesicle

- Seminal vesicle of bull is a thick-walled sacculated tube bent on itself several times in a tortuous manner, to form lobules separated by heavy smooth muscular septa. The capsule and the septa contain abundant plain muscle fibres, a feature characteristic of all accessory glands. The mucosa is thin shows primary folds which branch into secondary and tertiary folds.
- These project into the lumen and forms by anastomosis numerous cavities of different sizes separated by thin partitions of lamina propria, all open into the large central cavity. Epithelium is pseudostratified columnar being composed of columnar cells and irregularly shaped basal cells.
- Seminal Vesicles are absent in carnivores. In horse they are true vesicles showing mucosa, muscularis and adventitia.

Prostate gland

- Prostate is a compound tubulo-alveolar gland surrounded by a capsule, which contains abundant plain muscular tissue. From this capsule broad septa penetrate and form a network in the interior of the gland.

- The septa and the abundant stroma, which separates the alveoli, contain plenty of plain muscle fibres. The alveoli are lined by columnar epithelium. They show folds, which subdivide the lumen into compartment. The columnar cells may be tall or short, cytoplasm of cells is finally granular. Each lobule is traversed by an axial duct. Ducts are lined by columnar epithelium, but near termination in the urethra it becomes transitional.

Cowper's gland

- Each is a lobulated compound tubuloacinar gland covered by a fibrous capsule overlaid by striated muscle. The stroma between the alveoli consists of fibro-elastic tissue with a few plain muscle fibres.
- The secretory portions may be tubular or alveolar. Lining epithelium shows variations depending on functional stage. It may be columnar or cuboidal. Most of the columnar cells are of the mucous type, but the nucleus is spherical, located at the base of cells.
- The cytoplasm stains basophilic but some cells may show a granular acidiphilic cytoplasm. Smaller ducts are lined by simple columnar epithelium and main ducts stratified columnar epithelium. Cowper's glands are absent in carnivores.

URETHRA

Male

- The urethra is a long mucous tube, which extends from the urinary bladder to the glans penis.
- It consists of *pelvic* and *extrapelvic or penile part*. The pelvic part is lined by transitional epithelium.
- The vas deferens, seminal vesicles, prostate glands are opening into the urethra in its initial part and the ducts of bulbourethral glands open further behind.
- In the bull and boar, the pars disseminata of prostate gland forms a glandular layer in the wall of entire pelvic urethra whereas in horse and carnivore, they are in the form of scattered small glands.
- The penile part of urethra is also lined by transitional epithelium, which changes to stratified squamous epithelium near its termination. In the stallion and boar scattered glands may be present as in the pelvic part.

PENIS

- It consists of a body and glands. Body consists of
  - The erectile *corpus cavernosum penis*, whose two crura are attached to the ischial arch.
  - *Corpus cavermosum urethrae or corpus spongiosum penis* surrounding urethra muscles.
- Glans penis forms the tip of penis.

Body of penis

- Consists of the corpora cavernosa, which have a capsule, a system of trabeculae and the true erectile tissue.
- The fibrous capsule the tunica albuginea is a thick membrane of dense collagenous tissue with elastic fibres.
- It gives off similarly constructed trabeculae which are inter-connected to form a coarse frame work.
- The trabeculae forms a median septum between two corpora, between the trabeculae is the erectile tissue proper, which is a vast-sponge like system of irregular vascular spaces intercalated between afferent arteries and efferent veins.
- It consists of a fine framework of lamellae and cords, continuous with the trabeculae and albuginea and encloses communicating spaces called *cavernous spaces*. The spaces are longitudinal and are best developed in the crura. The spaces are lined by endothelium, which is continued into that of arteries and veins.
- They are bounded by the intercavernous lamellae and trabeculae, which carry vessels and nerves. The spaces are largest in the central zone of corpus cavernosum penis.
- Erection of the body of penis is brought about by filling in of the cavernous spaces with arterial blood and prevention of regress of blood through veins. Constriction of arteries and slow emptying of cavernous spaces by contraction of smooth muscle and elastic fibres terminate erection.
- The corpus spongiousum or corpus cavernosum urethrae have a similar structure but the albuginea is thin and contains more elastic fibres. The trabeculae are thin lacunae are more or less of uniform size. The urethra (penile part) passes through the corpus spongiosum. The mucous membrane is thrown into folds and is lined by transitional epithelium.

Species differences

- In man, three distinct bodies form penis and a median septum clearly demarcates the two corpora cavernosa. The median septum is present only near the root of the penis in ruminants and boar but is continuous throughout the body in dog. In stallion and cat, the septum is not continuous.
- The intercavernous framework is composed of fibroelastic tissue in ruminants and boar and smooth muscle is also present in the horse and dog.
- Scattered adipose tissue occurs in the penis of domestic animals. In the bull, the corpus cavernosum largely consists of fibrous tissue but the erectile tissue is also present to a limited extent, which serves to stiffen the penis rather to enlarge it.

MODULE-20: FEMALE REPRODUCTIVE SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about
    - ovary,
    - oviduct (Uterine tube or Fallopian tube),
    - uterus,
    - vagina and
    - mammary glands.

FEMALE GENITAL ORGANS

- The female genital apparatus consists of the ovaries, oviducts, uterus, vagina and vulva.
- The entire apparatus is in the scene of regularly recurring process of growth and involution which constitutes the *sexual cycle*, which is interrupted only by pregnancy and old age.
- Ovary like the testis is a *cytogenous gland*.
- It produces the female germ cells - ova and also hormone - female sex hormones.

OVARY

- This histological picture depends on the plane of section and phase of sexual cycle.
- Ovary can be divided into two zones - ***cortex*** (zona parenchymatosa) and ***medulla*** (zona vasculosa).
- It is surrounded by a *tunica albuginea* which itself is covered by a germinal epithelium. In the young this germinal epithelium is a single layer of cuboidal or columnar cells, which become flattened or squamous in adult. It is continuous with peritoneal *mesothelium*.
- Tunica albuginea is rich in collagenous fibres. The cortical stroma is made up of a special type of connective tissue, which is predominantly cellular.
- The connective tissue cells are fusiform or spindle shaped with elongated nuclei and is placed in a network of delicate collagenous fibres. Elastic fibres are practically absent.
- Scattered in this stroma are the glandular structure of ovary, the *ovarian follicles*. Each follicle consists of an ovum surrounded by follicular epithelial cells.
- In the embryo, germinal epithelium contains primordial germ cells. It forms cord-like proliferation, which grows down into the cortex as *egg tubes of Pfluger*.
- It contains primitive ova surrounded by a layer of small cuboidal cells. The cortical stroma grown in between these primitive ova or oocytes, thus forming primary follicles.
- At birth the tunica albuginea separates the germinal epithelium from the cortex. Thus at birth, the ovary contains all the primary follicles and no new follicles are supposed to form after formation of Tunica albuginea.
- In a mature or adult animal, the cortex will contain ovarian follicles, in various stages of development and regressions. Smaller follicles with the ovum surrounded by a layer of follicular cells are located near the periphery.

- They pass deeper into the ovary as they become larger and develop further but the matured follicle again approaches the surface. The follicle are described as primary, secondary, Graafian and mature Graafian follicles.

Primary follicle

- Are of 30-35 microns in diameter. Each contains an Oocyte surrounded by a layer of follicular cells and a basement membrane.
- The follicular cells are first later becoming cuboidal or columnar. The follicular cells proliferate and become two layered and then becomes multilayered surrounding the Ovum. These are the secondary follicles.
- The Ovum increases size and may occupy an eccentric position and develops a homogenous envelop *zona pellucida* between it and follicular cells and the stroma becomes more distinct.
- Further, growth of the follicle is characterized by proliferation of follicular cells which form a stratified layer around the ovum. Irregular spaces appear in the follicular mass which fuse to form a crescent shaped cavity the *anturm folliculi*.
- The cavity contains a fluid called the *Liquor folliculi*. These follicles with the formation of cavity are called *Graafian follicles*. The stromal cells surrounding the follicles form a sheath called *Theca folliculi*.
- As the follicle increases in size and matures, the follicular cavity with its contained fluid increases in size.
- In a mature follicle, the Ovum is pressed to one side where it is surrounded by an accumulation of follicular cells, it forms a definite projection into the cavity known as the *germ hill or discus proligerus or cumulus oophorus*.
- The Ovum with the nucleus (*germinal vesicle*) and nucleolus (*germinal spot*) is surrounded by a thick homogenous membrane the zona pellucida.
- Surrounding this are tall columnar follicular cells arranged radially forming the *corona radiata*. The follicular cavity is lined by several layers of cuboidal or polyhedral follicular cells forming the *membrana granulosa*.
- There is a homogenous basement membrane surrounding the membrana granulosa. The theca folliculi or the follicular sheath differentiates into a theca interna containing numerous epithelioid, connective tissue cells and extensive capillary network and a theca externa consisting predominantly of fibres circularly arranged and closely packed and spindle shaped cells.
- The mature Graafian follicle extends through the whole thickness of cortex and bulges on the surface of the Ovary. At this place, the stigma and the oocyte become thin and the follicle distended with fluid.

Ovulation

- It is the release of the fully grown oocyte from the follicle at the surface of the ovary. The projecting follicle ruptures at the stigma through the albuginea ova escapes with the corona radiata cells.

Oogenesis

- The ovum also undergoes maturation or reduction division, before it is fertilized. The egg cells of primary follicles are often described as *oogonia* but are actually primary oocytes, which have entered a period of rest.
- It is believed that proliferation of oogonia and differentiation into primary oocytes are completed before birth a period of rest.
- The primary oocytes give rise by reduction division to a secondary oocyte (containing the haploid number of chromosomes) and the first polar body. The polar body receives very little cytoplasm and soon degenerates.
- The secondary oocyte again divides giving rise to a ootid or mature ovum and a second polar body, which degenerates. Generally the first maturation division occurs in the developing follicle and the second division is completed after ovulation and at the time of or after fertilization.

Corpus luteum

- After rupture, the follicular cavity closes over by healing and becomes filled with a sero-fibrinous fluid, usually containing blood. This develops into temporary glandular structure known as *corpus luteum*.
- The granulosa cells enlarge, the nuclei become vesicular and stain lightly. The cytoplasm shows progressively greater accumulation of lipid droplets and yellowish *pigment* granules. These are known as *granulosa lutein cells*.
- The epitehlioid cells of theca interna also proliferate and show fatty droplets in the cytoplasm and form *theca lutein cells*. These are located peripherally and are smaller than granulosa lutein cells and have more compact, darker staining nuclei.
- Connective tissue fibres from the theca externa penetrates into the lutein mass and forms interlacing septa, in which are numerous capillaries present. The follicular cavity is greatly reduced and disappears as the corpus luteum enlarges further.
- If the discharged ovum is not fertilized, the corpus luteum develops after an initial period of development. This is known as *cyclical corpus luteum or corpus luteum spurium* (menstruations). The cells gradually decrease in size become vacuolated and are resorbed. The connective tissue increases in amount and finally there is transformation into a small body of connective tissue – the *corpus albicans*.
- It the ovum is fertilized and pregnancy occurs, the corpus luteum increases in size and becomes corpus luteum of pregnancy or *corpus luteum verum*. It persists until later months of pregnancy. After termination of pregnancy, it undergoes slow involution, becoming transformed into corpus albicans.

Atretic follicles

- Only a few of the oocytes in the follicle reach maturity. Most of the occytes together with their follicles undergo artesia. This may set in at any stage of development. The process involves degeneration of oocyte and invasion of the follicle by the internal cells.
- *Medulla of the Ovary*

    - There is network of fibro-elastic tissue with numerous blood and nerve fibres.
- *Hormones of the Ovary*
    - The ovary is under the direct influence of Gonadotrophic hormones of anterior pituitary.
    - The Follicular Stimulating Hormone (*FSH*) controls the maturation of the follicle and the Leutinzing hormone (*LH*) controls the formation of corpus luteum.
    - The maturing Graafian follicles of the Ovary produce *oestrogen* and the corpus luteum produces *progesterone*.
    - Since there is regular cyclical development of the follicle its maturation and subsequent development of corpus luteum after ovulation, there is a corresponding cyclical fluctuation in the levels of the two hormones secreted by the ovary. These are reflected in cyclical variations in the structure of oviduct, uterus and vagina in addition to changes in the behaviour of the animal.
    - The cycle itself is referred to as *Oestrus cycle* and considerable variations exist in different animals with regard to the duration of the oestrus cycle, different stages of the cycle, its periodicity and the nature and extent of changes in the various parts of the reproductive tract.

Species difference

- In the mare, there is no division of the ovary into the cortex and medulla. The peripheral part contains blood vessels (corresponding to the medulla of other animals) except at the ovulatory fossa, located at the free border, which is covered by germinal epithelium.
- The number of follicle that ripens in one cycle is more or less fixed for each species. Uniparous animals usually produce only one ovum at a time. The diameter of mature follicles is as follows: Women –9-12 m.m., mare –up to –10 m.m., Cow – 20 m.m., Ewe,Goat, sow-5-8 m.m., Bitch and Cat – 2 m.m.In carnivores and the sow, some follicles may contain 2 to 6 oocytes. (*Giant follicles*).
- The lutein cells of the corpus luteum in the bitch and cat contain a little or no pigment and the corpus luteum is pale in colour. In the ewe, goat and sow, it is grayish white or flesh coloured because of the absence of pigment in the lutein cells. In the cow, the colour varies from bright yellow to orange and brown as the corpus luteum develops and perists during pregnancy, finally turning brick-red in a regressing corpus luteum.

OVIDUCT

Uterine tube or Fallopian tube

- Wall of the oviduct is composed of a mucosa, muscularis and serosa. Mucosa bears a columnar epithelium, parts of which are psuedostratified in the rurminants.
- The epithelium contains columnar cells some of which are ciliated, whereas others are not ciliated. The mucosa forms large primary and small secondary folds. The lamina propria is composed of a richly cellular connective tissue. The muscularis chiefly consists of circularly arranged plain muscle fibres. The serosa has the usual structure of mesothelium.
- The structure of oviduct shows gradual variations from its ovarian to the uteine end. Mucosal folds are pronounced at the uterine end gradually decrease and become negligible at the uterine end. The muscular coat becomes thicker towards the uterine end.
- The epithelium also shows changes during different stages of oestrus cycle. The epithelium becomes taller with greater secretory activity just before and during the oestrus period.

UTERUS

- Wall of the uterus is madeup of a mucosa, muscularis and serosa.
- *Muscosa or Endometrium:* bears a columnar epithelium. The cells are secretory in type. Lamina propria contains *uterine glands*. These glands are simple branched tubular glands which are coiled towards their ends. The connective tissue stroma resembling mesenchyme or embryonal connective tissue surrounds the glands. Epithelium of the glands is simple columnar which are sometimes ciliated.
- *Submucosa:* It is absent.
- *Muscularis or myometrium:* consists of three layers of plain muscle fibres - an inner longitudinal, a middle circular and a thin outer layer composed of both longitudinal and circular fibres. The middle circular layer is thickest and forms the bulk of the muscular coat. Between the middle and outer layers is layers is layer of connective tissue *stratum vasulare* containing numerous blood vessels.
- *Serosa or Perimetrium:* is continuous with the broad ligament and has the structure of mesothelium.
- The uterus undergoes considerable structural changes during the various stages of oestrus cycle and during pregnancy. The cyclical changes consists of congestion, edema and proliferation of glandular epithelium during pro-oestrus and oestrus, followed by the secretory phase, when glands develop to the maximum become highly coiled and with high columnar cells (during metoestrus and early diestrus). In the absence of fertilization and Pregnancy, regressive changes appears in the mucosa accompanied by hemorrhage (*menstruation*) occurring in woman, is not characteristic in animals.
- During pregnancy, the endometrium undergoes considerable alterations and contributes to the formation of placenta. The myometrium also shows pronounced hypertrophy and hyperplasia of the muscle fibres.

Species differences

- The endometrium is line by stratified epithelium in ruminants and sow. The uterine glands in carnivores show least branching and coiling. In the mare they are highly coiled and branched and in the ruminants and sow, they are much wider superficially and in the deeper portion they are narrow, strongly coiled and branched.
- In the ruminants, the mucosa bears non-glandular projections, the *caruncles* which are small prominences in non-pregnant animals but develop into large, complex structures in pregnant animals. They consist of highly cellular connective tissue covered by epithelium. The uterine glands open on the intercaruncular mucosa.

VAGINA

- The wall of the vagina consists of a mucosa, muscularis and fibrosa.
- The mucosa is non-glandular and is thrown into folds. It is lined by stratified squamous epithelium. The lamina propria consists of loose connective tissue especially rich in elastic fibres. It contains diffuse infiltration of lymphocytes and solitary lymph nodules may also be present.
- The muscularis consists of an inner thicker circular layers and a thin outer longitudinal layer of plain muscle. The fibrosa consists of dense connective tissue with many coarse elastic fibres and contain large blood vessels and nerves. At the anterior part there is serosa which has the usual structure of serous membrane.
- The vagina also undergoes structural changes during the various stages of oestrus cycle. The changes are chiefly in the mucosa which increase in thickness and number of layers of the epithelium during proestrus and oestrus. Cornification to varying degrees in different species at oestrus followed by desquamation at metestrus, the epithelium being low in height at diestrus.

Species differences

- In the cow, the anterior end of the vagina has an epithelium which is lined by high columnar cells and secrete mucous.
- The cornfication of the vaginal mucosa is pronounced in rodents, carnivores and ewe and is not distinct in cow.

MAMMARY GLANDS

- The mammary gland is a compound tubuloalveolar gland. The capsule is fibroelastic and from the capsule, tough connective tissue septa containing elastic fibres, smooth muscle and adipose tissue enter the gland and separate the gland into lobes and lobules.
- The amount of inter lobular connective tissue varies considerably with the functional status of the gland, being greatly reduced in a lactating gland.
- The parenchyma consists of secretory tubules with alveoli lined by short columnar or cuboidal epithelium resting on a delicate basement membrane.
- The appearance of epithelium depends on the phase of secretion.

- During the onset of milk formation the granular cells are taller and show fat globules at the luminal end.
- After extrusion of secretion, cells become flattened because the apical portions are cast off as secretion (apocrine gland).
- The cell borders are indistinct. In a lobule, alveoli in different phase of secretion may be seen, with high or flattened epithelium.
- *Ducts:* (lactiferous ducts) smallest ducts are lined by secretory epithelium. Larger ducts by columnar and still larger ones by two-layered columnar epithelium. Towards the termination there is stratified squamous epithelium.
- *Non-functional gland:* Shows abundant interstitial connective tissue. Parenchyma shows only ducts and few alveoli.

MODULE-21: ENDOCRINE SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about
    - thyroid gland,
    - parathyroid gland,
    - adrenal or suprarenal gland and
    - pituitary gland (Hypophysis Cerebri).

ENDOCRINE GLANDS

- These are organs of internal secretion.
- They are rich in blood vessels.
- They have no excretory ducts.
- They secrete specific substances called *hormones*.

THYROID GLAND

- The gland is surrounded by a connective tissue capsule, which gives off septa of varying thickness into the interior. These divide the organ into interconnected lobule consists of vesicles of varying sizes called *thyroid follicles*.
- In young animals they are smaller than in adult. Between follicles there is fine connective tissue fibres, which contain many blood vessels and capillaries.
- The follicles are completely enclosed and surrounded by fine reticular fibres. They are usually spherical or ovoid.
- Cells lining these are cuboidal with large round nuclei. The cells may be flattened or squamous in distended follicles. The epithelium rests on a thin, delicate basement membrane.
- The cavity of the follicle is filled with a semifluid or gel-like substance, the *thyroid colloid*. The colloid generally stains acidophilic but may be basophilic especially in activated glands. In young animals, between the follicles, small groups of cells may be seen. These are the primitive or embryonic cells, which may give rise to more number of follicles.

- The secretion produced by the cells is stored in the vesicles as *thyroglobulin*.
- The thyroglobulin is hydrolysed by enzymatic action of cells and the thyroxine is secreted into the capillaries at the base of the cells.

PARATHYROID GLAND

- They are situated very close to or embedded in the thyroid glands. They have connective tissue capsule, but when deeply embedded in the thyroid gland both may have a common capsule.
- The parenchyma consists of anastomosing cords of cells between which are numerous capillaries. Two types of cells are described.
- *Chief cells:* These are polygonal with lightly stained or clear cytoplasm. The cells may be small, with darkly stained nuclei.
- *Oxyphile cells:* These are larger than chief cells but have smaller and darker staining nuclei. The cytoplasm contains fine granules and stains deeply with acid dyes.
- The oxyphile cells are present only in man and ox, and only in adults or aged ones among them. The secretion parathyroid glands (*parathormone*) play an important role in regulation of calcium metabolism.

ADRENAL OR SUPRARENAL GLAND

- The adrenal gland is divisible into two distinct different parts - Cortex and medulla that are developmentally and functionally independent.
- It has a connective tissue capsule containing a few elastic and smooth muscle fibres.
- From this many delicate trabeculae, enclosing capillaries, penetrate into the cortex and the corticomedullary junction.
- The framework of cortex consists of a network of reticular fibres.

Cortex

- The cells which occupy greater part of the gland are divided into three zones.
  - The outer thin *Zona glomerulosa*, next to capsule.
  - A middle thick *Zona fasciculata*
  - An inner moderately thick *Zona reticularis* which abuts on the medulla.
- *Zona glomerulosa:* consists of short columnar cells, closely packed, in groups or in columns forming arcs immediately below the capsule. They have deep staining nuclei and basophilic cytoplasm. (In the horse it is called as zona arcuata).
- *Zona fasciculata:* consists of columns of large polyhedral cells arranged radially in the form of anastomosing cords extending between both the zones above and below. Cell have central nuclei, one or two in each cell, and cytoplasm is basophilic and appear vacuolated because in routine staining technique, the lipoid droplets in the cytoplasm gets dissolved. The vacuolation gives a spongy appearance and hence the cells are often referred to as spongiocytes.

- *Zona reticularis:* consists of anastomosing cells cords. The cells are cuboidal and have deeply staining spherical nuclei. The cytoplasm stains deeply in some, lightly in others and may contain pigment. Lipoid droplets are less in number in these cells. There are sinusoids in the zone.

Medulla

- The cells of this part are arranged in groups or irregular cords surrounded by sinusoids. The cells are polygonal and show numerous fine granules in the cytoplasm. The nuclei are large, centrally located and stain lightly. The granular content of the cytoplasm varies in different cells.
- The cells are arranged in such a way that one pole of the cell is directed towards a capillary and the other pole towards a vein. When the gland tissue is fixed in fluid containing potassium dichromate, fine brown granules are seen throughout these cells. This is due to chromaffin reaction. The cells are therefore called *pheochrome* cells.
- These granules are readily stained with basic stain. In addition to chromaffin cells there are single group of sympathetic ganglion cells.

Functions

- The adrenal cortex produces numerous substances mostly steroids and based on their action they have been grouped into three classes. There is also some evidences to indicate that each of these classes is apparently secreted by one particular zone of cortex.

  - *Mineralo-corticoids* - (aldosterone) regulate water and electrolyte balance chiefly Na and K secreted by zona glomerulosa cells.
  - *Gluco-corticoids* - (cortisone and hydrocortisone) influences carbohydrate metabolism, favour catabolism of proteins and also have anti-inflammatory, anti-allergic, anti-rheumatic properties. They inhibit lymphoblastic activity and also antibody formation. These are produced by cell of zona fasciculata.
  - *Sex anabolic hormones* (weak androgens, 17-ketosteroids oestrogen and progesterone) These are concerned with the development of secondary sexual characteristics and have an anabolic action on protein metabolism. These are produced by cell of zona reticularis.
- The Medulla secretes *Epinephrine* and *Nor-epinephrine*. These increases blood pressure and cardiac output, and cause vasoconstriction and raise blood sugar level.

PITUITARY GLAND

Hypophysis cerebri

- The gross structure of this gland includes two lobes - an anterior and a posterior.
- Histologically the anterior lobe includes *pars distalis* or *pars anterior* and the posterior lobe includes *pars nervosa* and *pars intermedia*.
- *Pars tuberalis* surrounds the upper part of pars nervosa and is continuous with pars intermedia. Between the pars intermedia and pars anterior there is a cleft.

Pars anterior

- Contains a fine network of connective tissue, which supports tortuous and anastomosing cell cords. Sinusoids between cell cords are numerous. The cells of these cords are of two main types;
  - The *chromophobes* are characterized by pale staining non-granular cytoplasm,
  - The *choromophils* are granular and lager.
- The chromophils are classified as *acidophils* and *basophils* on the basis of the staining reactions of their cytoplasmic granules. Of these the acidophil cells take eosin stain in H and E preparations.
- Chromophobes: These appear in small groups. The nuclei are surrounded by a small amount of diffuse light staining non-granular cytoplasm. The cell boundaries are usually not distinguishable in ordinary preparations. These are considered to be reserve or undifferentiated cells, which give rise to granular varieties.
- Chromophils
  - *Acidophils:* These are larger than chromophobes and their cytoplasm contains granules, which take acid dyes. Two types of acidophils showing

preference to azocarmine (epsilon acidophils). *Orangeophils* or alpha acidophils showing preference to Orange G-stain.

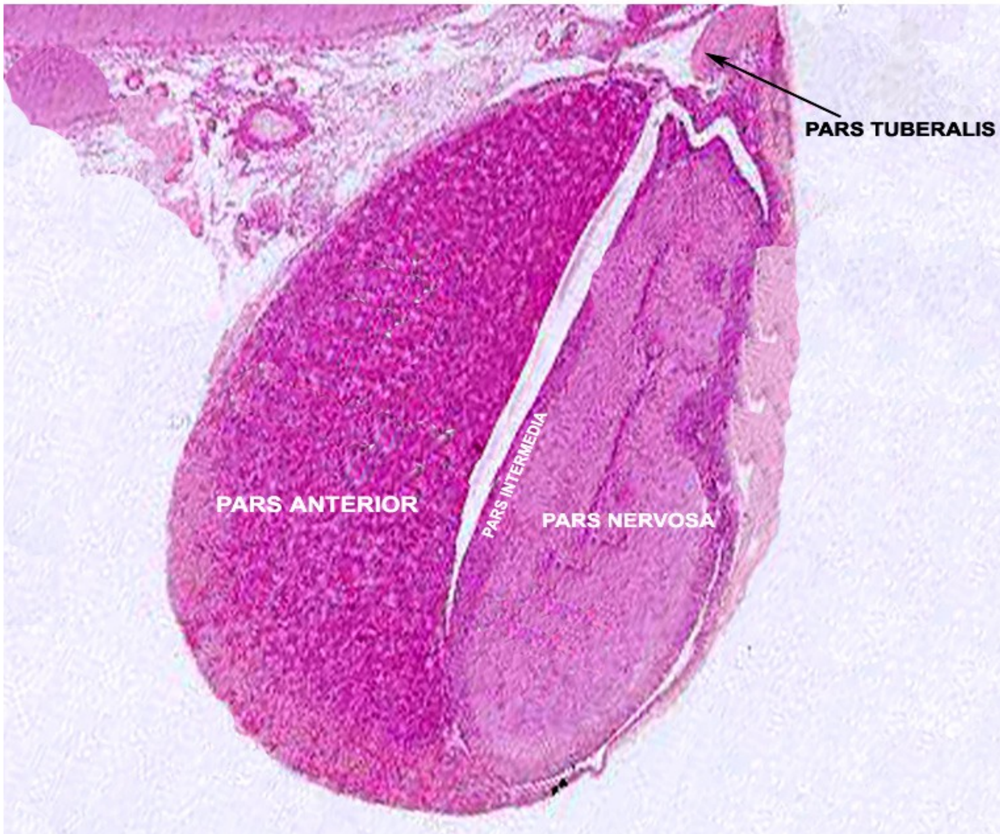
    - Carminophil (epsilon acidophil) - Prolactin or Luteotrophic hormone.
    - Orangeophil or alpha acidophil – Somato trophin or Growth stimulating hormone.

- *Basophils:* The cytoplasm of these contain granules of irregular size and considerable variation has been found in their staining properties. The morphological characters vary form large angular cells to small rounded ones.
    - A number of staining techniques have been used to differentiate the different types among the basophils. (Periodic Acid Schiff reaction, Aldehyde-fuchsin, aldehydethionin) etc.
    - Based on the staining reaction to these procedures and on their morphological characters, the basophils have been classified into Beta-1 and Beta-2 and delta-1 delta-2 types.
    - Pars anterior is known to secrete a number of hormones and a number of attempts have been made to connect the secretion of one hormone with one particular cell type. The cell types have not been identified uniformly in all animals nor the correlation between secretion and cell type has been conclusively demonstrated in many animals. The present evidence indicates the following association between secretion and cell type.
    - Beta-1 cell – Adreno-corticotrophin
    - Beta-2 cell - Thyroid stimulating hormone.
    - Delta cell - Luteininzing or Interstitial cell stimulating hormone
    - Delta-2-cell - Follicle stimulating hormone.

Pars intermedia

- Consists of a connective tissue framework containing (basophilic) cells which with form dense masses.
- Colloidal vesicles are often seen. The cells in pars in intermedia produce the melanocyte stimulating hormone.

PITUITARY GLAND



Par tuberalis

- Contains numerous sinusoids and has cuboidal cells with faintly basophilic cytoplasm.
- The cell form vesicles, which contain colloid. Functional significance of this part is not known.

Pars nervosa

- Has a vascular connective tissue framework housing **neuroglia like cells**.
- The cells *pituicytes* show granules in their cytoplasm.
- The nuclei of these cells are round or oval, with a fine chromatin network.
- The cytoplasm is drawn into a number of fine processes which often end either on the walls of blood vessels or on the connective tissue septa.
- In routine preparations the cytoplasm and the processes cannot be made out. Between the cells, there is a fine mesh work of interweaving processes, which stain lightly with eosin.
- Contrary to earlier beliefs, it is now known that pars nervosa by itself does not secrete any hormone. The nerve cells located in the supraoptic and paraventricular nuclei of the hypothalamus are the actual secretory cells. Their

secretions are conveyed by their axons to the pars nervosa, where they are released into capillaries, adjoining axon terminations.

- Accumulations of neuro secretion appear as homogenus stainable masses in pars nervosa and are known as *Herrings bodies*.
- Two hormones have been isolated form pars nervosa.
    - *Oxytocin* causes contraction of uterine musculature at the end of pregnancy
    - *Vasopressin or Antidiuretic hormone* – increases blood pressure and water resorption in kidney tubules.

MODULE-22: LYMPHOID SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about
    - tonsils,
    - lymph nodes (Lymph gland),
    - spleen and
    - thymus.

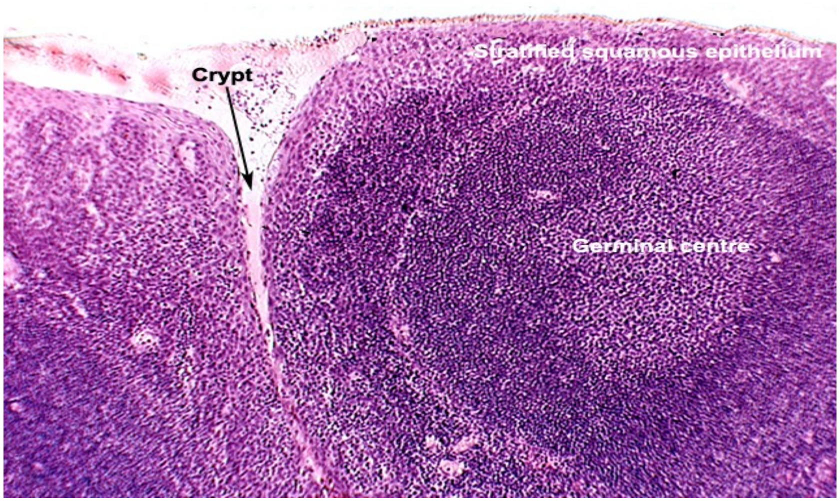
LYMPHOID ORGANS

- All these structures contain a matrix of reticular tissue the meshes of which are filled with lymphocytes.
- In addition to formed lymphatic structures like lymph glands, tonsils, thymus and spleen, there are diffuse lymphatic infiltrations in the body in the mm. Of digestive, respiratory and genital systems and conjunctiva.

TONSILS

- The palatine tonsil is an egg-shaped mass, which bulges into the oral cavity.
- The oral surface is covered by *stratified squamous epithelium*.
- The epithelium passes down into the crypts in the substance of tonsil. Between the crypts the masses of dense.
- lymphoid tissue arranged in folds containing the individuals follicles.
- At intervals, between folds of lymphatic tissue; connective tissue septa pass up form the basal layer of connective tissue, which separates the tonsil form the subjacent structures.
- Below this basal layer of connective tissue, lie bundles of skeletal muscle fibres.
- Round the periphery on the luminal edge are mucous gland – *tonsilar glands*.

TONSIL



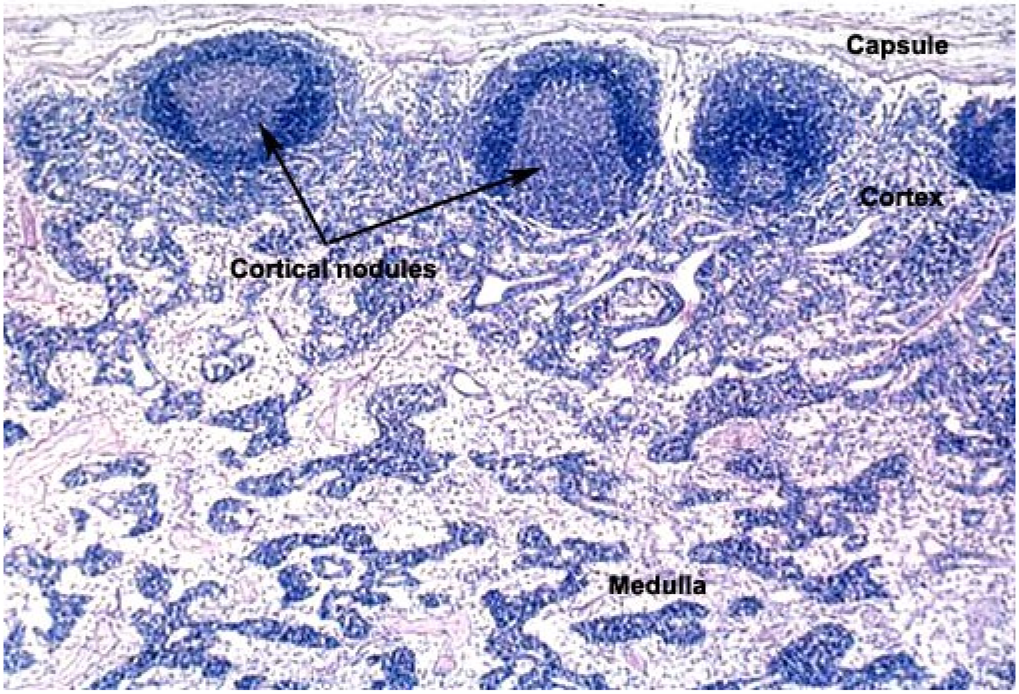
LYMPH NODES

Lymph gland

- These occur in the of lymphatics of lymph vessels. Lymph flows through them. These vary in size form those just visible to naked eye to those several centimeters in diameter.
- They are flattened and bean-shaped with a definite hilum. They have a connective tissue capsule containing a few elastic and smooth muscle fibres. Septa or trabeculae detached form the capsule pass towards the interior to form shallow compartments.
- In the inner zone the tarabeculae anastomose ad pass into the hilus. This framework divides the node into compartments, which communicate and are filled with reticular tissue.
- The reticular tissue of the node consists of reticular cells and fibres, which form a framework. The reticular fibres are continuous with the collagen fibres at the trabeculae.
- The Reticular cells have an irregular shape with processes and pale staining nuclei. These are phagocytic reticular cells, which form part of the reticuloendothelial system. There are also non-phagocytic undifferentiated primitive reticular cells (which may give rise to the phagocytic reticular cells or lymphocytes).
- ***The lymphoid tissue*** is arranged differently in;
    - the outer part of the node or the ***cortex*** and
    - the inner part of the node or ***medulla***.
        - Cortex
            - The trabeculae are more or less perpendicular to the surface and divide the cortex into a number of compartments. The trabeculae pass deeper and become continuous with the irregularly arranged trabeculae of the medulla.

    - In the cortical compartments the lymphocytes are closely packed together to form cortical nodules. These are more or less spherical discrete masses of closely packed lymphocytes but in some nodes, the nodules may be irregular and ill defined becoming continuous laterally with adjacent nodules.
    - The cortical nodules often contain lighter staining central areas called *germinal centers* because lymphocytes are formed in them by proliferation. In these area, many medium sized and a few large lymphocytes have a greater amount of cytoplasm and the undifferentiated large lymphocytes have pale vesicular nuclei.
    - These lightly stained central areas are also referred to as secondary nodules. Active proliferation of cells in the germinal center pushes outward to the surrounding cell and thus the primary nodule contains peripheral darker zone consisting of closely packed small lymphocytes.
    - The cortical nodules are separated from the capsule and the trabeculae by channel-like spaces called *lymph sinuses* through which lymph circulates. The marginal or cortical sinus receives lymph from the afferent lymphatics. The lymph then flows down the trabecular sinuses to enter the sinuses in the medulla.
- Medulla
    - The trabeculae of connective tissue are irregularly arranged and anastomose freely.
    - The lymphocytes do not form nodules as in the cortex, but form annstomoising *lymph cords*.
    - The medullary sinuses are wider and passing between the lymph cords and the trabeculae.

LYMPH NODE



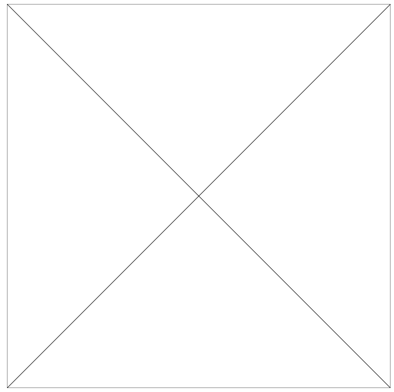
Lymphatic vessels

- The afferent lymphtics are numerous and pierce the capsule on the convex side of the node-and open into the marginal sinus.
- The lymph flows through the trabecular and medullary sinuses and from here it is collected by a plexus of vessels, which penetrate through the capsule at the hilum, from where it flows through the efferent lymphatic vessels.

Blood vessels

- The artery enters at the hilus and branches pass in the trabeculae and give branches to capsule.
- Other branches pass through medullary cords to form capillary nets in the center of the cortical nodules.
- The veins follow the same general course as the arteries.

Lymph capillaries



- Structure similar to blood capillaries but their diameter is greater and they show dilations.

Lymphatcis

- Structure similar to venules and veins; show a much thinner poorly defined three layered wall. T.intima lacks internal elastic membrane, T. media is made up of smooth muscle, elastic and collagenous tissue, T.Adventita is made up of collagenous tissue with few muscle fibres.
- They have numerous valves.

Species differences

- In pigs the arrangement of nodules in the lymph node is entirely different.
- The nodules occupy the central zone and the lymph cords are distributed peripherally.
- The afferent lymphatics penetrate the capsule, pass to the interior and open into the sinuses surrounding the nodule.
- The efferent lymphatics leave on the convex surface of the node at several points.

Haemolymph glands (Haemal nodes)

- Occur only in ruminants.
- They are independent of lymphatic system.
- They have no lymph vessels.
- The structure is similar to that of lymph nodes but blood circulates through the sinuses and not lymph.

SPLEEN

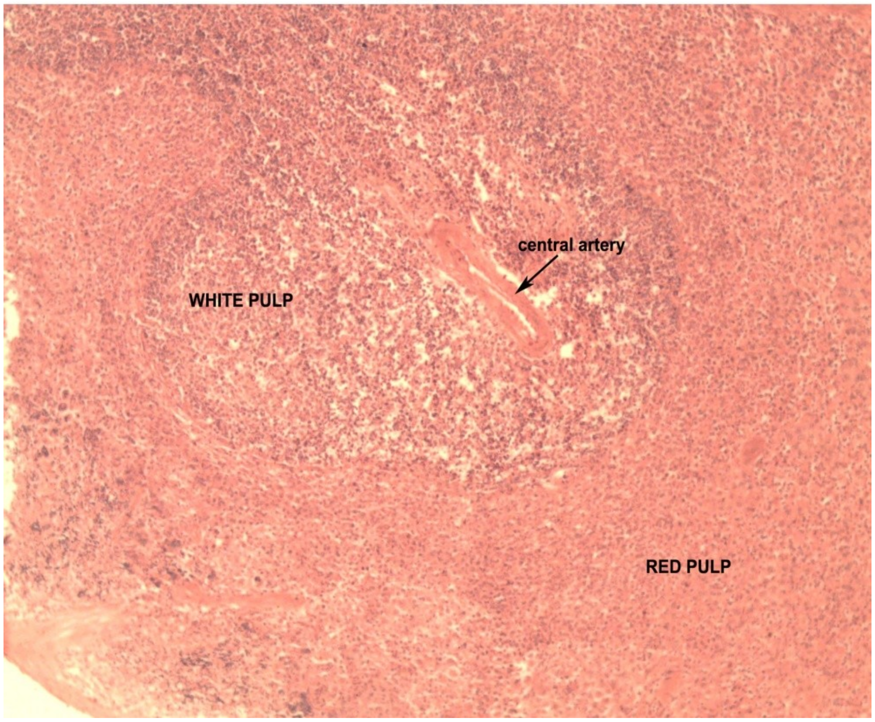
- Spleen has a capsule of connective tissue rich in elastic tissue and smooth muscle, over the capsule is serosa. Trabeculae from the capsule extend into the interior and form complicated framework by anastomoses.

- The spaces within the connective tissue framework are filled with a soft sponge like tissue known as *splenic pulp*. On the basis of colour difference seen in the fresh preparation different regions have been named as *white pulp* and *red Pulp*. Both types consists of lymphoid tissue, (i.e) reticular tissue with lymphocytes but with different arrangement and different relations to blood vessels.
- The white pulp is composed of lymph nodules distributed diffusely throughout the substance of the spleen and passing through each nodule often eccentrically is a branch of an artery. These spherical or ovoid lymph nodules with an eccentrically placed artery passing through them are referred to as *Splenic or Malpighian Corpuscle*.
- The Red pulp consists of anastomosing lymph cords or *cords of Billroth* between which are numerous venous sinuses filled with blood. The lymphoid tissue itself (i.e. spaces between reticular network and lymph cords) is infiltrated with erythrocytes, the number varying under different conditions. The presence of venous sinuses and infiltration with erythrocytes are responsible for the colour of red pulp.
- The framework of the splenic pulp is made up of reticular tissue. The cells of the reticulum like those in the lymph node are of two types - Phagocytic cells belonging to the reticulo endothelial system and non-phagocytic undifferentiated cells.
- Lymphocytes, large, medium and small are present forming the nodules in White pulp and lymph cords in red pulp. The Red pulp also contains monocytes, granular leucocytes, megakaryocytes or giant cells.
- The structures of spleen are best understood by following the course of blood vessels, in their passage through the organ.
- The *Splenic artery* enters the hilum and divides into a number of branches, which enter the trabeculae as *trabecular arteries*. After a short course in the trabeculae, the trabecular artery leaves the septa and enters the splenic pulp.
- The tunica adventitia of the artery is replaced by reticular tissue, which is infiltrated with lymphocytes. The artery becomes enclosed within a sheath of dense lymphatic tissue or a nodule forming the splenic or Malpighian corpuscle. This artery is called the *central artery* or artery of white pulp, but this is actually located eccentrically within nodule. From this artery numerous capillaries are given off which supply the lymphoid tissue and then enter the red pulp.
- The central artery after passing through the splenic corpuscle, becomes reduced in size, looses the sheath of lymphoid tissue and enters the red pulp. As it enters the red pulp the artery divides into a number of straight branches, which lie close together at the origin and later diverge like the bristles of a brush. These are called *penicilliform artery*.
- Each penicillus pursues a course through the red pulp, which can be divided, into three successive parts. The pulp artery, sheathed artery and terminal arterial capillary.
- The *pulp artery* is the longest of the three segments and has the thin coat of plain muscle surrounding the endothelium and external to the muscle in the tissue of red pulp. The pulp artery becomes smaller and divides into sheathed arteries.
- The *sheathed artery* has no muscular layer and the endothelium is surrounded by a compact mass of concentrically arranged reticular cells. These become

continuous peripherally with the reticulum of red pulp. This sheath is known as the *Schweiger-Seidel sheath* and the entire arrangements are referred to as an *ellipsoid*.

- The sheathed artery divides into two or more terminal arterial capillaries. The terminal arterial capillary may have conical shaped enlargement or ampulla at its termination.

THE SPLEEN



- The exact manner in which these capillaries terminate has been a controversial subject. Some suggest that the empty into intercellular space of the red pulp reticulum and that blood finds its way from the pulp spaces into the venous sinuses through perforation in the walls of the sinuses. This is called the theory of open circulation. Other workers believe that capillaries empty directly into venous sinuses. This is called the theory of closed circulation. An intermediate view that some capillaries connect directly with the venuous sinuses and that others open into pulp spaces has also been put forward.
- The venous sinuses form an anastomosing plexus through out red pulp. The cells lining the sinuses are elongated and are arranged longitudinally along the course of the sinus. The cell bodies are enlarged at the level of the nuclei and bulge at these sites into the lumen. "Surrounding these elongated cells are circularly disposed reticular fibres, which resemble the "staples" and "hoops" arrangement of a barrel.
- Some believe that clefts are present between the lining cells through which blood may escape and other hold the view that a thin homogenous membrane exists between the cells. These lining cells are believed to be phagocytic and considered to be not a true endothelium but belonging to the reticuloendothelial system.

- The venous sinuses unite to form large pulp veins or collecting venules line by endothelium. These venules reach the trabeculae to become trabecular veins which reaches the hilum to form the splenic vein.
- Recent studies on circulation in spleen have shown that there is a cyclical activity in the venous sinuses, regulated by sphincters at various levels including the terminal capillaries.
- The activity is in different phases and consists of ;
    - *Conducting phase* with all sphincters open all the blood enters the sinus at the afferent and leaves it at efferent and
    - *Filtration phase* –The sphincter at the efferent end closes, blood enters the sinus through the afferent end, the fluid passes rapidly through the sinus wall and the sinus gets gradually distended and packed with erythrocytes
    - The afferent sphincter also closes and the sinus remains distended with both sphincters closed for some time. Then the storage phase terminates with the opening of the efferent sphincter and the movement of erythrocytes into the collecting venules. The afferent sphincter also opens and the conducting phase begins.

Species differences

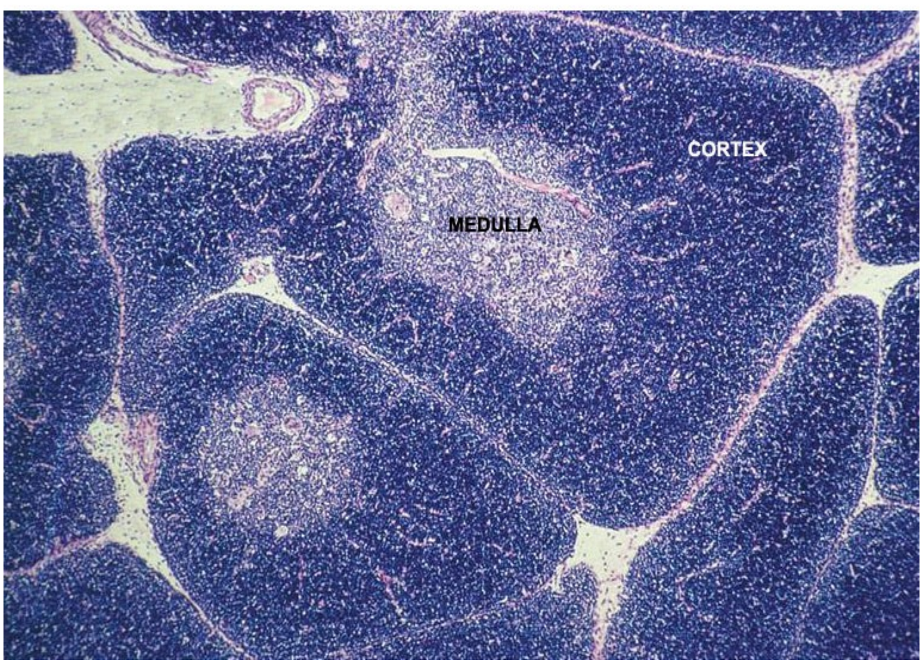
- Mammalian spleens, are of different types: The storage spleen of horse, dog and cat is relatively large, rich in tarbeculae and muscle and poor in white pulp. The abundant red pulp serves as storage space of blood elements and the muscular framework serves to empty the spleen.
- The defense spleen is small and has few trabeculae and smooth muscle fibres but abundant lymphatic tissue. The red pulp, the storage space of the spleen is poorly developed in the rabbit, only moderately so in man. The ruminant and swine belong to an intermediate type. The Ellipsoids are large in the pig and are will developed in the dog and cat.

THYMUS

- The thymus varies in size and development with the age of the individuals.
- It begins to decrease in size and undergone involution with advancing age and gets gradually replaced by fat and connective tissue.
- The thymus is covered by a connective tissue capsule, which gives off numerous septa, which divide the gland into a number of polygonal lobules.
- Each lobule consists of a cortex and medulla.
- Often the medullary substance is continuous through several lobules.
- Cortex
    - It consists of a compact, dense lymphoid tissue (reticular tissue and lymphocytes). The cells often called as *thymocytes* are closely packed but do not form nodules. The reticular cells are often obscured by the loosely packed thymocytes of lymphocytes.
- Medulla

- The thymocytes are less numerous and are not so closely packed together and hence the medulla presents a lightly stained appearance in sections in contrast to the darkly stained cortex. The Reticular tissue is more distinct.
- The medulla also contains spherical or oval bodies known as *Thymic* or *Hassall's corpuscles*. These are characteristic of thymus.
- Each corpuscle consists of a central eosinophilic hyaline mass surrounded by concentrically arranged flattened reticular cells which become continuous with the cells of the surrounding reticulum.
- The reticular tissue in thymus is different from the reticular tissue in other organs, in that it is derived from the endoderm, where as the reticular tissue in other organs is derived from mesoderm.
- A number of views have been held regarding the functions of thymus and it is now considered that thymus serves as a lymphocytes producing center during foetal and early postnatal life and the lymphocytes produced are distributed to other lymphatic organs, where they establish colonies and multiply.
- The colonization of the various lymphatic tissue of the body with lymphocytes of thymic origin begins at different times in different species. It has also been suggested that thymus produces a Lymphocyte stimulating factor, which is responsible for proliferation of lymphocytes in other parts of the body. The thymus has some interrelationship with the gonads, adrenal and thyroids.

THYMUS



MODULE-23: NERVOUS SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about
  - cerebrum,
  - cerebellum and
  - spinal cord.

NERVOUS SYSTEM

- It can be divided into;
  - Central nervous system (CNS) and
  - Peripheral nervous system (PNS). CNS includes the brain and spinal cord.

CEREBRUM

Note: The Brain consists of many parts (studied in gross anatomy) having its own histological structure only the motor area of the cerebral cortex is described below as an example.

- The cerebral cortex is the external layer of gray matter covering the convolutions and fissures of cerebral hemispheres.
- It contains the bodies of nerve cells, nerve fibres, neuroglia and blood vessels.
- It shows the following layers from without inwards:
  - *Piamater*
  - *Molecular or plexiform Layer:* It is poor in cells and has a framework of the reticulum formed by the glial process and dendrites of the pyramidal cells. There are fusiform cells directed horizontally.
  - *Layer of small pyramidal cells:* Contains cells with their apices directed towards the surface. They are 10-12 microns in size. From the apex a long main dendrite passes to the molecular layer where it forms a feltwork by its ramifications. Laterally and basally from the cells arise dendrites. The axon arises from the base and gets myelinated. Giving off collaterals, it passes into white matter.
  - *Layer of large Pyramidal cells* - giant cells of Betz: Found in the motor cortex. Apical dendrite long and goes towards molecular layer, there are also basal dendrites. Axon arises from the basis to the white matter giving off collaterals on its way.
  - *Layer of Polymorphous cells:* Cells are 5-8 microns in size, irregular and varied in shape. Their short dendrites ramify in all directions. Their axons enter white matter.

CEREBELLUM

- The cerebellar hemispheres are divided by *transverse fissures* into lobules. The surfaces of lobules are marked by folds (folia or lamina) running parallel to the fissure and runs transversely to the longitudinal axis of brain.

- In cross section of folds, it is seen that they give off secondary and tertiary lamina the whole producing the appearance known as arbor vitae. The surface of secondary cerebellum is composed of gray matter – the cortex that encloses white matter.

Cortex

- Has an *outer molecular layer* (plexiform layer) with few cells and few medullated nerve fibres, an *inner granular or nuclear layer*. Between these two layers a single row of large flask shaped cells called the *Purkinje cells* are present. These cells give off several antler like main dendrites which enter molecular layer and form a remarkably rich arborization extending to the surface.
- The dendritic arborization is fan-shaped and extends at right angles to the laminae. The axon is given off from the end of the cell opposite to the dendrites and acquiring a medullary sheath passes through the granular layer to the white matter.
- Purkinje cells are almost the only ones whose axons reach the white matter. Axons of the Purkinje cells give off collaterals, which enter molecular layer and appear to terminate there in "*end buttons*" upon the bodies of adjacent Purkinje cells. Cell bodies of Purkinje cells contain concentric chromophylic bodies.
- The cells in the molecular layer are either superficial stellate cells with irregular branching dendrites and short axon or deep stellate (basket) cells.
- Axon of the latter extend at right angles to the laminae for a distance of several Purkinje cells giving off to each Purkinje cell one or more collaterals which pass towards the granular layer and envelop with their terminal arborizations of the body and proximal non medullated portion of the axons of Purkinje cell. Collateral's of other basket cell axons may terminate around the same Purkinje Cell, thus forming the basket.
- The granular layer in ordinary preparations presents the appearance of closely packed nuclei with clear spaces here and there and a few larger cell. Most of these nuclei belong to granule cells. Their short dendrites 3 to 6 in number terminate in compact arborizations in the granular layer. Their nonmedullated axons ascent into molecular layer to end in varicosities.
- These are the parallel fibres of molecular layer and they run at right angles to and through the dendritic expansions of Purkinje cells and their cross sections together with terminal dendritic arborizations of Purkinje cells give the molecular layer its punctate appearance.
- In the cortex there are also the termination of afferent fibres, mossy fibres and climbing fibres.
- *Mossy fibres* are the coarsest of the white matter while in the white matter they bifurcate, branches going to different laminae. These main branches give off secondary branches which enter the granular layer and arborize there. The climbing fibres pass from the white matter to the cells of Purknije cells. The medullated fibres of cerebellum pass through the white matter into the granular layer, separating groups of granular cells.
- The above details are best demonstrated by the Golgi method.

SPINAL CORD

- Spinal cord is surrounded by spinal piamater. It is made up of outer white and inner gray matter. Surrounding the central canal of the spinal cord is the central mass of gray matter, the cross section of which is like *'H'*.
- The transverse bridge connecting the lateral halves of this is called the *gray commissure*. The central canal is lined by *ependyma*, enclosed by a layer of glia. The gray matter is covered all round by white matter.
- The gray matter on each side consists of a *dorsal horn* (column), which extends almost to the surface of the cord and a *ventral horn* (column), which is shorter and broader and does not reach the surface of the cord.
- The portion of gray matter connecting the dorsal and ventral horn is termed as intermediate part. The jelly-like substance called gelatinous substance of *Rolando* covers the summit of the dorsal horn.
- In the concavity between the ventral and the dorsal horn processes of gray matter extend into the white matter where they interlace with the longitudinally directed fibres form the reticular formation. In the thoracic and anterior lumbar region a small projection of gray matter on the upper part of ventral horn is present and is known as the *lateral horn*.
- White matter encloses the gray matter on all sides and is divided into two lateral halves by ventral median fissure and dorsally by a dorsal median septum, which contains a sheet of piamater.
- The outgoing ventral motor root and the entering dorsal sensory root into ventral, lateral and dorsal funiculi further divide each of these halves. A bridge of white matter - white commissure, connects the two ventral funiculi. At the entrance of the dorsal root on either side there is dorsolateral groove or sulcus.
- The gray matter of the cord consists of nerve cell and nerve fibres held together by neuroglia. The nerve cells are in different group,
    - *Motor cells* - large multipolar nerve cells upto 150 microns in size, present throughout the ventral gray (horn) column. Their dendrites extend into the dorsal gray horn and into the ventral and lateral funiculi of white matter. Their axon traverses the white matter where it receives a myelin sheath and enters into formation of ventral root of spinal nerve.
    - *Column cells* - make up the great majority. They are smaller than motor cells and distributed throughout gray matter but most abundant in the dorsal horn. Their axons pass out into the white matter.
- White matter is composed of predominantly myelinated and few non-myelinated nerve fibres neuroglia and blood vessels, most of the myelinated nerve fibres are directed longitudinally except in the region of the nerve roots and white commissure where they are radial or transverse. White matter contains neither nerve cells nor dendrites.
- In transverse section, spinal cord appears oval, more flattened on its ventral surface than on the dorsal. If the section has been cut through a dorsal nerve root, a bundle of dorsal root fibres can be seen entering the white matter dorsal and medial to the dorsal gray horn.

Different regions of spinal cord in transection

- *Cervical region:* Section is large and oval. White matter greater in amount than in any region. Ventral gray horn large and dorsal, slender.
- *Thoracic region:* Section smaller and circular. Both gray horns are slender Opposite the gray commissure on both sides, is a pointed projection called lateral horn. The lateral horn is present only in thoracic and upper lumbar segments of the cord.
- *Lumbar region:* Section is larger than in thoracic region and more of gray matter than white. Both dorsal and ventral gray horns are made of white matter.
- *Sacral region:* White matter is very small in amount. Section is smallest, gray matter is two large oval masses

MODULE-24: HISTOLOGICAL TECHNIQUES

Learning outcomes

- At the end of this module the learner will be able to know about
  - histological techniques,
  - fixation and
  - paraffin method of preparing tissue.

GENERAL HISTOLOGICAL TECHNIQUE

The technique includes methods of preparation and examination of tissues and cells.

Methods of preparation

- Dissociation or teasing of tissues: In this method details of individual cells are well seen but their anatomical relationships are destroyed. The organ or tissue is dissociated in some fluid medium and examined under microscope. The fluid medium used usually has the property of dissolving the intracellular cement substance at the same time fixes and preserves the cell structure. (Muller's fluid, 1% Normal saline, 30% Alcohol).
- Smear technique: Smears can be made by 'impression-smear' method, spreading with platinum loop or crushing and spreading material with another side. Preparation can be fixed stained and examined (e.g. Examination of blood smears). They can be cleared and mounted in a mountant.
- Sectional methods: here anatomical relations are preserved and maintained and extremely thins sections are cut. Finished preparation is mounted in a medium with high refractive index to enable its detailed study. Medium that is used for embedding tissues depends upon technique employed and type of material to be sectioned. Most common medium is paraffin wax. In certain cases celloidin, and occasionally gelatin are used.
  - *Paraffin Technique:* has the widest application. The tissue are embedded in a block of paraffin wax with melting point of 58° to 60°C after subjecting them to various processes which render them permeable to molten paraffin wax.

   - *Frozen Sections:* Unfixed or fixed tissue is frozen on a special microtome with carbon dioxide. This method is especially useful when rapid results are required or when demonstrating materials soluble in alcohol or cleaning agents like xylol.
- Vital staining: Some living cells take up certain stains (vital stains) which colour certain elements in cells (e.g. mitochondria). Some cells like phagocytes engulf microscopic coloured particles, which are then visible inside the cells (e.g. elements of R.E. system). Vital staining is subdivided into
- Supravital staining: This refers to staining living cells outside the body. Janus green and neutral red stains cytoplasmic organells like mitochondria. Living cells are treated with very dilute solutions of the stains. The cells are alive when they take up the stains but die subsequently as the stains are toxic.
- Intravital staining: Dyes like Trypan blue, Lithium carmine or Indian ink are injected subcutaneously or intravenously and tissues are collected from the site of injection (when subcutaneously injected) or pieces of organs containing phagocytic cells are prepared and processed by the usual methods. The dye will appear as fine granules in the cytoplasm of phagocytic cells.

Methods of examination of tissue

- Using optical microscope with direct or transmitted illumination.
- Using polarizing microscope.
- Using dark ground illumination.
- Using phase-contrast microscope to examine living cells and tissues without staining.
- Using electron microscope for obtaining magnification upto 1,00,000 times.
   - Of these, the most common method is using ordinary optical microscope with direct or transmitted illumination.

FIXATION

- Fixation is the method of preserving the cell and tissue constituents as in life like condition as possible. Adequate and complete fixation are the foundation of good histological preparation. It is essential that tissues are fixed as soon as possible after death or removal from the body.
- The amount of fixative (that is an agent used for fixation) should be 15 to 20 times the bulk of tissue to be fixed. Tissues or sectioning should be sufficiently thin to be adequately fixed throughout in a reasonable time. The best thickness for routine use is 3 to 5 m.m.

Aims and effects of fixation

- Fixation is required to prevent putrefaction and autolysis to preserve and harden, to solidify colloid materials and to aid visual differentiation of structures. Certain fixatives have effects on subsequent staining and this should be remembered.

- Fixation also renders cells insensitive to hypotonic and hypertonic solutions. Fixation alters the refractive indices of various components of cell and tissue into varying degrees so that details are easily seen. Fixative must be used in solutions either with normal saline or distilled water.

Common fixatives employed

- Formalin is the most common fixative used in 5 to 10% strength in normal saline.
- Mercuric chloride in combination with other fixatives.
- Osmium tetroxide (Incorrectly named Osmic acid) to fix fat and lipids used as a 2 to 5% aqueous solutions).
- *Chromic acid:* used as a 2% solution preserves carbohydrates.
- Potassium dichromate used a 3% aqueous solution. This is another common fixative used in combination with others.
- Picric acid used as a saturated aqueous solution in combination with others.
- Acetic acid-used in varying strengths in combination with other.
- Trichlor-acetic acid used with others in varying strengths.

Type of fixatives

- Generally the fixatives are named after their inventors
    1. Formal Saline 5-10%
    2. Heidenhain's Susa
    3. Bouin's fluid
    4. Zenker's fluid and Zenker formaldehyde
    5. Flemming's fluid
    6. Carnoy's fluid
    7. Helly's fluid
- Of these Numbers 1,2,3 and 4 are micro anatomical fixatives, that is they accurately preserve the relations of tissue layers and large aggregates of cells to one another and are useful in routine work. Numbers 5, 6 and 7 are cytoplasmic and nuclear fixatives.
- In general, fixatives are either;
    - *Precipitant fixatives* (that is they precipitate or coagulate colloidal constituents (e.g. mercuric chlorides, alcohol, picric, chromic acid) or
    - *Non-precipitant fixatives* (that is they fix proteins not by chemical combination but by denaturing them which involves a change in the shape of protein molecule and results in making it insoluble (eg.) Formalin, Osmium tetroxide and Potassium dichromate).

PARAFFIN METHOD OF PREPARING TISSUE

- The Scheme given below refers to procedures commonly employed for routine preparations of histological sections.

- It should be noted that procedures may have to be considerably modified or additional new process introduced when other fixatives are used or special methods followed.
- The method given below deals with fixations, using formal saline, embedding in paraffin and staining by Heamatoxylin and eosin.
    - Fixation in 100% Formal saline
    - Washing in water
    - Dehydration in ascending grades of
        - 50%
        - 70%
        - 90%
        - Absolute alcohol (usually three changes)
    - Clearing commonly in xylol (sometimes benzene, toluene, or cedar wood oil).
    - Inclusion in paraffin embedding oven at 56° to 60°C
        - Permeation with paraffin three changes
        - Casting of tissues (orientation and cooling the mass).
    - Sectioning
        - Sectioning (microtomy)
        - Fixing section to slide
    - Staining

MODULE-25: EMBROYOLOGY - INTRODUCTION

Learning outcomes

- At the end of this module the learner will be able to know about
    - introduction and divisions of embroyology and
    - general features of development.

INTRODUCTION

- Embryology is the science that deals with the origin and development of the individual organism or it deals with the formative history of animals from the time of fertilization of the female germ cell or ovum by a sperm to the adult condition.
- Exceptionally an ovum may develop into an organism without being fertilized by a sperm, which is known as parthenogenesis.

Historical background

- The study of Embryology becomes more interesting with discussion on the historical background of the subject. Aristotle, (384-322 B.C] Greek philosopher studied the embryos of many animals without the aid of microscope. He wrote the first treatise on embryology. He formulated that the embryo was a preformed structure and only enlarging during its development or it must be actually differentiating from a formless beginning.
- Galen (165-200 A.D) learned much about the structure of relatively advanced fetuses but the minute dimensions of early embryos was not studied due to the lack of the invention of the microscope.

- Regnier.de. Graaf (1672) described the ovarian follicles and Antony van Leeuwenhoek (1677) described the sperm of man and mammals. But significance of sperm and ovum was not known to these scientists.
- All this time two groups were emerged. According to the Homanculist or Spermatist view the sperm contained a minute individual, which grew into a fully formed baby by taking nourishment from the ovum. According to the other view, the minute human being was situated inside the ovum. The sperm merely activated its growth. This was called as the Ovist view. These views are also known as Preformation doctrine or view, which says that human being is preformed either in sperm or in ovum.
- The preformation theory was destroyed by the Spallanzani and Wolff (1759). According to them, there is no minute individuals either in a sperm or in an ovum. But the development takes place by progessive growth and differentiation of basic buildings in it known as cells. This is called as Epigenesis.
- Karl Ernst Van Baer (1828) first described the germ layers ectoderm and endoderm and he was honoured as the Father of Modern Embroyology.
- Cleavage or subdivision of the cell into the building units of the embryo was described by the Prevost and Dumas (1824). This was followed by Schleiden (1838) and Schwann (1839) who propounded the cell theory which states that the body of an organism is com posed of innumerable microscopic cells, form the tissues.
- Errnst Haeckel, (1866) a German scientist formulated the Bio-genetic law as "Ontogeny recapitulates Phylogeny". Ontogeny means development of an individual organism whereas Phylogeny denotes the development of a race. According to this, the mammalian embryo looks like an embryo of fish and then like the embryo of reptile before the mammalian shape is obtained. The early stages of embryos of fishes, amphibians, reptiles, birds and mammals looks somewhat similar.
- Van Beneden (1883) proved that the male and female sex cells contribute the same number of chromosomes to the fertilized eggs.

Fields of embryology

- *Descriptive embryology*
  - This branch of study is based on the observations and descriptions of different embryonic stages of the ontogenic development of a species. It is the chief concern of the early embryologists.
- *Comparative embryology*
  - Comparative studies are made between the embryology of most animal types and are classified, compared and common trends and principles are sought.
- *Experimental embryology*
  - It is the branch of embryology that attempts to understand the fundamental development mechanisms or the factors, which active or regulate the developmental process. It is also called as developmental mechanics, casual embryology, and analytical embryology.
- *Chemical embryology*
  - To understand the developmental phenomena in molecular terms, various biochemical, molecular, biological, biophysical and physiological techniques are employed to the developing embryo.
- *Teratology*
  - The study of malformations/abnormalities.
- *Developmental biology*
  - It is the study of post-natal processes such as normal growth, metamorphosis, regeneration and tissue repair at the levels of complexity ranging from the molecular to the organism level along with the embryonic development. It is the study of processes and concepts rather than specific morphological structures.

Scope of embryology

- To the student of Veterinary medicine the study of embryology is of great practical value as it helps
  - To provide a comprehensive and rational explanation of the many facts of anatomy which are otherwise meaningless or anomalous.
  - To interpret rudimentary structures, variations, anomalies and monstrosities.
  - To understand the origin of certain tumors and other pathological changes in tissues.
  - To unlock the secrets of heredity, determination of sex and organic evolution.
- A general conception of how man and other animals develop from a single cell by orderly and logical processes should share in the cultural background of every educated mind.

GENERAL FEATURES OF DEVELOPMENT

- A multi-cellular begins life as a fertilized egg or zygote. The further development depends on the following processes.

Growth

- Growth occurs by the following three basic mechanisms:
  - An increase in the number of cells — In the early stages of development increase in size by cell proliferation is a major growth mechanism.
  - An increase in the size of the cells – A good example of growth that occurs by an increase in cell size is the growth of muscles brought about by an increase in exercise. Muscle cells are unable to undergo mitosis and therefore cannot grow by cell proliferation. Thus well – exercised muscle grow because the individual cells increase in size.
  - An increase in the amount of exrtracellular material – the best example for this is found in the various connective tissues, which are primarily composed of extracellular material.

Differentiation

- Differentiation occurs in two ways.
  - Morphogenesis: This refers to a change in the shape and organization of the body and its parts.The more morphogenetic processes in molding of the body and its organs into form and pattern are as follows
    - Cell migration
    - Cell aggregation forming
      - Masses
      - Cords
      - Sheets
    - Localized growth resulting in
      - enlargements of various kinds
      - Constrictions
    - Fusion and splitting
    - Folding including circumscribed folds which produce
      - Anterior pocketing or evaginations
      - Bending where folding is due to unequal growth.

        - The differential growth resulting in enlargements, bending and folding of all sorts is the chief process utilized by the embryo in molding its general form and producing new organs.
        - The term "*primordium" or "anlage"* is applied to the celluar beginnings of a future tissue, organ or part before it assumes the characteristic differentiation and grow features.
    - Histogenesis
        - This applies to a change in the substance and structure of the cells and therefore various tissues are created.
        - The total process by which cells differentiate into distinctive kinds and assume specific tissue characters is known as histogenesis.
        - At this early period of differentiation in form and structure they are often designated by the suffix – blast. Eg.Neuroblast will complete its differentiation into a nerve cell and a Myoblast into a muscle cell.
        - Further the histogenic differentiation is the history of the originally single germ layer. Eg. The cells from the ectodermal layer proliferate and gradually change their form and character as they produce
            - A layers of epidermis
            - More specialized epidermal products are the hairs, nails, lens of the eye and enamel of the teeth.
            - Glandular derivative of the ectoderm vary from salivary gland, sweat gland, mammary gland and anterior lobe of pituitary gland.
            - Other local specializations produce the sensory epithelium of the organs of smell, hearing and vision.
            - Part of the ectoderm becomes thickened neural plate from which both nerve cells and supporting elements arise.
- *Morphogenesis* and *histogenesis* are the processes resulting in the organogenesis, which resolve the early embryo into complete organs.

Integration

- Although the new organs and organ systems possess structural coherence and unity, they need to be reintegrated into co-operative working mechanisms. This control is given by the nervous system and endocrine glands, which constitute the primary mechanism of physiological control and co-ordination.
- The supplying of organs with adequate nervous, vascular and hormonal influences will make the development to pass from a prefunctional period to a functional period.

MODULE-26: GAMETOGENESIS

Learning outcomes

- At the end of this module the learner will be able to know about
    - spermatogenesis,
    - oogenesis,
    - comparision between spermatogenesis and oogenesis,
    - comarision between the spermatozoa and ova,
    - significance of meiosis and
    - structure of gamete.

GAMETOGENESIS

- The most important characteristic of every living organism is the ability to reproduce to perpetuate the species.
- The reproductive cells, which unite to form the new individual, are known as gametes. In all higher vertebrates, the gametes from male are called spermatozoa and the larger, food – laden gametes formed within the female are termed ova/ovum.
- The gametes themselves and the cells that give-rise to them constitute the germplasm of an individual. The other cells of the body, which take no direct part in the production of gametes, are called somatic cells.
- The process by which the gametes are produced is known as ***gametogenesis***.
- It includes
    - *Spermatogenesis* in male
    - *Oogenesis* in female.
- Generally, gametogenesis is divided into four major phases
    - Origin of germ cells and their migration into gonads.
    - The multiplication of germ cells by mitosis.
    - Reduction division/Meiosis.
    - The final stage of maturation and differentiation of the gametes into spermatozoa/ova.

SPERMATOGENESIS

- The development of sperm in the testes is called spermatogenesis. The testis is a glandular organ composed of several coiled seminiferous tubules and their wall is formed by a multi-layered epithelium called germinal epithelium.
- The germinal epithelium is formed by two types-spermatogonia, primary spermatocyte, secondary spermatocyte and spermatids. When the male animal becomes sexually mature, these spermatogonia begin to produce sperms. This process includes three phases.
    - Multiplication/Mitotic Phase.
    - Growth Phase
    - Spermatogenesis/Maturation Phase.

Multiplication phase

- Mitosis of spermatogonia occurs throughout the life and they are situated near the outer wall of the seminiferous tubules.
- The spermatogonia are the rounded cells and they are the mother cells from which primary spermatocyte are produced. These are also rounded cells situated near to the spermatogonia.

Growth phase

- During this phase, limited growth occurs. This growth phase is insignificant.

Maturation phase

- Each primary spermatocyte is divided into two secondary spermatocyte by I meiotic division. From each of the secondary spermatocytes, two spermatids are produced by II meiotic division. Thus from one primary spermatocyte four spermatids are produced.
- The spermatids do not divide any more. Each spermatid is gradually transformed into a fully formed, potentially functional male gamete, the spermatozoa. This final phase of spermatogenesis where spermatogenesis does not begin until puberty but is then continues throughout life.
- The transformation of the spermatid into mature spermatozoa is known as spermiogenesis.
- During the spermatogenesis the following changes occur;
    - The nucleus becomes the sperm head and the cytoplasm appears to be arranged in tail side leaving a thin layer covering the nucleus.
    - The centrioles become more conspicuous and form the flagellum.
    - The mitochondria become the middle part of the spermatozoan.
    - The part of the cytoplasm with golgi apparatus in the apical end forms the acrosomal cap. The remaining part of the cytoplasm disintegrates and leaving the mature

spermatozoan stripped off all non-essential parts and consisting only concentrated nuclear material bearing the genes and the tail for the motility.

OOGENESIS

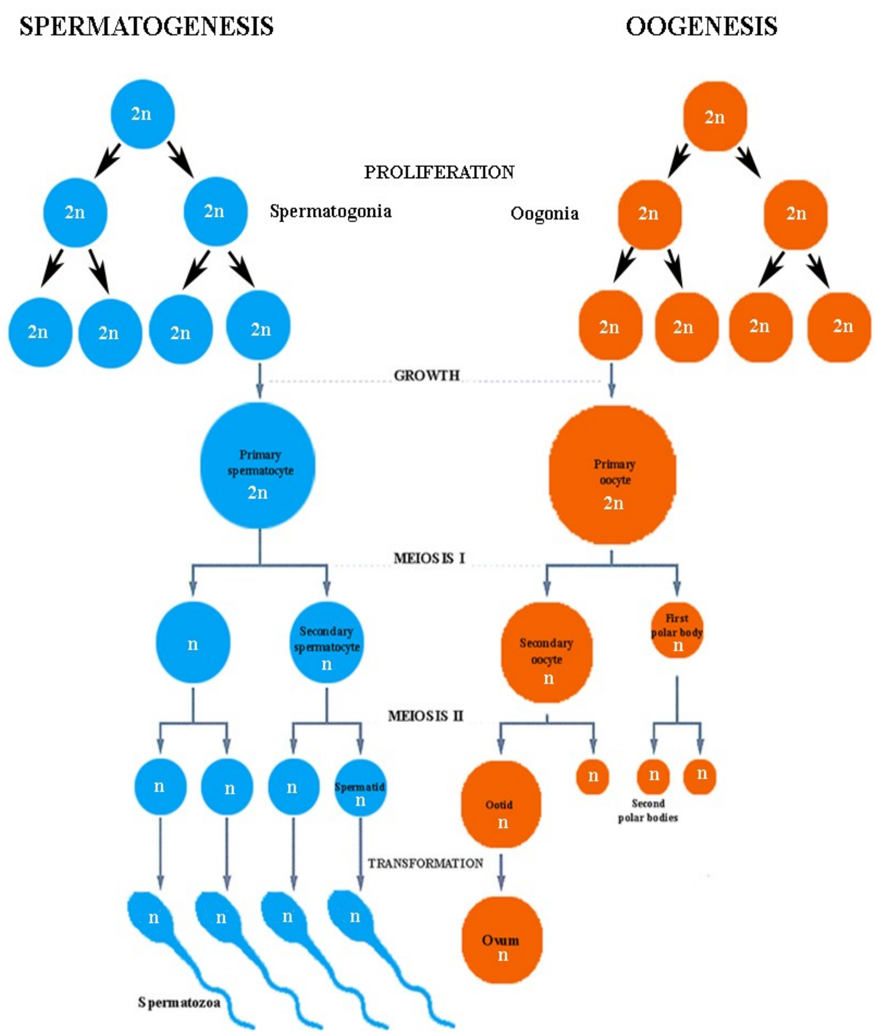
- Oogenesis is the process by which the female gamete or ova is produced. It takes place in the ovary.
- The ovary is a compact mass of connective tissue, smooth muscle fibres blood vessels, nerves and ovarian follicles at different stages of development. The entire ovary is covered by a thin germinal epithelium. From this, the germinal cells dip into the substance of the ovary and these are the oogonia. Like spermatogenesis, the oogenesis takes place in three phases namely,
    - Multiplication phase
    - Growth phase
    - Maturation phase
- The process of oogenesis is more complicated. It involves not only the production of the ova but also the acquisition of food reserves for the developing embryo.

Multiplication phase

- The ova are derived from the primordial germ cells, which undergo proliferation by mitotic division and the resulting cells are called Eugenia or egg mother cells.
- When the division stops, the cells are termed primary oocyte which enter a period of growth.
- The nucleus of primary oocyte is in diploid state (2n).

Growth phase

- Growth plays a much greater role in oogenesis than in spermatogenesis.
- During this period, nutritive substances and other materials necessary for the development of embryo are synthesized.



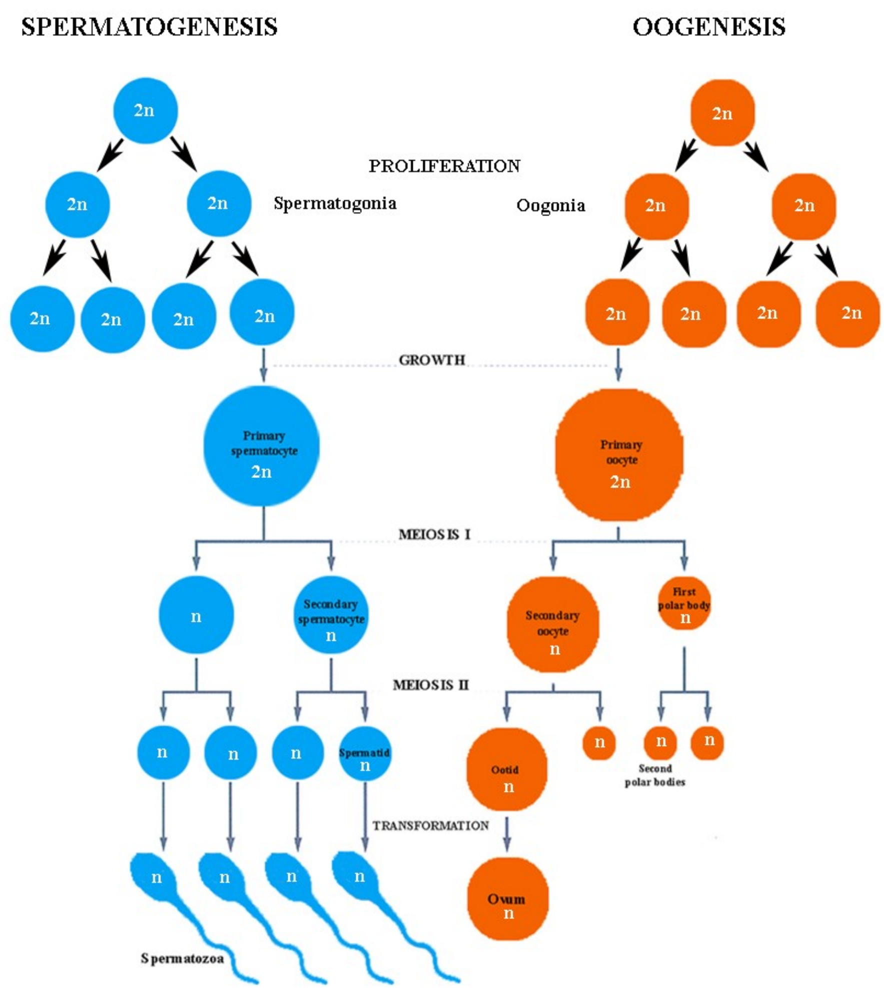
Maturation phase

- The primary oocyte under goes the I meiotic division to form two haploid unequal cells- a large secondary oocyte with more cytoplasm and a small polar body with little cytoplasm.
- Then the secondary occtye undergoes II meiotic division resulting in a large cell ootid and a small second polar body.
- Sometimes the I polar body divides into two polar bodies. Thus in oogenesis, one ootid and three polar bodies are formed from a single primary oocyte.
- The ootid then becomes the mature ovum. The three polar bodies are soon degenerates.

COMPARISION BETWEEN THE SPERMATOGENESIS AND OOGENESIS

Spermiogenesis	Oogenesis
Occurs in germinal epithelium of testes.	Occurs in germinal epithelium of ovary.

It involves 3 phases namely multiplication, growth and maturation phases.	It involves 3 phases namely multiplication, growth and maturation phases.
Meiotic divisions are equal.	Meiotic divisions are unequal.
At the end of the II meiotic division 4 spermatids are formed.	One Ootid and 3 polar bodies are formed.
Polar bodies are not formed.	Three polar bodies are formed.
Growth phase is insignificant.	More significant.
Spermatid undergoes spermiogenesis to become functional spermatozoa.	No such changes in Ootid to become ovum.



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COMPARISON BETWEEN THE SPERMATOZOA AND OVA

Spermatozoa	Ovum
Small and elongated	Large and spherical
Motile	Non-motile
No envelope	Egg envelope present
Centrosome present	No centrosome
XY chromosome	XX chromosome

SIGNIFICANCE OF MEIOSIS

- It affords a mechanism for selection and recombination of the genes of unit characters and there by ensures variation.
- It prevents accumulation of chromatin and a numerical duplication of chromosomes from generation to generation.
- It also provides for sex determination of individual.

STRUCTURE OF GAMETES

Spermatozoa

- The normal spermatozoon is composed of head and a tail that is divided into a mid-piece, main-piece and end-piece.
- The important component of the head include the nucleus containing the genetic code, which is the sire's contribution to the new offspring, the postnuclear cap covering the posterior portion of the nucleus and the acrosome. The acrosome covers the anterior part of the nucleus and contains enzymes needed for penetration of the corona radiate and zona pellucida during fertilization.
- The point where the tail joins the head contains the proximal centriole, and is called the implantation region. The head and tail get separated at this point during fertilization.
- The mid-piece is just posterior to the proximal centriole. The mitochondrial sheath, which forms the mitochondria of the spermatid , is a apart of the mid-piece. The mitochondrial sheath contains enzymes which convert fructose and other energy substrates into high energy compounds that can be used by spermatozoa.
- The main-piece and end-piece differ in that the end-piece does not have a protective sheath. A major feature of the tail is the axial filament. The axial filament is the small bundle of tiny fibrils that starts at the proximal centriole and runs through the entire tail. One center pair of small fibrils surround the circle of nine pair of small fibrils. Nine larger fibrils surrounds the circle of nine pair of small fibrils. Contraction of these fibrils cause a lashing of the tail which propels the spermatozoa forward.

Ovum

Types of Vertebrate Egg

- The fully developed female sex cell is termed as Ovum or Egg. The ova are relatively larger in size and inert as compared to the spermatozoa. An animal egg has three main functions.

- It supplies a haploid set of chromosomes to the future embryo.
- It provides most of the cytoplasm to the embryo.
- It supplies food reserves for the developing embryo.

Shape

- As a general rule, the mature eggs are spherical in shape, but in few animals the eggs are elongated.
- The eggs of birds are oval in shape.

Size

- Generally vertebrates, the size of the egg vary from 0.07 mm in mouse to about 3.5 inches diameter in ostrich whereas the eggs of mammals are very minute and measure about 100 u in a diameter.
- The size of the egg chiefly depends upon the amount of yolk present in them. Sharks, reptiles and birds lay eggs of larger dimensions.

MODULE-27: OVUM/EGG, OVULATION AND FERTILIZATION

Learning outcomes

- At the end of this module the learner will be able to know about
    - classification of egg,
    - polarity of egg,
    - membranes of ovum,
    - ovulation ,
    - types of ovulation,
    - type of ovulators,
    - mechanism of ovulation and
    - fertilization.

CLASSIFICATION OF EGG

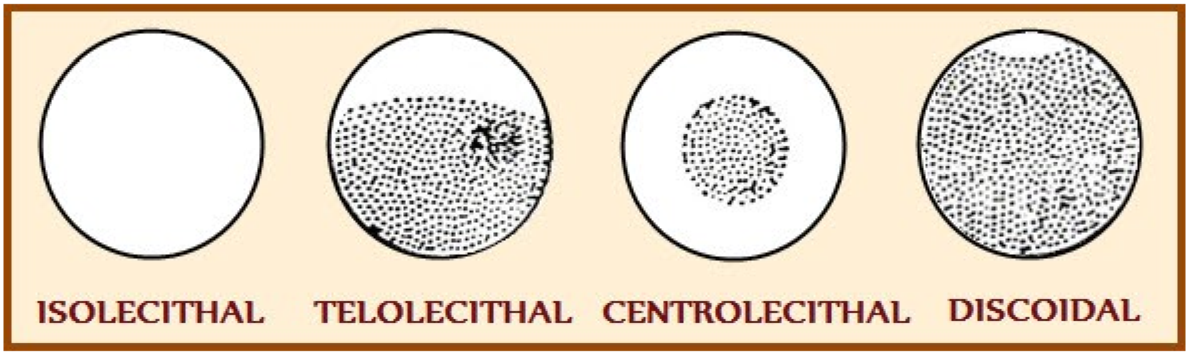
- The animal eggs are classified according to the following criteria:
    - Amount of yolk
    - Distribution of yolk
    - Presence or absence of shell
    - Type of development

According to the amount of yolk

- *Alecithal:* Yolk is absent. If present, it is in a negligible quantity. **E.g.** Mammals.
- *Microlecithal:* The eggs containing small amount of yolk and they can also be called as oligolecithal eggs. **E.g.** Amphioxus.
- *Mesolecithal:* Moderate amount of yolk is present in these eggs. **E.g.** Amphibians.
- *Macro/Megalecithal:* Enormous amount of yolk is present. **E.g.** Reptiles and Birds.

According to the distribution of the Yolk within the cytoplasm of eggs

- *Isolecithal:* The amount of yolk is small and scattered fairly and evely throughout the cytoplasm. **E.g** Amphioxus.
- *Telolecithal:* The distribution of yolk is unequal. It is collected more at lower part (Vegetal pole) than at the upper part (Animal pole). **E.g.** Amphibians.
- *Centrolecithal:* The amount of yolk is large and it is concentrated in the center of eggs. **E.g.** Insects.
- *Discoidal:* The amount of yolk is enormous and occupies the major portion except a small disc shaped area of cytoplasm called the Blastodisc. The blastodisc is found at the top of the yolk mass. **E.g.** Reptiles and Birds.



According to the presence/absence of shell

- *Cleidoic (box-like):* These eggs are laid on dry land, self contained, fully laden with yolk and surrounded by albumin and a waterproof shell. **E.g** Reptiles and Birds.
- *Non-cleidoic:* These eggs are laid in water and are not protected by the shell. **E.g.** Amphibians.

According to the type of development

- *Determinate/Mosaic eggs:* In the development of certain animals, the fate of each and every part of the egg is fixed before or at the time of fertilization. If a particular portion of the egg is removed, the developing embryo will be deficient in particular organ. **E.g.** Annelids and Arthropods.
- *Indeterminate/ Regulative eggs:* In this type, there is no predetermination and the fate of various parts of eggs is usually not fixed until the cleavage divisions (8-cell stage) completed. So at this stage if any of the blastomeres (the cells resulting form cleavage) are separated, each blastomere can develop as a whole embroyo. The ability of the balastomere to develop into a whole embryo is known as Totipotency. **E.g.** Chordates and Echinoderms.

POLARITY OF EGG

- The egg consists of two poles namely animal and vegetal pole.
- The animal pole is the one where the nucleus of the egg lies.
- The opposite pole, where the yolk is accumulated is called the vegetal pole. This type of arrangement is seen in amphibians, reptiles, and birds.
- In domestic animals and man, the nucleus is at the center of the egg and the animal pole refers to the pole where the polar bodies are accumulated.

MEMBRANES OF OVUM

- Like any other cell ovum also has a membrane – *oolemma*, inside which the cytoplasm, nucleus, yolk and other organelles are situated. In addition to the oolemma, the other egg membranes also surround the ova. The egg membranes surrounded the ovum itself are called the primary egg membranes. They are
    - *Vitelline membrane:* It is the primary egg membrane of amphioxus, amphibian and birds. Initially they are very closely applied to the surface of the oolemma. But at the later stage, a space filled with fluid may appear between the oolemma and vitelline membrane and is known as *perivitelline space*. The vitelline membrane contains mucopolysaccharides and certain fibrous proteins. Its envelope is essential for species-specific binding of sperms.
    - *Zona pellucida:* It is the primary egg membrane of mammal, which is a clear, non-cellular membrane situated outside the oolemma of the mammalian ovum.
    - The mammalian egg also surrounded by several layers of cells called the cumulus cells. These represent the ovarian follicular cells and are actively involved in the transfer of yolk constituents to the ovum. The mammalian sperm has to pass through these cells to fertilize the egg.
    - The egg membranes secreted by the follicular cells of the ovary are called secondary egg membranes. **E.g.** Corona radiata – the layer of cumulus cells immediately outside the zona pellucida of the mammalian ovum.
    - The egg membranes secreted by the glands of oviduct and uterus are called tertiary egg membranes. **E.g.** Albumen and shell membranes in birds.

OVULATION

- The process of release of ovum from the follicles in the ovary is called ovulation.
- On the surface of the ovary the matured graaffian follicles looks like blisters and continues to swell and finally it ruptures at one point of swelling to release the ova along with the corona radiata cells.
- The released ova are picked up by the ciliary movements of the fimbriated end of the oviduct and are carried to the site of fertilization.
- Commonly there is a seasonal period during which ovulation occurs.
- The ovulation occurs during estrus in all domestic animals except cow where it occurs 12 hours after the end of estrus.

TYPES OF OVULATION

- *Spontaneous ovulation:* No stimulus is required for ovary. The mating acts as stimulus. Hence the ovulation is independent of mating. **E.g.** All domestic animals & man.
- *Induced ovulation:* Stimulus is a must for ovulation. Mating stimulates the release of Leutinizing Hormore (LH) which inturn brings the ovulation. **E.g.** cat, rat, rabbit and mink.

TYPES OF OVULATORS

- Based on the side of the ovary which ovulates in mammals are classified as
    - Left ovulators – Swine, Mare and Chicken.
    - Right ovulators – Cow and Sheep.
    - Both side ovulators – Owl, Hawk and Women.

MECHANISM OF OVULATION

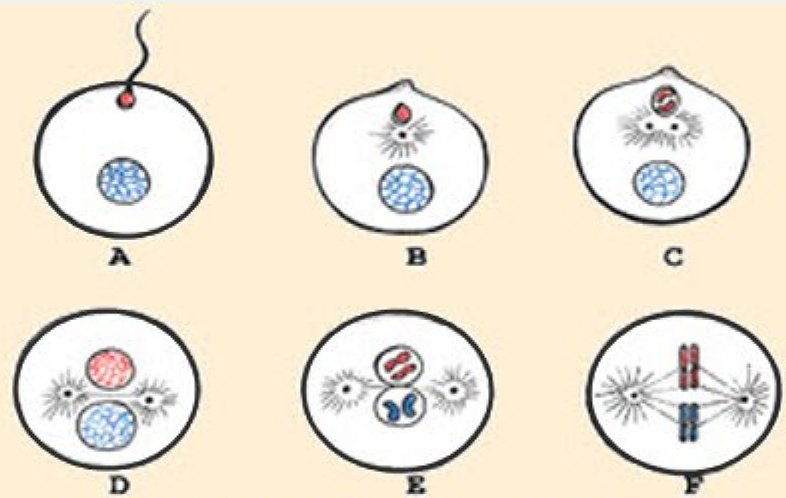
- As the follicle matures it bulges from the surface of the ovary. At the apex of the follicle an avascular spot appears and it is called stigma.
- The follicle ruptures at the stigma and the liquor folliculi is liberated carrying with it the ovum and the discus proligerous.

Theories of ovulation

- *Pressure theory:* As the follicle matures, the follicular fluid increases in quantity and the pressure brings about the rupture of the follicle. This theory is not accepted in cow, ewe and sow where at the time of ovulation the follicle will be flabby but still ovulation occurs.
- *Massage theory:* The follicle ruptures by massage action, which lacks proof.
- *Hormonal theory:* The ovulation takes place by the influence of hormones and is the most accepted theory.

FERTILIZATION

- The sperm can enter the ovum at any point on its circumference. In many mammals, entire sperm is known to pass into the cytoplasm of the ovum. After the entry of the sperm, the second polar body is extruded and the chromosomes, which remain in the ovum, reconstitute themselves into a vesicular nucleus, the female pronucleus. The vitellus shrinks so that a distinct perivitelline space is present.
- The head of the sperm undergoes changes after it enters the ovum. It swells up and becomes transformed into the male pronucleus. The middle piece and the tail persist for sometime and later disappear and are probably absorbed into the cytoplasm of the ovum.
- After the head of the sperm becomes detached from the middle piece and tail, it probably rotates through 180 ° and the two pronuclei meet roughly in the center of the ovum.
- A centrosome, which is possibly derived from the proximal centriole of the sperm, now becomes distinct. It divides into two parts, each of which is attached to a pole of the spindle, which now makes its appearance. At the same time, each pronucleus resolves itself into chromosomes and the nuclear membranes disappear. The chromosomes of both pronuclei arrange themselves on the spindle and each splits into halves passing towards the chromosomes.
- The polar bodies persist for a variable time in the perivitelline space but later they degenerate and disappear.



Stages of the events in fertilization

The chromatin of the ovum is colored blue, that of the spermatozoa red.

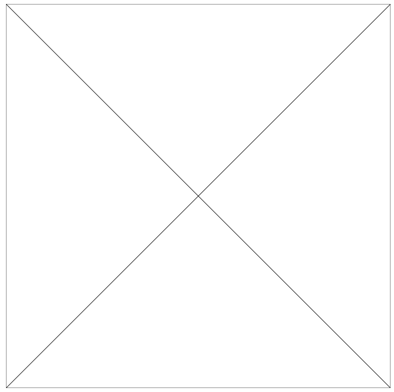
MODULE-28: CLEAVAGE AND GASTRULATION

Learning outcomes

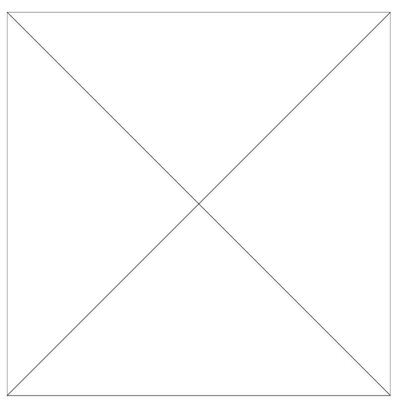
- At the end of this module the learner will be able to know about
  - cleavage in chick,
  - cleavage in amphioxus,
  - cleavage in mammal,
  - gastrulation in amphioxus,
  - gastrulation in chick and
  - gastrulation in mammals.

CLEAVAGE

- The fertilized ovum enters on a series of cell division. The initial period, the development of a new multicellular individual is called the cleavage period. The process of cellular division without growth is called cleavage. During the period, the zygote split up into a number of smaller cells called the blastomeres. The mitotic division tends typically to follow the doubling sequence, 2, 4, 8, 16 etc. The total mass of living substance does not increase appreciably when the cleavage comes to an end.



- It is the active protoplasm of the egg that accomplishes the division and the inert stored yolk retards mitosis. In this way the relative amount of yolk and its even or uneven distribution throughout the egg, influence on cleavage. On this basis, the cleavage is classified as follows:
    - Total Holoblastic cleavage: Entire ovum divides
        - *Equal:* In isolecithal ova (evenly distributed yolk) blastomeres are of approximately equal size. **Eg.** Amphioxus, marsupial and placental mammals.
        - *Unequal:* In moderately telolecithal ova (uneven distribution of yolk) accumulated at the vegetal pole retards mitosis and fewer but larger blastomeres form there. **Eg.**Lower fishes and amphibians.
    - Partial Meroblastic cleavage: Protoplasmic region alone cleaves.
        - *Discoidal**:*** In higly telolecithal ova, mitosis is restricted to the animal pole. **Eg.** Higher fishes, reptiles, birds and monotreme mammals.
        - *Superficial:* In centrolecithal ova (the yolk substance is accumulated in the centre and protoplasmic mass located peripherally), the mitosis is restricted to the peripheral cytoplasmic investment. **Eg.** Arthropods.
- All the animals under the phylum chordate have certain similarities in their early development. It is therefore necessary to compare the rarely stages of development, in Amphioxus (a lower chordate), Chick and Mammal for gaining a broad understanding of the subject.



CLEAVAGE IN CHICK

- The egg is large and highly telolecithal and the cleavage is of meroblastic type (partial and discoidal). The protoplasm is located as a cap over the huge yolk mass and is involved in the cleavage. The large yolk never divides.
- The first 2 planes of division are vertical furrows which cross at right angles. Succeeding furrows pass first radial and then in circumferential planes and the original disc of cytoplasm is transformed into a mosaic of separate cells. Following this stage, cleavage divisions take place in a horizontal plane to produce a certain amount of layering.
- The end result, after one day, is a discoidal plate of cells perched on a surface of the yolk and separated from it by a cleft. At the periphery, the cellular disc progressively gains new cells from a proliferating, syncytial margin that blends into the yolk. The cellular cap is termed as germinal disc or blastoderm. The space between the blastomeres and yolk mass is called the blastocoel. Cleavage thus produces a modified blastula corresponding to the blastula of the amphioxus.

CLEAVAGE IN AMPHIOXUS

- The egg of amphioxus is isolecithal and the cleavage is of holoblastic type. About one hour after fertilization, the egg is divided into 2 blastomeres.
- The plane of this first cleavage is passing through the egg axis from pole to pole.
- Next, the cleavage is in a vertical plane, but at right angles to the first plane.
- In the third series of division, the planes of separation are horizontal. By the 16 to 32-cell stage, the cells are crowded together into a compact mass within the zona pellucida. The embryo is now known as *morula*.
- Soon the balstomeres arrange themselves in a circular manner forming a blastula around a central space, the blastocoel. This marks the end of the cleavage period.

CLEAVAGE IN MAMMALS

- The egg of all marsupial and placental mammals are isolecithal and the cleavage is of holoblastic type and takes place within the zona pellucida of the ovum.
- The first two planes are vertical and third is horizontal.
- The darker blastomeres with slower cleavage are destined to become the embryo proper whereas the clear cells with rapid cleavage differentiate into auxillary tissue known as the Trophoblast.
- At about 16 cell stage, the future trophoblast cells begin to flatten against the zona pellucida and produce a kind of cellular capsule.
- By the time some thirty cells have formed, the definite hollow sac known as blastocyst. The cells destined to become embryo proper, constitute the inner cell mass attached to the trophoblast at one end.

GASTRULATION

- Gastrulation is the process through which the three ***primary germ layers- ectoderm, mesoderm*** *and* ***endoderm*** are ultimately segregated. The blastula possesses polarity, and bilateral symmetry.
- It contains predetermined cell area, which would become the future ectoderm, mesoderm, endoderm, notochord and the neural plate.

GASTRULATION IN AMPHIOXUS

- The animal pole of the blastula corresponds roughly to the front end of the future embryo. The animal and vegetal poles are the future ectoderm and endoderm respectively. In between, is a girdling zone, which is subdivided into prospective mesoderm, notochord and neural plate.
- Invagination of vegetal cells is followed by involution of cells, around the margin of the double walled cup, thus being formed. The continuation of these movements carries endoderm, mesoderm and notochord to the interior and obliterates the original *blastocoel*.
- The central cavity now formed is *archenteron* and its mouth at the vegetal pole is *blastopore*. At this period, the young embryo is termed a *gasturla*.
- The margin around which involution took place is the lip of the blastopore. Backward growth of this lip-region, lengthens the embryo and upward growth of the ventral lip elevates the blastopore, thus tilting up the mesodermal portion.
- Now, the roof of the archenteron consists of a median strip of notochordal cells, flanked on each side by a strip of mesodermal cells (which were tilted up by the elevation of the ventral lip of the blastopore). The entoderm then closes the dorsal defect caused by the loss of notochord and other mesoderm and thus produces the definitive, tubular gut.
- The cells left on the external face on the gastrula form the ectoderm. Dorsally they constitute the neural plate while the rest of the area forms the general covering of the embryo, which will become epidermis.

GASTRULATION IN CHICK

- Gastrulation is confined to the blastoderm, which contains the cells of all the three future germ layers. The process, as a whole, is accomplished in two stages.
- The gastrula is formed by a process involution of the blastoderm. The caudal part of blastoderm rolls and tucks itself under the blastodermal cells. It divides until a new inner layer, the endoderm and an outer layer, the ectoderm are formed. The region where the ectoderm and endoderm meet represent dorsal lip of the blastopore of amphioxus. The space between the endoderm and the yolk is the *archenteron*.
- At the end of gastrulation a median band appear posteriorly on the surface of the blastoderm. It is a linear thickening of ectoderm and acquires an anterior knob called *primitive knot*. The thickening is called as the *primitive streak* which encloses a primitive groove and close to the primitive knot the primitive pit.
- The major function of the primitive streak is the formation of the third germ layer, the mesoderm. The adjacent cells on the surface of the blastoderm move medially enter the primitive streak and leave it as mesodermal cells.
- Soon the germinal disc is comprised of an outer ectoderm and an inner endoderm and the mesoderm, which is between the ectoderm and endoderm. Due to the migration of cells from the primitive streak on both the sides, a middle pole like invagination occurs on the median line of the streak, giving rise to the primitive groove folded by the primitive folds. From the primitive knot, a column of cells arise from the head process which becomes the notochord.

GASTRULATION IN MAMMALS

- The inner cell mass delaminates into an inner layer of ectoderm. The endoderm forms the roof of the yolk sac and the two layers together are spoken as embryonic disc.
- The primitive streak appears caudally on the upper face of the disc and proliferation of the cells in this area produces the cells of the mesoderm, which spread out in all directions between the other two germ layers. This forms the middle germ layer or mesoderm and this differentiates into the axial cord, the notochord and two lateral sheets.
- The sheets split tangentially into two layers, the somatic and splanchnic layers to enclose the coelom or body cavity. The ectoderm and the somatic mesoderm together is

the *somatopleurae* or body wall and endoderm and the splanchnic mesoderm is the *splanchnopleurae* or gut wall.

MODULE-29: FOETAL MEMBRANES

Learning outcomes

- At the end of this module the learner will be able to know about
    - foetal membranes in chick,
    - placentation in higher mammals,
    - placenta,
    - classification of placenta,
    - stages in prenatal period and
    - twins and twinning.

FOETAL MEMBERANES

- In the development of a higher vertebrate embryos like those of chick and mammals, only part of the cleavage cell mass forms the actual embryo, whereas other parts lie outside the embryonic territory and are called extra embryonic.
- The extra embryonic parts form *foetal membranes*, which are the auxiliary organs to protect the embryo and provide for its nutrition and excretion. All these membranes eventually are discarded.
- The placenta is a distinctive membrane that is developed only in higher mammals (placentalia) chiefly from the chorion, allantois and the uterine lining. The umbilical cord connects the foetus and its placenta.

FOETAL MEMBRANES IN CHICK

- The blastoderm, originally a small disc soon spreads by peripheral growth and covers the entire egg surface. But only the most central, is directly concerned in the formation of fissures all round. The extra embryonic blastoderm furnishes the foetal membranes. The blastoderm consists of somatopleurae and splanchnopleurae separated by a coelom.
- Yolk Sac
    - As the embryo enlarges, its circular connection with the extra embryonic blastoderm grows at a slower rate. This produces an apparent constriction of the splanchnopleurae that unites the rapidly elongating gut with the yolk sac.
    - The region of constriction soon lengthens into tubular yolk stalk and the yolk overlaid and enveloped by the extra embryonic splanchnopleurae constitutes the yolk sac.
    - The vitelline blood vessels arising in the splanchnic mesodermal wall ramify on the surface of the yolk sac, and through them yolk substance is absorbed and conveyed to the embryo during the incubation period. Shortly before hatching, the shrunken yolk sac slips through the naval into the body cavity.
    - The yolk sac is a very important structure in the chick as it supplies the yolk necessary for the development of the chick till it hatches. In mammals, it is vestigeal but is important as the earliest organ in which angioblasts first make their appearance.

- Amnion and chorion

    - These two foetal membranes are synchronous in development. They are concentric layers, which arise by folding of the extra embryonic somatopleures. The earliest fold to appear is the head fold located in front of the head of the embryo. The second is the tail fold just behind the embryo.
    - As these crescentic folds arch higher and higher and draw over the embryo like hoods, their lateral extensions also unite in lateral folds which flank the embryo on the sides gradually to complete a circular fold which closes in, from all sides as a purse is closed by drawing its strings.
    - The final stage is brought about by fusion of similar parts of the somatopleurae ectoderm with ectoderm and mesoderm with mesoderm, the result being production of two completely separate compound membranes an inner amnion of ectoderm internally and mesoderm externally and an outer chorion of ectoderm externally and mesoderm internally.
    - The amniotic sac contains fluid within which the embryo is suspended. The embryo is thus protected from drying and is able to maintain its shape free from distortion and muscle fibres developing in the mesodermal layer produce rhythmic contractions, which agitate the embryo gently and prevent adhesions. The chorion lies next to the shell membrane enclosing the other layers and is separated from them by the extra – embryonic coelom.
- Allantois
    - This is a temporary sac for storage of urine of the foetus. It arises as an outgrowth of the ventral part of the hind gut and its wall is made up of an external layer of splanchnic mesoderm and internal layer of entoderm. It soon grows into the extra – embryonic coelom and is connected to the hind gut by the allantoic stalk.
    - It completely fills up the extra embryonic coelom and lines the entire shell. Fusion of the outer wall of the sac with the overlying chorion produces a common membrane in contact with the porous shell. Blood vessels ramify in this common mesodermal layer – allantochorion constituting the respiratory organ for exchange of gases.

PLACENTATION IN HIGHER MAMMALS

- Placentation includes the events of implantation and development of placenta.
- *Implantation:* At the 8 to 16-cell stage, the embryo has reached the uterus in about 2 to 51/2 days in most species of mammals. However, the pig embryo enters the uterus relatively in the 4-celled stage, while in the bitch; the time taken is 6 to 8 days.
- The blastocyst – enlarges and fills up the uterine lumen. Zona pellucida is shed and the free-living embryo is nourished by uterine secretion. The embryo is said to be implanted when it is fixed in position and does not float freely in the uterine lumen. In farm mammals the attachment to the uterine wall of the blastocyst is loose prior to formation of placenta. Implantation takes place about 11 to 40 days in cow and 10 to 22 days in sheep, after coitus.

PLACENTA

- Placenta is the intimate apposition or fusion of extra embryonic membranes to the maternal tissue for the physiological processes of respiration, nutrition and excretion. In addition placenta protects the embryo.

Foetal membranes (or) Extra Embryonic membranes

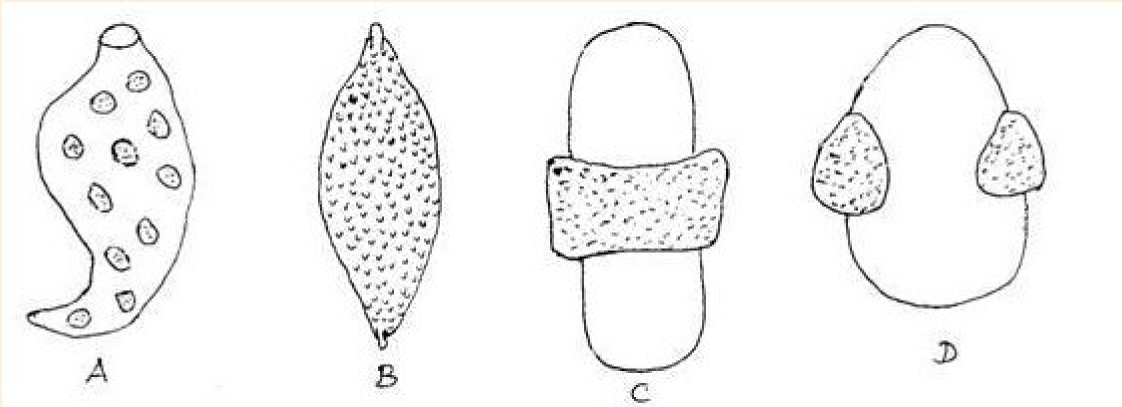
- *Yolk Sac:* The endoderm lines the inner border of the blastocyst, converting the blastocoele into the yolk sac cavity.

- *Amnion and Chorion:* The newly formed chorionic sac in the early stages encloses a large cavity – the extra embryonic coelom (exocelom) that lies between chorion and amnion. In later stages the amniotic membrane fuses with chorion in the cow, ewe and sow to form an amniochorionic membrane.
- *Allantois:* The allantois grows into the exocoelom and surrounds the amnion. During this period the yolk sac regresses. The allantois which is highly vascularised by foetal vessels, fuses with the chorion bringing foetal vessels to the periphery of chorionic sac and thus into closer apposition with the maternal tissue. This is the formation of the chorioallantoic membrane.
- The compound allantochorionic membrane together with the uterine tissue is designated as chorioallantoic placenta and is classified on the basis of its form and also the number of layers of tissue separating foetal and maternal vascular system viz., degree of placental union.
- The chorion which is beset with vascular villi that are in intimate association with the endometrium, constitutes the placenta which sub serves the functions of nutrition, respiration; excretion – and protection of the embryo.

CLASSIFICATION OF PLACENTA

- The placenta is of two varieties:
  - Deciduate: in which the foetal part of the placenta is very closely associated with the maternal part and hence part of endometrium also is shed off after parturition, e.g., man and primates;
  - Non-deciduate: in which the association between the parts is not so close and hence the maternal endometrium is not shed, e.g. all domestic mammals.
  - The non-deciduate placenta are of three types:
    - *Cotyledonary:* The chorionic villi are grouped in well marked prominent projection called cotyledons which are separated by stretches of smooth chorion and these foetal cotyledons are received into the maternal caruncles e.g., *ruminants*
    - *Diffuse:* The chorionic villi are diffusely scattered all over the chorion e.g. *mare and sow*
    - *Zonary:* The chorionic villi occupy a girdle-like band about the middle of the chorionic sac and these are received into crypts of endometrium around a circular zone which is shed off at parturition. Hence it is partly deciduate, e.g., *carnivores*.

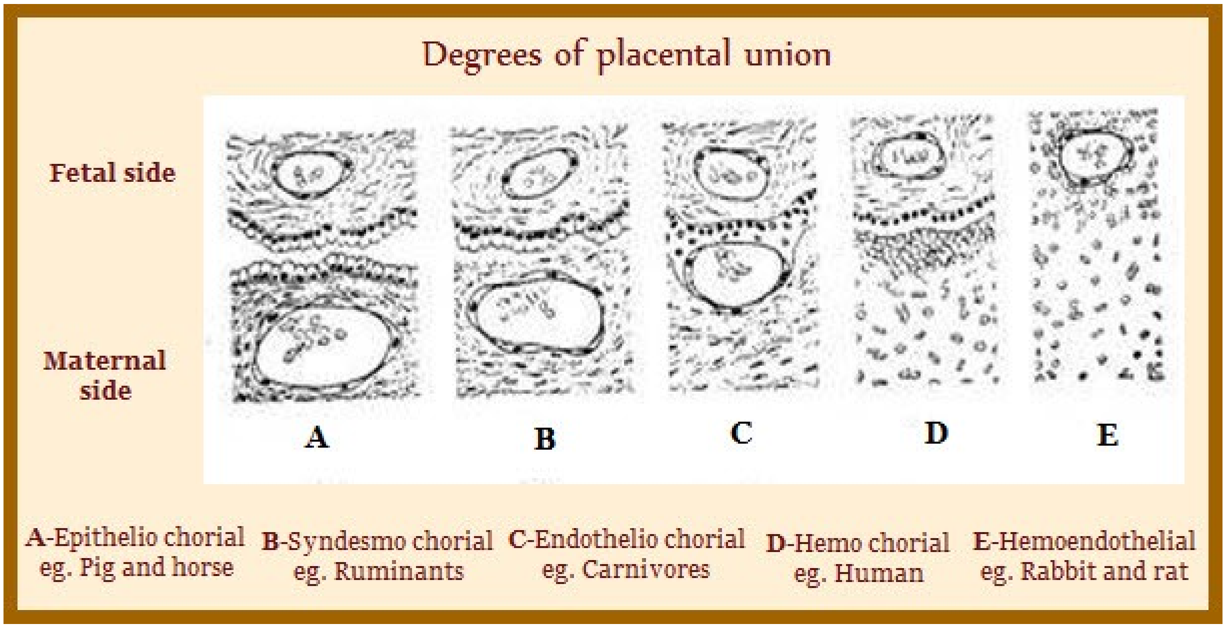
Placental types based on the distribution chorionic villi



A-Cotyledonary eg. **Ruminants** | **B-Diffuse** eg. **Pig** | **C-Zonary** eg. **Carnivores** | **D-Discoid** eg. **Monkey**

Degrees of placental union

- All mammals, above the egg laying monotremes have placenta, but the degree of development and the intimacy of placental union vary. The ascending series with the names of the different types of placental structure follows in a brief form.
    - *Temporary imperfect placenta:* (Marsupials, such as Opossum and Kangaroo) Epithelium of chorion makes short duration contact with epithelium of endometrium.
    - *Epithelio–Chorial placenta:* (non–ruminant ungulates such as horse and pig) chorionic villi occupy pits in endometrium.
    - *Syndesmochorial placenta:* (Ruminants such as cow, sheep and goat) Epithelium of endometrium destroyed in local areas. Epithelium of chorion comes into contact with connective tissue core of the endometrium.
    - *Endothelio–chorial placenta:* (carnivores such as dog and cat). Epithelium of villi in contact with endothelium of blood vessels.
    - *Haemo–chorial placenta:* (Man, monkey, and lower rodents). Endometrial blood vessels open, forming sinus of maternal blood which bathes the epithelium of the villi.
    - *Haemo endothelial placenta:* (higher rodents, such as rat, guinea pig and rabbit). Epithelium of villi is destroyed. Endothelium of chorionic capillaries bathed by maternal blood in sinus.



STAGES IN PRENATAL PERIOD

- *Period of the ovum:* In which male and female germ meet, unite and form the zygote which develops into the blastula and gastrula covering the first 14 days of intra uterine life.
- *Period of the embryo:* From end of the second week, it extends to the eighth week. Differentiation of embryonic parts is completed. Placenta is formed, embryo shows resemblance to parents.
- *Period of the fetus:* From the ninth week to the end of gestation.

TWINS AND TWINNING

- Twins are either identical twins or fraternal twins. In uniparous animals usually only one ovum is fertilized at a time. If two individuals are derived from a single fertilized egg, each member acquires the same chromosomal heritage and hence the similarity between the twins is so striking in physical, mental and other characters. They are identical, true or duplicate twins. They are always of the same sex.
- Two or more individuals, derived due to independent ripening of two or more number of ova and fertilization, have the same, degree of family resemblance, as between brothers and sisters of different ages. They can be of the same or opposite sexes. They are fraternal twins. In animals, e.g. the cow there is identical twinning.
- Also in bovines, a condition called Freemartin is recorded, which is the female fraternal twin of a male. It is sterile, as the internal genital organs are of the male type and the external genital organs are of the female type. This is caused by placental anastomosis and the influence of the male hormone which is earlier to appear in circulation.

MODULE-30: SPECIAL EMBROYOLOGY

Learning outcomes

- At the end of this module the learner will be able to know about the development of

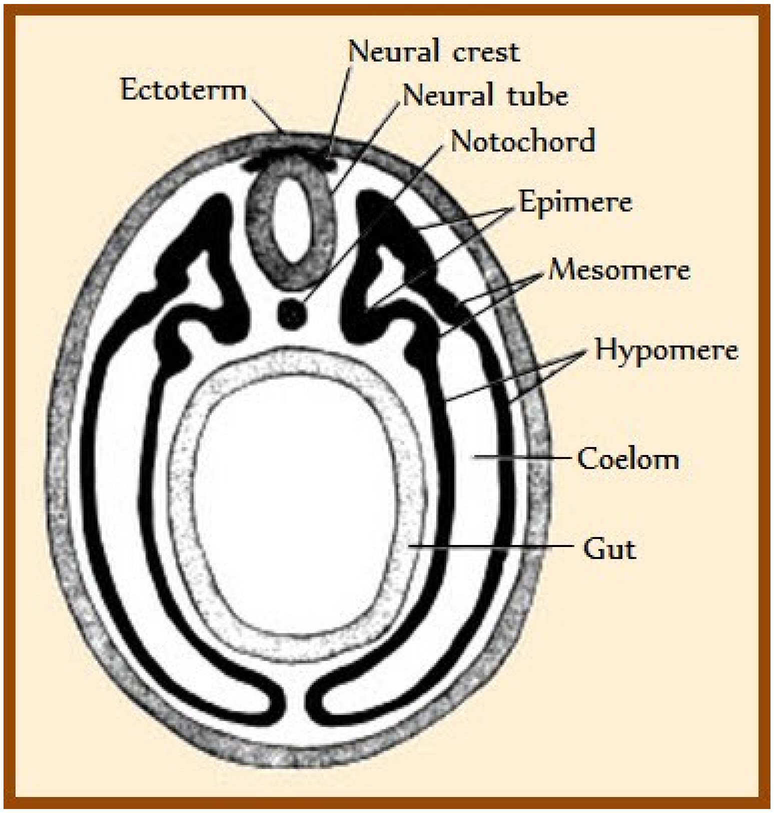
    - head region,
    - trunk and body wall,
    - branchial region,
    - pharyngeal pouches,
    - liver and heart and
    - other external features.

DEVELOPMENT OF GENERAL BODY FORM AND EARLY FEATURES

- As a result of Gastrulation, the embryonic part of the gastrula consists of a flat structure in addition to the formation of three basic germ layers. The basic body pattern in adult vertebrate is found to have one tube within another, the outer being synonymous with the body wall the inner being the digestive tube.
- The space between the two is the ***coelomic cavity***. Therefore, in order to achieve the adult body pattern, the early embryo must undergo developmental processes that transform it from a flat structure to a tubular one. These processes begin shortly after the first somites appear and initially take place in the future head region of the embryo.

DEVELOPMENT OF HEAD REGION

- Neural Plate and neural groove
    - The first indication of the formation of the head is a thickening of the ectoderm over the cranial end of the notochord.
    - The thickening is the precursor of the brain which is referred as *neural plate*.
    - The folds develop from neural plate fuse with one another forming the *neural tube*.
    - The neural tube differentiates into the major parts of the *brain*.



- Notochord
  - The *notochord* is a rod shaped aggregate of cells that extends along the entire length of the embryo. Although it does not form a major structure in the adult mammalian embryo, it is of great developmental significance.
  - It defines the cranial and caudal axis of the embryo and serves as the inductor for the formation of the central nervous system and head of the embryo.
  - It is located on the midline of the embryo just ventral to the developing neural tube.
  - It is an organizing center for the formation of the vertebral bodies and the basal parts of the sphenoid and occipital bones.
- Formation of Cylindrical Shape
  - The period in which the growth of the neural tube occurs, differential growth of all the layers of the embryo also occur. However, the growth of the neural ectoderm predominates.
  - The growth patterns are in such a way that the cranial end of the embryo grows up and forward so that it extends over the area just in front of the head area to fold back under the head ventrally. This folding is referred as *head fold*.
  - At the same time, there is lateral infolding of the ectoderm on each side of the embryo which also surround the underlying mesenchyme of the cranial end of the embryo. These two lateral folds fuse with one another ventrally resulting in a cylindrical outgrowth, the *head*.
  - These two morphogenic growth processes that form the head enclosing layers and structures present in the area namely, the neural plate and attached ectoderm. Between these two are the endoderm and mesenchymal cells. As a result, the head has an outer cylindrical form covered by ectoderm and an inner tube lined by endoderm. The inner tube is the future cranial part of the digestive tube called the *foregut*.

- The head once formed is elongated by the continued growth and the folding of the area, which is just in front of the primitive knot. The elongation of the head is also facilitated initially by the regression of the primitive knot caudally due to the disappearance of the primitive streak.

DEVELOPMENT OF TRUNK AND BODY WALL

- The lateral folding and ventral fusion described in the formation of the sides of the head continues caudally.
- As the lateral folding behind the head form the cylindrical shaped embryo, it partitions a part of the coelom and part of the yolksac.
- These are incorporated into the body of the embryo forming the intra-embryonic coelom and the future gut of the embryo.
- When the folds are fused ventrally and the basic body plan of the embryo is established, the somatopleurae of the folds form the body wall of the embryo.
- The splanchnopleurae of the folds form the gut and supporting mesentries.
- A tail fold is formed in a manner similar to that of head. The resulting endoderm lined cavity in the tail area is the *hindgut*. The gut between the hindgut and the *foregut* is referred as *midgut***.**
- With the completion of the body wall along the entire length of the embryo, the basic hollow cylindrical tube within a tube, the body pattern is complete.

DEVELOPMENT OF BRANCHIAL REGION

- Another early feature that is distinct in the head region involves the mesenchymal structure around the cranial most part of the foregut. Around this area of the foregut, the mesenchyme aggregates and proliferates to form five pairs of arch like structures lateral and ventral to the foregut.
- The part of the foregut that is bounded by these arches will be the pharynx of the embryo and adult and the arches are called ***branchial arches***.
- There are grooves between the consecutive branchial arches that are apposed to the pharyngeal pouches, called the branchial grooves.
- In these grooves, the ectoderm is in close association with the endoderm of the pouches. Thus between each pair of arches, there is a thin membrane consisting of endoderm and ectoderm with only a negligible amount of mesoderm between them.
- The mesenchyme in each of the branchial arches forms the specific components of the musculo skeletal system of head, especially of the face.

DEVELOPMENT OF PHARYNGEAL POUCHES

- The forming branchial arches encroach on the wall of the pharynx. Lateral outpouchings of the pharyngeal endoderm are formed between the branchial arches as the foregut in the pharyngeal region is compressed dorsoventrally. These are called ***pharyngeal pouches.***
- Each pharyngeal pouch has specific derivatives.

DEVELOPMENT OF LIVER AND HEART

- The liver and heart are the largest structures in the early embryo and form a distinctive bulge that can be seen externally.

OTHER EXTERNAL FEATURES

Flexures

- A series of three differential growth centers develop that result in several flexures along the axis of the embryo soon after the branchial arches begin to form. These flexures transform the embryos from a linear structure to 'C' shaped structure.
- The first flexure occurs in the area of midbrain, the second flexure occurs in the future neck region and the final flexure occurs in the tail region.

Limb buds

- Limb buds also appear at an early stage, which are the primordial for the future limbs. These are the mesodermal outgrowths from the body that are covered by the ectoderm of the region.

FATE OF BRANCHIAL ARCHES

- The *branchial arches* are bar like ridges separated by grooves which appear on the lateral surface of the embryonic head. Usually there are five pairs of branchial arches develop which are separated by four external ectodermal grooves, the branchial grooves. The forming branchial arches encroach on the wall of the pharynx.
- Since the endoderm of the pharynx pushes the mesenchyme subjacent to the *branchial grooves*, pharyngeal pouches are formed. The ectoderm of each groove and endoderm of the pouch meet and unite to form thin plates. Sometimes, these plates rupture forming temporary openings, reminiscent of gill slit condition in fishes. Failure of these openings to close constitutes branchial fistulae. The mesenchyme in each branchial arch forms components of musculo skeletal system of the head, especially of the face.
    - The *first branchial arch* divides into an upper *maxillary and lower mandibular* process.
        - The maxillary process undergoes degeneration and the surrounding mesoderm develops into maxilla and palatine bones.
        - The mesenchymal core (*Meckle's cartilage*) of the mandibular process becomes enveloped by surrounding mesenchyme and is transformed into spheno-mandibular ligament, malleus and incus.
    - The mesoderm of *II branchial arch (Reichert's cartilage*) contributes to the stapes, styloid process of the temporal bone and small cornua of the hyoid.
    - The cartilage of the *III arch* forms the styloid cornua and the body of the hyoid.
    - The *IV arch* differentiates into epiglottis and thyroid cartilages of the larynx.
    - The *V branchial arch* furnishes the cricoid and arytenoids cartilages of larynx.

MODULE-31: DEVELOPMENT OF FACE AND SALIVARY GLANDS

Learning outcomes

- At the end of this module the learner will be able to know about the development of
    - mouth,
    - lips ang gums,
    - cheeks,

- palate and
- salivary glands.

DEVELOPMENT OF FACE

- The *stomodeum* or the primitive buccal cavity is formed by the formation of the cranial and lateral foldings and subsequent cranial flexures. It is separated from the pharyngeal cavity by the oropharyngeal membrane which breakdown following the fusion of the left and right mandibular processes. During the foetal development, the stomodeum becomes greatly elongated as a result of the growth of the maxillary, mandibular and nasal process.
- Neural crest mesenchymal cells initially located over the dorsal and rostral surfaces of the procencephalon are brought to the rostral and ventral surfaces of the head as a result of >90 ° cranial flexure. This population of cells called the *frontonasal mesenchyme*, will form the forehead and nasal regions of the face. At the early stage, the fronto nasal mesenchyme, will form the forehead and nasal regions of the face. At the early stage, the fronto nasal process represents forehead. A thickening of ectoderm on each side o this process forms the *olfactory placode (nasal placode)*.

- Each nasal placode invaginates to form the nasal pit which deepens and subsequently contacts the roof of the stomodeum. The nasal pit is circumscribed by two swellings, the *medial nasal process* and the *lateral nasal process* derived from fronto nasal mesenchyme.The area between the two medial nasal processes extending dorsally over the forebrain is the *frontal prominence*. The line of fusion of the two medial nasal process is the *philtrum***.**
- Each medial nasal process unites with the maxillary process of the respective side to form the upper jaw and cheek regions. The lateral nasal process fuse with the maxillary process closing the *oculo-nasal sulcus* and thus completing the socket. The lateral nasal processes become the sides and wings of the nose.
- The two mandibular processes unite in front to form the lower jaw. The bifurcation of maxillary and mandibular processes is reduced by the establishment of the lips and cheeks forming the *rima oris***.**

DEVELOPMENT OF MOUTH

- The first indication of the embryonic mouth is the *stomodeum* - an indentation of the ventral surface of the embryo at the level of first branchial arch.
- The stomodeum enlarges and becomes deeper. A defnite stomodeal cavity is formed at two weeks of gestation in most of the embryos. Shortly thereafter,the *oropharyngeal memberane* ruptures which allow the communication between the stomodeum and the floor of the pharynx.
- The rupture of the memberane allows structures arising from the pharynx to extend into the adjacent part of the stomodeum.
- After the rupture of the oral memberane,it is impossible to determine the exact junction of the ectoderm and endoderm in the mouth cavity.
- The terminal sulcus on the root of the tongue marked by the presence of circumvallate papillae is the only demarcation.
- The stomodeal part is lined with the ectodermal epithelium and the pharyngeal part with endodermal epithelium.

DEVELOPMENT OF LIPS AND GUMS

- The maxillary and mandibular prominences that form the jaws are originally solid masses of mesenchyme covered with the ectoderm.
- At about 3 ½ weeks, in the ectodermal epithelial lining of the mouth, a horse-shoe shaped thickened band of cells appear on each jaw.
- The band of epithelial cells begins to grow into the underlying mesenchyme thereby causing bands to become the grooves.
- Along the course of the original band, the epithelial lamina is formed because of the sufficient penetration of epithelium into the mesenchyme.
- Then the lamina splits forming a peripheral layer of tissue to form the lips (labia oris) and a medial layer of tissue to form the gums (gingiva). Thus, the grooves and the lamina are called labio-gingival groove and lateral lamina respectively.
- The space created by the labio-gingival lamina is called the vestibule.

DEVELOPMENT OF CHEEK

- The fusion of the jaws results in the formation of cheeks.
- The degree of the fusion is a factor determining the size of the opening into the oral cavity (rima oris).
- The labial and buccal muscles differentiating from the mesenchyme of the second branchial arches which migrates between the epidermal covering and mucosal lining of these parts.

DEVELOPMENT OF PALATE

- Following the fusions of the facial mesenchyme, the roof of the stomodeum is bounded by the maxillary process laterally and by the medial nasal process and fronto nasal prominence rostrally. A pair of openings from the short nasal cavities enter the roof of the stomodeum.
- The mesenchymal cells located between the nasal cavities initially form the medial nasal process and ventral aspect of the frontal prominence. These cell population aggregate in the rostral midline to form the *medial palatine process*, part of which will become the primary palate. Later, the premaxillary bone is formed within the mesenchyme. The palatine fissures mark the caudal margin of the primary palate. The mesenchyme located superficially between the nasal cavities contributes to the rostral cartilages of the snout, philtrum and median part of the upper lip.
- The oronasal cavity is partially partitioned by two vertical tissue masses, the nasal septum which projects from the roof of the cavity ventrally between the two nasal cavities. Broad mesnchymal process grows into the oronasal cavity from the maxillary processes on both the sides. These are lateral palatine processes, which unite with each other and then with nasal septum and medial palatine process. Bone appears in the anterior part of the fused lateral palatine processes forming the hard palate. Ossification fails at the posterior part, which results in soft palate. The medial palatine process forms the premaxillary portion of the upper jaw.

Anomalies

- *Cleft palate* – Failure of fusion of lateral palatine process.

DEVELOPMENT OF SALIVARY GLANDS

- The salivary glands are ectodermal in origin. The primodium arises as epithelial bud from the respective location of the salivary gland, which grows into a branched duct system. The end of these ducts twigs round into spherical masses of cells, which form the secretary acini.
- Canalisation of the ducts through the disintegration of the central cells and the specialization of acinar cells complete the epithelial differentiation. The mesenchyme, in which the primordium lies furnishes the capsule, interlobular connective tissue and vessels of the gland.
- Parotid salivary gland
    - The primordium of the parotid gland first appears at the angle of the mouth. This grows away from the labial grooves, elongates itself from the parent epithelium and forms a tube. The tube grows away backward towards the region of the ear and develops into the body of the gland. The stream of the tube becomes the parotid duct.
- Mandibular and sublingual salivary glands
    - The primordia for both the glands are in the labio-gingival groove between the lower jaw and tongue on either side on the floor of the buccal cavity. The difference in the development of sublingual gland is that the epithelial furrow giving rise to this gland is just lateral to that forming the mandibular gland.
    - The ducts of the two glands are located along the sides of one another. They either open together through a common opening or adjacent to each other under the tongue, near the attachment of the franulum. In those cases where these ducts of the two glands have a common opening, the rostral ends of the respective primordial grooves have fused or overgrown one another during development.
- Zygomatic gland
    - In carnivores, several ectodermal epithelial cards form from the labio-gingival lamina just caudal to the origin of the parotid gland. The glandular elements of these form the zygomatic gland in carnivores.

MODULE-32: DEVELOPMENT OF NERVOUS SYSTEM, TEETH AND TONGUE

Learning outcomes

- At the end of this module the learner will be able to know about the development of
    - peripheral nervous system,
    - pituitary gland,
    - teeth,
    - tongue and
    - pharyngeal pouches.

DEVELOPMENT OF NERVOUS SYSTEM

- The primordium of the nervous system is one of the first structures to appear in the embryo. A thickening of the dorsal ectoderm called neural plate develops first along the mid dorsal line of the embryo. By unequal growth the neural plate is folded into a neural groove bounded by neural fold.
- The groove deepens and the folds meet above thus forming a neural tube. At this point of formation of a neural tube, some of the neural plate cells escape into the space between the neural tube and surface ectoderm.
- The escaped cells form two ridges parallel to the dorsal half of the neural tube called neural crest.

Central Nervous System

- The cranial end of the neural tube presents two constrictions separating three brain vesicles. An expansion at the most rostral end of the neural tube forms the *prosencephalon*. An evagination growing outwards from each side of the prosencephalon is the optic vesicles. Caudal to this, two enlarged regions are formed, the *mesencephalon* and *rhombencephalon*.
- The rostral end of the neural tube begins to expand bilaterally marking the division of prosencephalon into *telencephalon* and *diencephalons*. The paired telencephalic vesicles will develop into the cerebral hemispheres. The diencephalons is located in the midline and connected to the expanding optic vesicles. The thalamus, hypothalamus and neural component of pituitary gland develop in this part of the brain.
- The *rhombencephalon* divides into *rostral metencephalon* and *caudal myelencephalon*. The metencephalon gives rise to cerebellum dorsally and pons ventrally. The myclencephalon forms the medulla oblongata. The rest of the neural tube develops as spinal cord.
- Within each telencephalic vesicle lateral ventricles are formed. The third ventricle is developed in the diencephalons. The cavity of the midbrain vesicle remains as cerebral aqueduct. The lumen of the rest of the neural tube forms the central canal of the spinal cord.

DEVELOPMENT OF PERIPHERAL NERVOUS SYSTEM

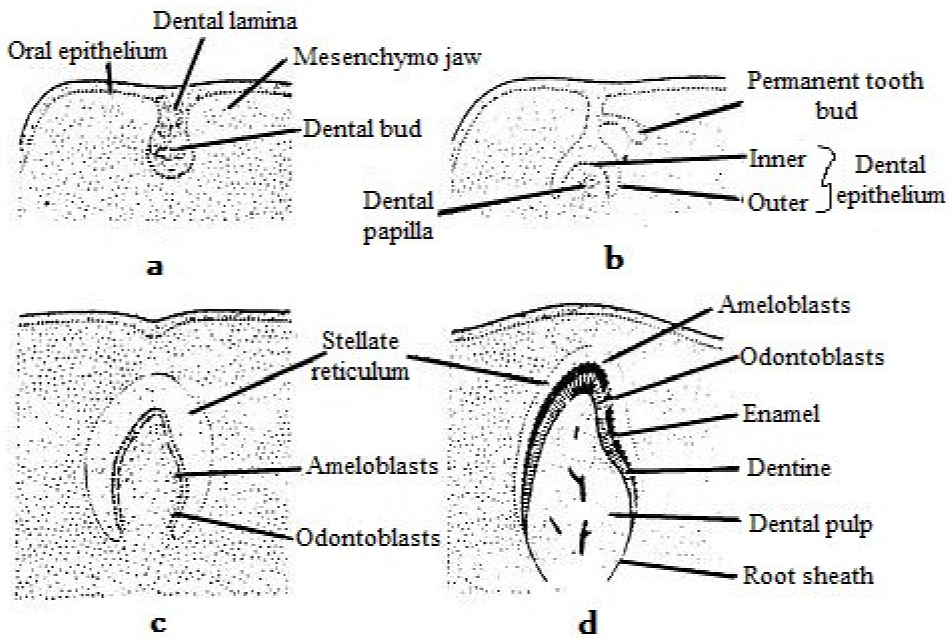
- The neural crest cells form the ganglionic elements and supporting structures of the peripheral nervous system.
- The neural crest cells migrate from the dorsal midline. Some of the crest cells aggregate dorsolateral to the aorta forming sympathetic trunk ganglia. Other crest cells continue to migrate ventrally to form abdominal sympathetic ganglia.
- The crest cells also form the spinal ganglia and parasympathetic ganglia.
- The afferent and efferent fibres of the cerebro spinal and autonomic series are formed from neuroblasts located in the neural crest.

DEVELOPMENT OF PITUITARY GLAND

- The hypophysis cerbri or pituitary gland is an ectodermal derivative and an endocrine gland of double orgin. One part glandular in nature is derived from the epithelium of the stomodeum while the other not so plainly secretory is a specialized extension from the brain.
- A dorsal evagination the *Rathke's pouch* from the roof of the buccal cavity just in front of the oral membrane forms the epithelial part of the gland. The pouch elongates and the stalk degenerates. The pouch enlarges and embraces the infundibulum, an invagination from the floor of the forebrain vesicle. The infundibulum forms the non-epithelial part of the gland.
- At about four months, the cranial wall of the pouch thickens greatly and differentiates into pars anterior and the caudal wall remains thin and forms pars intermedia. Very early in development, a pair of buds detaches from the pouch and encircles the infundibulum and forms pars tuberalis.
- The original lumen of the Rathke's pouch becomes reduced t the oblique cleft between the pars anterior and pars intermedia in the adult and is filled with a glairy fluid. The tubular primordium of the neural lobe is transformed into a solid structure composed of nerve fibres neuroglial tissue and certain spindle shaped cells and this forms the pars nervosa of the gland.

DEVELOPMENT OF TEETH

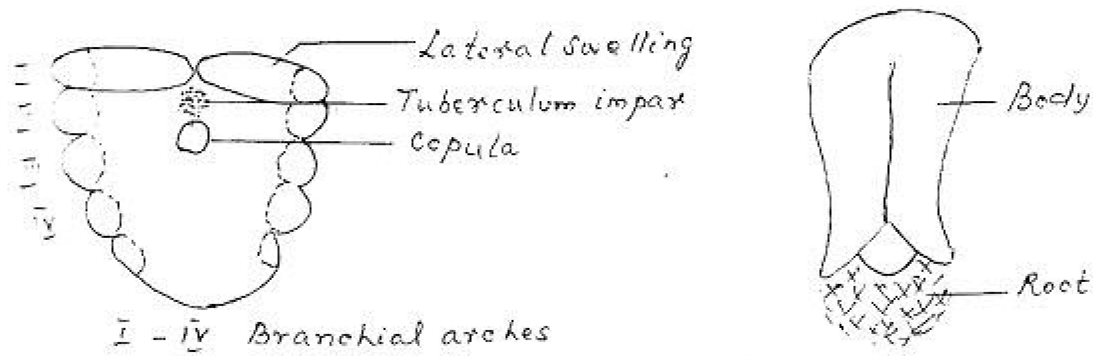
- Teeth are derived from both ectoderm and mesoderm. A tooth is a highly modified connective tissue papilla that has undergone a peculiar ossification into dentine and caged by hard enamel elaborated from the epidermis. In addition the cement a bony deposit encrusts the base. The enamel is from ectoderm arid the dentine pulp and cement are from mesoderm.
- The earliest indication of the development of teeth is the appearance of a dental groove on the surface of the gum about the seventh week of the embryo. From this groove a lamina the dental lamina projects from the bottom of the groove into the underlying mesoderm.
- From this lamina a series of knob like thickenings – the enamel organs appear at definite intervals as many in numbers as there are milk teeth. In the third month the underlying mesoderm forms a dense papilla the dental papilla and this meets the enamel organ, which forms a cup shaped covering over the papilla. The rudiment of a future tooth is thus said.
- The enamel organ gradually becomes a double walled sac composed of an outer convex wall and inner cancave wall enclosing in between a stellate reticulum the enamel pulp. The walls are made up of columnar cells and the cells of inner layer afre taller and constitute the *ameloblasts* which produce the *enamel* at their free surfaces.
- The cells of the outer wall form the circular covering of the unworn tooth the enamel substances arise as a circular scretion from the ends of the *ameloblasts*. Classification of the '*Tomes Process'* is secondary and this completes the formation of enamel prisms.
- At the end of the fourth month the superficial cells of the dental papilla arrange themselves in a definite layer that stimulates columnar epithelium. These specialized connective tissue cells are called "*odonto-blasts*" which deposit their exoplasm on their free surface a dentine and withdraw themselves into the underlying mesoderm. As they withdraw they leave a process of cytoplasm the dentinal fibre in the midst of the column of exoplasm. Calcium salts are deposited around these processes in the dentinal tubules. Thus dentine is formed. The odontoblasts continuously from the dentine and skin deeper into the dental papilla which becomes a very narrow structure and which persists as the dental pulp occupying the root canal of the tooth.
- The mesoderm surrounding the root of the developing tooth becomes condensed and highly vascular to form the dental sac. The elements of the dental sac are *cementoblasts,* which deposit their exoplasm in the form of a uniform matrix and this gets ossified by deposition of calcium salts. These cells occupy the lacunae and canaliculi in this ossified matrix.
- The tooth thus formed erupts on the gum. The cuticular membrane of *Nasmyth* covers its crown, which is the persisting outer layer of the enamel organ. The temporary tooth is connected to the dental lamina by an epithelial sheath from which the permanent tooth grows in much the same way and pushes the temporary tooth out of its alveolus and at the same time, giant cells absorb the root of the temporary tooth.



Schematic representation of the formation of the tooth at successive stages of development
a) At 8 weeks b) 10 weeks c) 3 months and d) 6 months

DEVELOPMENT OF TONGUE

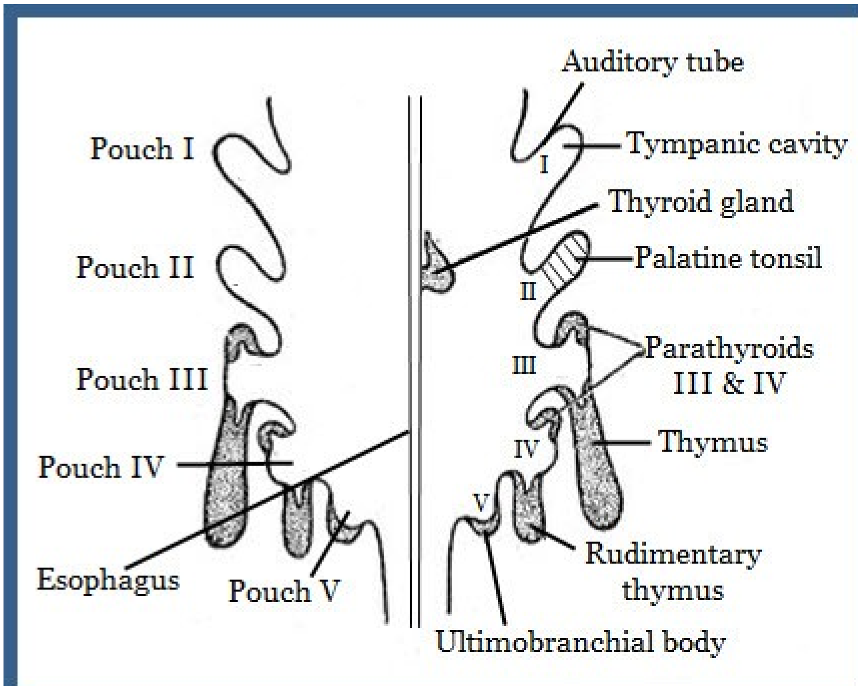
- The tongue develops from the ventral ends of the branchial arches. It consists of two parts oral and pharyngeal.
- The oral part is the body occupying the mouth cavity and arises from the mandibular arches in front of the oral membrane and hence is covered by ectodermal epithelium. It bears papillae and is concerned with mastication.
- The pharyngeal part is the root, which develops from the second, third and fourth – arches and is covered by endodermal epithelium. It is concerned with swallowing.
- The junction between ectoderm and endoderm is in front of the row of vallate pupillae whereas the body and root are demarcated by a V-shaped terminal sulcus behind them.
- The body arises from three primodia – a median triangular *tuberculum impar* and a pair of lateral swellings from the first arch. At the same time the root arises from a median primordium – *copula* from the union of the base of second arches. Copula is encroached by the third and fourth arches.
- Anomalies
  - Bifid tongue
  - Trifid tongue



Development of Tongue

DEVELOPMENT OF PHARYNGEAL POUCHES

- The lateral walls of the pharynx present a series of paired sacculations that bulge outward towards the ectodermal grooves. Five sets are formed but the last pair is rudimentary and merges in the fourth pair. Each pouch develops a dorsal and ventral wing.
- Each pouch in its outward expansion, pushes aside the mesenchyme, comes in contact with the overlying ectoderm fuses with it and forms a closing plate.
    - The first and second pouches open into a broad lateral expansion of the pharynx. The third and fourth grow outwards and communicate with the pharynx through narrow ducts.
    - The first pharyngeal pouch retains its lumen and differentiates into the eustachian tube and the tympanic cavity of the middle ear. The overlying ectodermal groove forms the external acoustic meatus and the drum of the ear.
    - The second pouch is greatly reduced and becomes the fossa and covering epithelium of palatine tonsil.
    - The third, fourth and fifth pouches lose all traces of lumen and give rise to the ductless glands thyroid thymus and parathyroid.



Pharyngeal pouches

MODULE-33: DEVELOPMENT OF DIGESTIVE SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about the development of
  - esophagus,
  - monogastric stomach,
  - ruminant stomach,
  - intestine,
  - liver,
  - pancreas and
  - spleen.

DEVELOPMENT OF DIGESTIVE SYSTEM

- The digestive tube consists of an internal tube of endoderm which is the primary tissue that becomes the epithelial lining and an investing layer of splanchnic mesoderm that specializes into the connective tissue, muscle and peritoneum.
- The primitive gut is made up of three portions, the foregut, midgut and hindgut.
- The cranial part of the foregut forms the oesophagus and the caudal part of the foregut forms the descending duodenum.
- The midgut develops into ascending duodenum, jejunum, ileum, caecum, ascending and transverse colon.
- The hindgut differentiates into decending colon and rectum.

DEVELOPMENT OF ESOPHAGUS

- From the foregut, just behind the pharynx, the oesophagus develops which maintains its tubular shape throughout the life.
- The musculature in the oesophagus is comprised of smooth muscle that comes from splanchnopleurae of the foregut.
- The distribution of skeletal muscle may be from mesenchyme present in the area of bronchial arches (I – VI) and migrates to the nearby foregut wall.

DEVELOPMENT OF MONOGASTRIC STOMACH

- The 1^{st} indication of the stomach appears as dilation in the foregut. The dilation enlarges but is not uniform and most of the enlargement is dorsal.
- Once the dorsal enlargement is over, the stomach undergoes a 90° rotation along cranio-caudal axis. Thus the dorsal enlargement rotates forward the left side of the embryo.
- Hence the stomach lies with its dorsal part on the left and ventral part on the right. The cranial part of the dorsal enlargement of the stomach grows more than the caudal part forming the fundus.
- The boundry of dorsal enlargement becomes greater curvature and of the ventral part is lesser curvature.

DEVELOPMENT OF RUMINANT STOMACH

- Monogastric days reached in 33 days and 90° rotation is completed by this time. The area corresponding to fundus becomes rumen. Other differential growth area appears along the greater curvature of embryo stomach just caudal and ventral to the forming rumen. This area is the reticulum.
- A third area appears along the lesser curvature. This is the omasum. The abomasum forms from the pyloric region. By 40 days, further differentiation occurs by two cranially directed outgrowths from fundus. One is dorsal and the other is ventral (dorsal and ventral sacs).
- By 43 days, rumen is growing caudo-dorsally and forward to the right. This results in reversal positions of the dorsal and ventral sacs. The sacs become directed caudally and the dorsal sac is dorsal to the ventral sac. Now the rumen is on the left side of the abdominal cavity, followed by reticulum, omasum and abomasum towards right.
- When the rumen enlarges, it forces the reticulum cranially and ventrally. As the rumen grows, it begins to encroach toward the right. This encroachment pushes the omasum and abomasum ventrally.
- Once the adult positions are reached (14 weeks of gestation) the growth of the rumen slows. By birth rumen is 1 1/2 size of abomasum. After birth rumen enlarges till 8 weeks and by 12 weeks, becomes twice the size of abomasum. In adults around 1- ½ yrs of age the size depends on roughage diet.

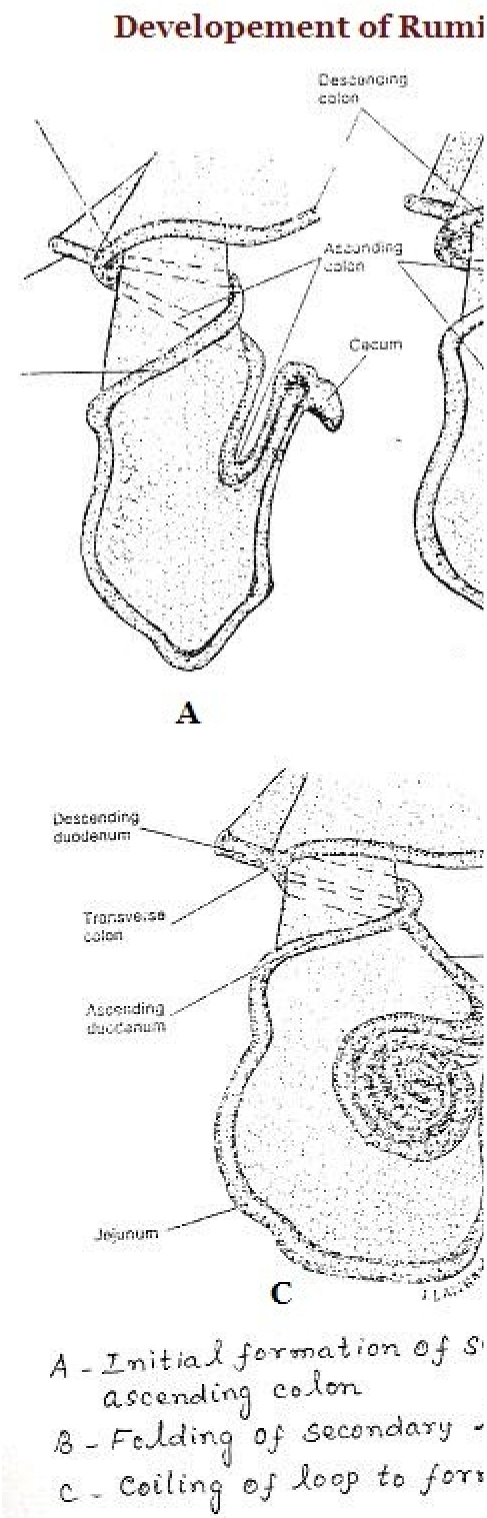
DEVELOPMENT OF INTESTINE

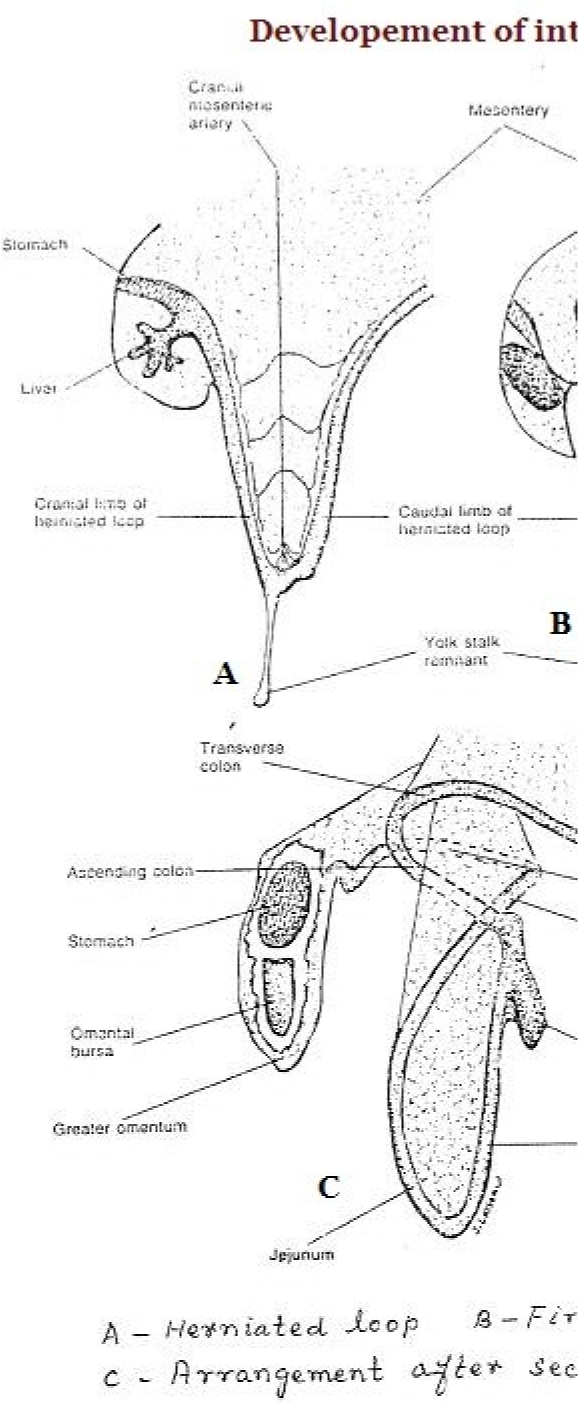
- The intestine is a simple tube beginning in the stomach and ending in the cloaca.The narrow caudal part of the foregut forms the descending duodenum.
- The midgut develops into ascending duodenum, jejunum, ileum, caecum, ascending and transverse colon. The hindgut differentiates into decending colon and rectum.
- Around 20 days, or even earlier, the midgut grows in length farther than it could be accommodated in abdominal cavity.

- The midgut looses connection with the yolksac and at this stage, it is in the form of a loop. This loop has a cranial and a caudal limbs and it undergoes an anti-clockwise rotation. Due to this, the cranial limb goes to the right and behind.
- The caudal limb is taken forwards and to the left. Now the gut begins to elongate rapidly and the loop herniates into the umbilical cord. Then cranial and caudal limbs undergo 180^{o} rotation.
- The original cranial limb of the intestinal loop forms the ascending duodenum, jejunum and ileum. The caudal limb of the loop forms the ceacum and the first part of the colon.
- The hindgut forms the terminal part of the colon. The caudal end of the hindgut forms the cloaca.
- The subdivision of the cloaca results in the rectum. The endodermal lining obliterates the lumen of the gut in the early stages which later on gets canalized and the lumen gets restored. The lining gets villi throughout initially but later the large intestine loses the villi.

Anomalies

- *Stenosis or Atresia of oesophagus* - absence of canalization.
- *Situs inversus* – organs found in exactly opposite situation.
- *Umbilical fistula* - persistent yolk sac opening to exterior.
- *Umbilical hernia* – failure of withdrawal of intestine.
- *Meckle's direrticulum of ileum* – Persistence of proximal part of yolk stalk.
- *Imperforate anus* – failure of rupture of the anal membrane.





DEVELOPMENT OF LIVER

- Liver is an endodermal derivative. Its primordium lies between the pericardial cavity and attaching yolk stalk. Here the floor of the future duodenum continues to give rise to definite sacculations named hepatic diverticulum. This consists of a cranial portion which will differentiate into the glandular tissue and its bile ducts.
- The caudal portion will become the gall bladder and cystic duct. The hepatic diverticulum forces its way to splanchnic mesoderm which forms the primitive diaphragm, the septum transversum.
- A little later, the region of the septum occupied by the liver becomes drawn out as ventral mesentery and the final relation to the liver is more related to the mesentery than the diaphragm.
- The cranial portion of the hepatic diverticulum buds off epithelial cords which invade the septum transversum and continue to proliferate into a spongy work.
- The paired vitelline veins flanking the gut and send the branches into the region of proliferation. The result is a mutual, intimate intergrowth of tortuous liver cords and sinusoidal channels.
- The diverticulum in the meanwhile elongates and differentiates into duct system. The main portion of the diverticulum forms the hepatic duct and ductus choledochus.
- From the hepatic duct, large intra hepatic ducts buds off and from these small inter lobular ducts arise. The system of branching of vitelline veins are responsible for creation of hepatic lobules from the parenchyma.
- The gall bladder and cystic duct develop from caudal portion of hepatic diverticulum. The septum transversum furnishes the peritoneal covering and the connective tissue framework.

DEVELOPMENT OF PANCREAS

- It is an endodermal derivative. The outpocketings from the endodermal lining of the gut are the indications of future pancreas. These buds arise on the opposite sides of duodenum, one on the dorsal side and the other on the ventral side.
- The dorsal bud lies in front of the hepatic diverticulum. The ventral bud lies in the angle between the gut and the hepatic diverticulum.
- Unequal growth of duodenal wall shifts the bile duct dorsally and the ventral primordium of the pancreas is shifted dorsal and is brought nearer to the dorsal primordium. During futher development two primordia fuse.
- By proliferation, the duct system develop into acini, some epithelial buds loose connection with ducts and develop as islets.

DEVELOPMENT OF SPLEEN

- The spleen is a mesodermal derivative. It is developed in the dorsal mesogastrium.
- At first an accumulation of mesenchymal cells is seen just beneath the surface of the peritoneal epithelium. This mass increases in size and projects above the omental surface as several hillocks which soon merge.
- The part of the dorsal mesogastrium which is attached to the spleen becomes reduced to narrow band called the gastrosplenic omentum. The mesenchyme is soon vascularised and the capsule, trabeculae and pulp cords are differentiated.

MODULE-34: DEVELOPMENT OF RESPIRATORY AND URO-GENITAL SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about the development of
    - respiratory system,
    - uro-genital system,
    - adrenal gland,
    - genital ducts,
    - mullerian ducts,
    - mesonephric or wolffian ducts,
    - external genitalia and
    - mammary gland.

DEVELOPMENT OF RESPIRATORY SYSTEM

- The epithelium of respiratory tree is derived from endoderm. The primordium of this system is the *laryngo-tracheal groove*, which runs lengthways in the floor of the foregut just behind the last pair of pharyngeal grooves.
- On the ventral surface, the endoderm projects as a ridge. This ridge is the primordium for caudal part of larynx, trachea in front and caudally the bronchi and lungs.
- A lateral groove appears on each side at the junction of the ridge and the oesophagus, which becomes deeper and thus separates the oesophagus from the trachea and lung bud.
- The ridge extends forwards up to the level of the fourth branchial arches. The mesenchyme of the fourth and fifth arches gives rise to the thyroid, cricoid, epiglottic and arytenoid cartilages and laryngeal muscles. The primitive opening of the pharynx into the trachea forms the glottis.
- The trachea elongates and bifurcates into two *bronchial buds* on the right side and one on the left. The end of each main tube continues as stem bronchus.
- As the bronchial buds elongate and branch, the tubular system in each pulmonary lobe becomes bush-like with dorsal, ventral, lateral and medial rami.
- The splanchnic mesoderm within which the early respiratory tree has developed is later named as the mediastinum and the mesenchyme furnishes the connective tissue and cartilage plates of the tracheal and bronchial wall, where the blood vessels and nerve fibres grow.
- A series of anomaly in connection with the development of this system is a fistula between the trachea and oesophagus due to incomplete separation of the laryngo-tracheal groove from the gut.

DEVELOPMENT OF URO-GENITAL SYSTEM

The urinary and genital system both arises from the mesoderm. Both drain into a common urogenital sinus and hence these two systems are intimately associated in their origin, development and relation.

Urinary organs

- Nowhere in the development of the individual can be found a better example of the principle of recapitulation than in the development of kidneys of mammals. The earliest excretory organ is the *pronephros* (functional in adult amphioxus). In fishes and amphibians, the pronephros is replaced in the adult condition by the *mesonephros*. This is present in the embryos of reptiles, birds and mammals but the final permanent kidney in these classes is the *metanephros*. All the three types of kidneys are formed in succession, one behind the other during development of a mammal.

- The kidney arise from the mesoderm of the *intermediate cell mass or nephrotome* which lies next to the mesodermal somites. The series of nephrotomes from the urino-genital ridge which splits up into an lateral nephric and a medial genital ridge, which project into the coelom from the dorsal wall.
- The pronephros arises as a series of about seven simple paired pronephric tubules arranged segmentally. One end of each tube opens into the coelom while the other end opens into a longitudinal pronephric duct which is excretory in function and drains into the cloaca. The arterial tuft projecting into the coelom is the external glomerulus which serves to filter the waste products from the blood into the coelom. These degenerate early in foetal life.
- The *mesonephros* or *Wolffian body* is larger and it consists of about 30 tubes which are longer and complicated, situated about the middle of the ridge. These mesonephric tubules are tortuous and are connected to the pronephric duct which is now termed as the mesonephric or Wolffian duct. At one end each tubule is invaginated like a gastrula. Bowman’s capsule and is associated with a glomerulus (internal glomerulus) and at the other end with the duct. These tubules degenerate about the fourth month.
- The *permanent kidney or metanephros* arises far behind in the body. The final kidney consists of an aggregate of tubules which drain into a common duct. The excretory ducts (ureter, pelvis calyces, papillary ducts and straight collecting tubules are derived from a bud called ureteric-bud which is growing off the mesonephric duct. On the other hand the secretory unit, the nephron (Bowman’s capsule, both convoluted tubules and Henle’s loop) differentiates from the substance of the nephrogenous cord (*metanephrogenic mass*), which surrounds the pelvic dilation as a cap. The collecting (drainage duct) and secretory tubules then unite secondarily to complete a continuous uriniferous tubule. In structure and function, therefore these two components remain as different as was their origin.

- The mesonephric duct makes a sharp bend before opening into the cloaca. At this angle, the ureteric primordium (*ureteric-bud*) appears as a hollow outgrowth from the mesonephric duct and grows forwards. The proximal, rapidly elongating portion of this invagination is the future ureter, while the blind end expands into the renal pelvis. This ureteric-bud pushes itself into a mass of condensed tissue, which is the caudalmost portion of the nephrogenous cord, which also forms a cap over the ureteric-bud. The ureteric-bud differentiates into the calyx’s majores, calyx’s minores, papillary ducts and collecting tubules for making up a large part of the medulla of the kidney. The metanephrogenous tissue differentiates into the secretory tubules forming the cortex. Then the formation of capsule and interstitial tissue are established between the secretory and excretory portions of the tubules. Soon the metanephros migrates toward the sublumbar region.

Anomalies

- *Horse shoe kidney :* Due to fusion of the metanephric primordia of the two sides
- *Cystic kidney :* Want of communication between the secretory and excretory tubules.
- *Pelvic kidneys:* Due to retention of their primitive pelvic position.
- *Forked or double ureter:* Due to partial or complete splitting of the ureteric bud.

DEVELOPMENT OF ADRENAL GLAND

- The origin of adrenal gland is of double origin.

- The gland develops in the intermediate mesoderm at the cranial pole of the mesonephric kidney.
- The *adrenal cortex* is derived from the surrounding intermediate mesoderm.
- The *adrenal medulla* is ectodermal in origin, being formed by cells derived from the neural crest.

DEVELOPMENT OF GENITAL SYSTEM

- The genital organs are undifferentiated when they first appear (indifferent period), either by gross or microscopic appearance and hence during this period the term gonad is applied to them.
- The gonad appears within a thickening called the genital ridge on the medial aspect the urino-genital ridge.
- The ventral surface of the genital ridge shows rapid proliferation of the mesothelium which becomes thickened and many layered. The gonad consists of a superficial germinal epithelium and an internal epithelial blastemal mass.
- The primordial germ cells from the yolk sac endoderm migrate by way of the dorsal mesentery of the gut and locate themselves in the epithelium of the genital ridge.
- In the male, genital glands as they increase in size, shorten into more compact organs and begin to show branched and anastomosing cords of cells called the testes cords. These arise from the superficial germinal epithelium which dips into the interior of the mesenchyme forming cords of cells. These cords differentiate into the tubuli contorti and tubuli recti.
- The original germ cells descend into the tubuli contorti and the mesenchyme forms the interstitial tissue and the mediastinum testis. When the migration of the germs cells is complete, the mesenchyme surrounding the gland forms the tunica albuginea and cuts off the germinal epithelium, which becomes mesothelium. Certain cells of the mesenchymal stroma transform themselves into large cells lying in the intertubular connective tissue forming the interstitial cells.
- In the female, the gonad does not exhibit any distinctive ovarian features until several weeks after the gonad of the male has declared itself as a testis. Then the blastemal mass shows clusters of small indifferent cells and one or more primordial germs cells. Soon a primary cortex appears beneath the germinal epithelium and a primary medulla appears internally.
- Later, the ovary enlarges by addition of a new (secondary) definitive cortex upon the original blastemal mass. In the primary medulla and cortex, the earlier ova decline, regress and are replaced by vascular fibrous stroma-the definitive medulla.
- In the definite cortex, ova and the primary follicles develop. Later vesicular (Graafian) follicles develop from the primary follicles during the active sexual cycle.
- It is to be remembered that while the primary medulla and primary cortex correspond to the male component of a gonad, the definitive cortex of the gonad is a distinctive female characteristic.

DEVELOPMENT OF GENITAL DUCTS

- The male does not elaborate any ducts intended primarily for its own purposes. With the degeneration of the mesonephros it merely appropriates the mesonephric ducts and some to the mesonephric tubules and converts them into genital canals (mesonephric duct becomes, the duct of epididymis, ductus deferens and ureter and pelvis while the cranial group of mesonephric tubules become efferent ductules of epididymis. Seminal vesicle arises from the mesonephric duct).
- In the female, the mesonephric ducts mostly degenetrate, except for ureter, pelvis and some vestigial remnants.

DEVELOPMENT OF MULLERIAN DUCTS

Both sexes develop a pair of female ducts of Muller. But its fate in the two sexes is different, as described below:

Female

- These ducts arise by formation of a groove in the thickened epithelium of the urino-genital ridge which is lateral to the mesonephros near its cranial end. This extreme cranial end of the groove remains open like trumpet while caudally the lips of the groove fuse into a tube.
- In the most posterior part, the two Mullerian ducts approach each other, reach the dorsal wall of the urogenital sinus, fuse and end blindly at the Muller's tubercle-a median projection in the dorsal wall of the cloaca, caused by the opening of the mesonephric ducts into it. This fused region is the first indication of the uterus and vagina and the unfused cranial parts serve as uterine tubes.
- The fused part, by unequal growth of its walls, becomes trans formed into the uterus and vagina. The cranial end of the tube, which remains open, forms the fimbriated end of the fallopian tube. The Muller's tubercle becomes the site of hymen.

Male

- The same primordia also develop but remain rudimentary. Degeneration of the ducts occurs in the third month and only the extreme cranial end is spared which remains as a vestige-the appendix testis.
- The portion which forms the uterus and vagina persists in a rudimentary from as the uterus masculinus.
- The Muller's tubercle is represented by the colliculus seminalis.

DEVELOPMENT OF MESONEPHRIC OR WOLFFIAN DUCTS

Male

- Some of the cranial degenerating mesonephric tubules, unite with the seminiferous tubules and form the efferent ducts of the epididymis. The caudal group of degenerating mesonephric tubules persists as paradidymis. The upper end of the mesonephric duct becomes highly convoluted to form the duct of the epididymis and lower portion forms the vas deferens.
- The primordia of the seminal vesicles arise from the terminal part of the mesonephric ducts and so are mesodermal in origin. The prostate and Cowper's glands arise from the pelvic urethra which is entodermal in origin. The penile part of the urethra is ectodermal in origin.

Female

- The cranial group of mesonephric tubules persists as the epoophoron and the caudal group as the paroophoron.
- The greater part of the mesonephric duct atropies and the distal portion persists as Gartner's canals in the wall of the vagina.

DEVELOPMENT OF EXTERNAL GENITALIA

- Embryos of six weeks present a conical genital tubercle in the mid-ventral line between the umbilical cord and tail. Its caudal slope bears a shallow urethral groove, flanked on either side by slightly elevated urethral folds.
- The genital tubercle elongates into a cylindrical phallus whose tip is rounded into glans. Lateral to the phallus on either side appears a rounder ridge- the labio-scrotal swelling.
- Rupture of the urethral membrane in the floor of the-urethral groove provides an external opening for the urino-genital sinus. So far the development is identical in both the sexes.
- In the male, the phallus elongates to become the penis. The edges of the urethral groove progressively fold together in a distal direction to transform an open urino-genital sinus into the tubular urethra within the penis. The fused edges form the raphe. The scrotal swellings shift laterally and behind and develop into the scrotum. Each half of the scrotum is separated from its mate by a septum and a superficial raphe.
- In the female, the phallus lags in development and becomes the clitoris. The shorter urethral groove remains as the vestibule and the urethral folds constitute the labia minora. The primitive labio-scrotal swelling enlarge and fuse below the anus in the dorsal commissure, while the swellings enlarge to form the labia-majora.

Anamolies

- *Hypospadias* - failure of closure of the lips of the urethral grooves, on the ventral surface of the penis.
- *Epispadias* -urethra opening on the dorsal surface of the penis due to displacement of the cloacal membrane.

DEVELOPMENT OF MAMMARY GLAND

- An ectodermal thickening called milk line or mammary ridge extends on either side as longitudinal bands between the bases of limb buds.
- The primordial band is developed in the pectoral region (Primates, elephants) inguinal region (undulates) or throughout (axilla to groin region) in carnivores and pigs.
- The primordium of each gland becomes lens shaped, then globular and then lobed. From these, solid cords bud inwards into the - corium. These primary solid milk ducts branch and terminate in secretory portion of acini.
- Lumen is acquired by canalisation of the solid ducts and acini.

MODULE-35: DEVELOPMENT OF CARDIOVASCULAR SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about the development of
    - haemopoiesis,
    - heart,
    - arteries,
    - veins and
    - foetal circulation.

DEVELOPMENT OF CARDIO VASCULAR SYSTEM

- Both the blood vessels and blood cells arise from *mesenchyme*. The earliest formative tissue of this kind is the angioblast which differentiates in the mesodermal wall of the yolk sac where groups of angioblasts form the *blood islands of Pander*.
- Originally solid, these soon hollow out and in this process the peripheral cells become arranged as endothelium and central cells form blood cells. From the wall of the yolk sac, the blood vessels extend into the body of the embryo and spread into the different parts.

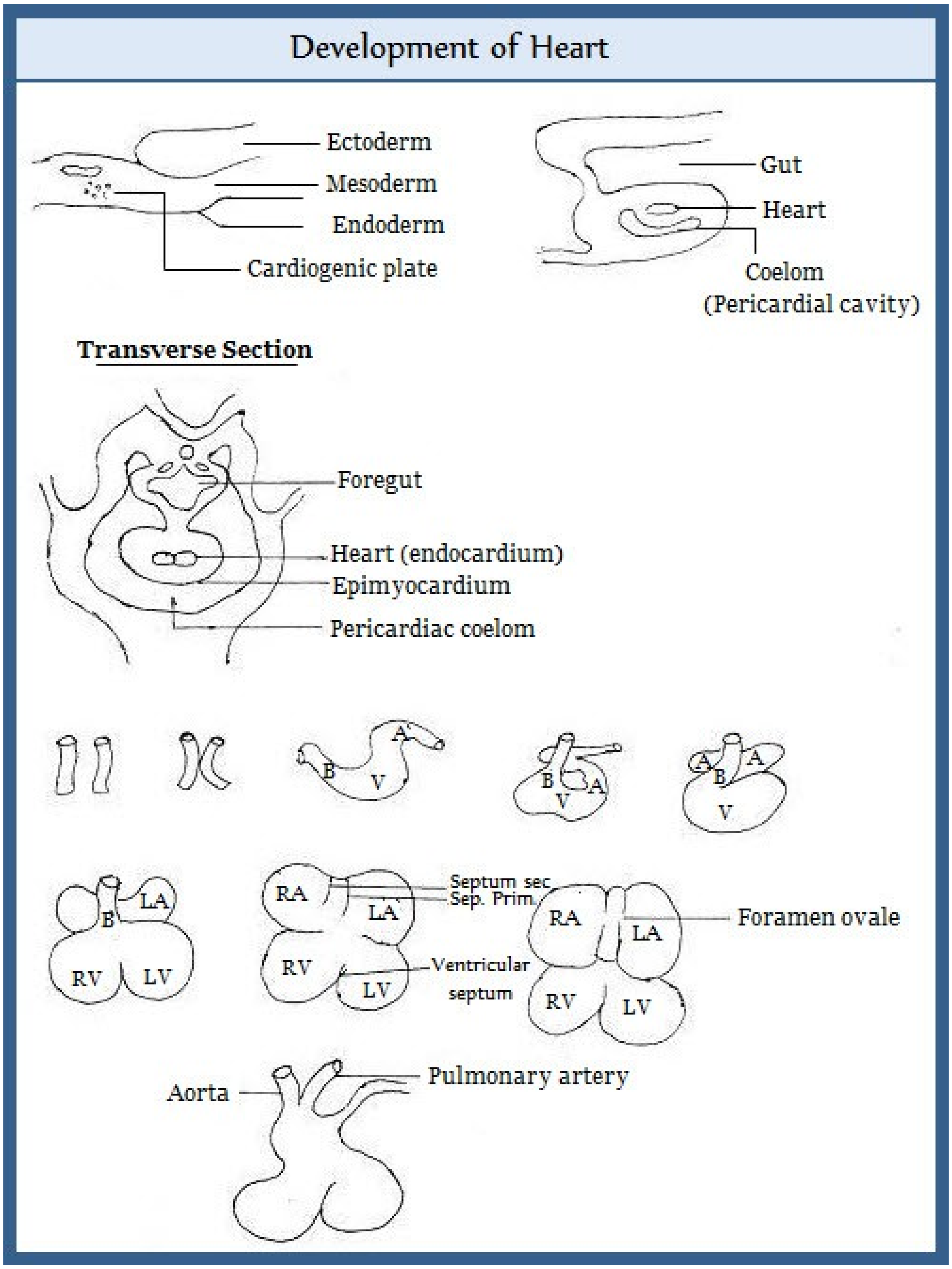
DEVELOPMENT OF HAEMOPOIESIS

- The first site of blood formation is in the *area vasculosa* of the wall of the yolk sac. Here between the extraembryonic splanchnic-mesoderm and endoderm the blood islands of Pander develop. These are solid masses of mesenchymal cells united by cellular stands to form a network.
- As they become differentiated the outer cells join to form the tubular wall of blood vessels, while the inner cells are separated by the secretion of plasma between them and become primitive blood cells, which multiply rapidly by mitosis. Formation of primitive blood cells also occurs for some time by the detachment of cells from the endothelial wall.
- These cells die out during embryonic life and do not form definitive erythrocytes. Other primitive blood cells remain as colourless proliferating hemocytoblast. Blood formation is soon transferred from the yolk sac to the body of the embryo-where it is continued by the body mesenchyme, endothelium liver, spleen, thymus, lymph nodes and bone marrow. The haemocytoblasts or stem cells are large amoeboid cells with large pale spherical nucleus and a basophilic cytoplasm. All the definitive blood cells develop from this stem or blast cell.
- According to monophyletic theory, a common stem cell gives rise to all the types of blood elements, both red and white. The polyphyletic theory holds that there are two stem cells-one stem cell for erythrocytes and granular leukocytes and the other for non-granular leucocytes.
- The hemocytoblast differentiates by the gradual elaboration of haemoglobin consequent to transformation of basophilic cytoplasm to the acidophilic cytoplasm, nuclear condensation and reduction in size of the cell. The successive stages are proerythroblast, erythroblasts, and normoblast. The normoblast (which have a size about equal to the erythrocytes, a small dense nucleus and an eosinophilic cytoplasm) lose their nuclei by extrusion and become erythrocytes.
- The haemocytoblast also gives origin to the differentiating granular leucocyte termed myelocytes. These elaborate within their cytoplasm specific kinds of granules, giving rise to neutrophilic, acidophilic and basophilic myelocytes. After a number of mitotic divisions, these myelocytes lose the capacity for division, the nucleus becomes indented and these cells enter the blood stream, as the different types or granular leucocyte.
- The lymphocytes are produced in the lymphatic tissue by differentiation of haemocytoblasts into large lymphocytes. The large lymphocytes give rise to small lymphocytes.
- As believed by some, the monocytes arise by the transformation of lymphocytes in the sinusoids of spleen, liver and bone marrow. Others believed that they are derived from the lining cells of sinusoids or from monoblasts in the bone marrow.
- The megakaryocytes are giant cells derived from haemocytoblast and occur in the embryo, in the hemopoietic organs (red marrow, liver spleen) and their processes extend through the walls of sinuses and by constriction and segmentation of these, platelets are formed.

DEVELOPMENT OF HEART

- The Heart is a specialized blood vessel with a lumen and thick muscular walls. In mammals, it arises from a *cardiogenic plate* located in front of the head in the splanchnic mesoderm and beneath the pericardial coelom. Due to a reversal in position, the heart primordium comes to lie above the pericardial coelom beneath the foregut.

- The earliest indication of the cardiac primordia is the formation of two endothelial tubes which fuse in front and later behind, to form a single tube. The internal endothelial tube becomes the endocardium and the mesodermal layer surrounding it forms the myocardium and epicardium. It is suspended by the dorsal mesocardium from the gut, which is also soon lost.
- At this stage, this single tube by constrictions, presents three regions viz., a) the paired atria receiving the veins, b) the single ventricle and c) the single bulbus continued in front by the ventral aortae. A sinus venosus is soon demarcated from the atrium. Due to the greater rate of the growth of the heart tube than the pericardial cavity, it is soon bent into a simple spiralled 'S'.
- A continuation of this growth process drops the *bulbo-ventricular* loop still further backward and downward. By development of septa, indicated externally by grooves, the heart presents the two ventricles and the aorta and pulmonary artery. The interatrial septum presents the foramen ovale.
- The two atria are separated by the development of the *septum primum* and the *septum secundum* which fuse to form the interatrial septum. The ventricular primordium is subdivided into two ventricles by the development of the *interventricular septum*. The bulbus is split into the aorta and the pulmonary artery by the development of two endocardial septa which fuse.



DEVELOPMENT OF ARTERIES

- The aorta is dilated at its origin forming the aortic sac from which the ventral aortae ascend and continue as right and left dorsal aortae. The dorsal aortae unite behind to form a single descending aorta.
- From the aortic sac, five pairs of aortic arches arise and connect themselves to the dorsal aortae. The pulmonary artery divides into right and left pulmonary arteries which connect themselves by the sixth aortic arches with the dorsal aortae.
- The first and second aortic arches of both sides degenerate. The dorsal aortae between the third and fourth arches degenerate, thus establishing continuity between the third arches and

the anterior segments of the dorsal aortae. The third aortic arch gives off a sprout - the external corotid artery, after which it is continued as the internal carotid artery.

- The common stem of the third arch before the sprout arises is the common carotid artery. The fourth arches are transformed into different structures on both sides. The right arch becomes the right subclavian artery (right axillary).
- The fourth arch on the left side persists as the arch of the aorta and gives off a sprout,the left subclavian artery (left axillary). The fifth arches degenerate. The sixth arches (pulmonary arches) on the right side degenerates, whereas on the left side it persists as the ductus arterious.
- The vagi detach the recurrent laryngeal nerves which pass round the sixth arches. During the migration of the heart downwards, the left recurrent laryngeal nerve, hooks around the sixth arch (ductus arteriosus) and is dragged down whereas the right nerve lags behind and is hooked around right brachial. The right dorsal aorta between the sixth arch and the descending aorta degenerates.

- In the domestic animals the right brachial and the right common carotid shift themselves on the arch of the aorta and fuse with the left common carotid and the left brachial.
- The dorsal aorta gives off the following branches:
    - The ventral splanchnic arteries which are represented in the adult by the coeliac anterior and posterior mesenteric arteries.
    - The lateral splanchnic arteries represented in the adult by the renal, adrenal, testicular and ovarian arteries.
    - The dorsal inter segmental arteries with divide into dorsal and ventral ramus. The dorsal ramus gives a spinal branch to form the inferior spinal artery and passes up to supply the muscles and skin of the back. The ventral ramus supplies the body wall and is represented in the adult by the intercostal arteries in the thoracic and lumbar arteries in the lumbar regions.
- The dorsal aorta terminates by giving off two umbilical arteries after which it is continued by the middle sacral artery. The external iliac arteries are sprouts from the umbilical arteries. A new connecting trunk from the junction of the umbilical artery with aorta, becomes the internal iliac.

DEVELOPMENT OF VEINS

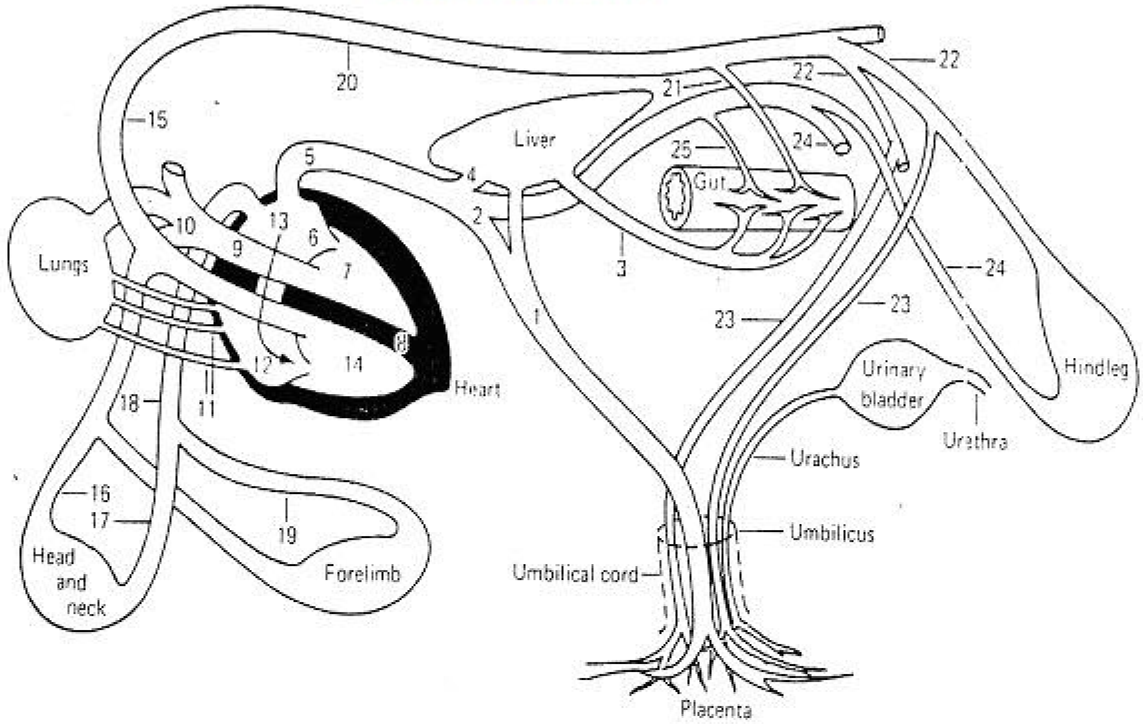
- All the veins of the body develop as modifications of the ground plan present in the developing embryo.
- The plan may be outlined briefly as consisting of:
    - Umbilical veins,
    - Vitelline veins,
    - Anterior cardinal veins,
    - Posterior cardinal veins,
    - Supracardinal veins and
    - Sub-cardinal veins and all the six veins are paired.
- The proximal ends of vitelline and umbilical veins are absorbed by the developing liver of form the portal system. The mesenteric veins draining the venous blood from the gut on enter the liver, persists as the portal vein.
- The anterior cardinal veins drain the venous blood from the head and neck. The posterior, sub and supra-cardinal veins drain the venous blood from the posterior parts of the body.
- The cranial segment of the anterior cardinal is transformed into the venous sinuses of the dura mater and the cervical segment persists as the internal jugular form which sprouts the external jugular. The thoracic segments of the anterior cardinals unite to form the anterior vena cava.

- The posterior cardinals degenerate without contributing anything except a small proximal part of the azygos vein. The sub-cardinals unite and are transformed into the posterior vena cava. The supra-cardinals are transformed into the azygos vein on the right and vena hemizygous on the left side.

FOETAL CIRCULATION

- Oxygenated blood returning from the placenta, enters the embryo by the large umbilical vein and is conveyed to the liver. From here it is conveyed to the posterior vena cava for the most part directly through the ductus venosus and to a certain extent through the hepatic- veins.
- The impure blood of the portal vein and posterior vena cava contaminates partially the large volume of Oxygenated blood from the placenta.
- In sharp contrast, the blood returning from the anterior venacava is very poor in oxygen.
- In the heart, the blood coming from the anterior venacava is directed into the right ventricle and through the pulmonary artery it leaves the heart.
- Some of this reaches the lungs but mostly it is conveyed through the ductus arteriosus to the posterior aorta.
- On the other hand the blood from the posterior venacava entering the right atrium passes mostly to the left atrium through the foramen ovale and reaches the left ventricle.
- From here it is pumped into the aorta. Thus the blood reaching the heart substance through the coronary arteries and the head and neck through bicarotid trunk and its branches contains comparatively more oxygen than that which is distributed to the other parts of body through the posterior aorta.
- The umbilical arteries arising from the aorta transport a large volume of this blood to the placenta for oxygenation.
- At birth, the lungs become functional and placental circulation ceases. This throws some foetal vessels into disuse. The umbilical vessels pass into sudden and complete disuse.
- The arteries become transformed into lateral ligaments of the bladder and the vein forms the *ligamentum teres of liver*.
- The *ductus venosus* also atrophies and is transformed into the fibrous *ligamentum venosus* embedded in the wall of the liver.
- The *ductus arteriosus* is transformed into the *ligamentum arteriosum* and the *foramen ovale* is obliterated and the site is marked permanently by the *fossa ovalis*.

Foetal Circulation



1. Umbilical vein
2. Ductus venosus
3. Portal vein
4. Hepatic vein
5. Posterior vena cava
6. Right atrium
7. Right ventricle
8. Interventricular septum
9. Pulmonary artery
10. Ductus arteriosus
11. Pulmonary vein
12. Left atrium
13. Foramen ovale (shown by arrow)
14. Left ventricle
15. Aorta
16. Brachiocephalic trunk (innominate artery)
17. Jugular vein
18. Anterior vena cava
19. Brachial vein
20. Abdominal aorta
21. Mesenteric artery
22. External iliac arteries
23. Umbilical arteries
24. External iliac vein
25. Mesenteric vein

MODULE-36: DEVELOPMENT OF MUSCULO-SKELETAL SYSTEM

Learning outcomes

- At the end of this module the learner will be able to know about the development of
    - muscular system,
    - skeletal system,
    - intramembranous ossification,
    - enchondral ossification,
    - bones of the skull,
    - vertebral column and

- limb buds and tail bud.

DEVELOPMENT OF MUSCULAR SYSTEM

- The muscular system consists of specialised cells - the muscle fibres which are of three varieties, skeletal, plain and cardiac.
- These are differentiated from the *myoblasts* which are derived from the mesoderm.
- The smooth muscle fibres of the iris and sweat glands are ectodermal.
- The muscles originate in the myotomes.
- The visceral (plain and cardiac) musculature is developed from the splanchnic mesoderm that surrounds the gut and heart.

DEVELOPMENT OF SKELETAL SYSTEM

- The skeletal system is a mesodermal derivative. Bone a always develops by a transformation of the embryonic or adult connective tissue.
- When development of bone takes place in cartilage, the method of ossification is termed *enchondral ossification*.
- When it occurs in membrane the process is termed *intramembranous ossification* but essentially the process is the same in both.
- Bone matrix is deposited the activity of specialised connective tissue cells called osteoblasts.
- The only difference between the two types of ossification is that the former occurs at first in cartilage which is destroyed - replaced and substituted by bone. Hence bones formed in this way are also known as substitution bones e.g. long bones of limbs.
- The *flat bones* of the *skull* are *membrane bones*.

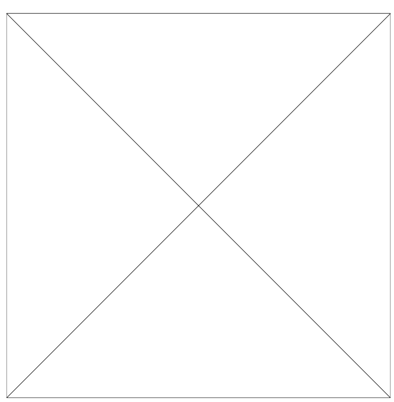
DEVELOPMENT OF INTRAMEMBRANOUS OSSIFICATION

- In an area where bone is going to develop, the mesenchymal cells are connected with one another by their processes and delicate bundles of white fibres run in all directions between them. In between the cells and bundles is a semifluid intercellular substance
- At one or more central points, ossification begins by appearance of osteoblasts, which promptly deposit bone matrix in the form, of acidophil bars or spicules, which unite a meshwork of trabeculae. As the matrix is laid down some cells remain imprisoned in the meshes as osteoblasts or bone producing cells, which takes up calcium, salts from the blood and deposit the same in the network of acidophil bars, thus converting them into plates of bone. Thus Ossification starts from the centre and proceeds towards the periphery.
- As this proceeds, the surrounding mesenchyme furnishes more and more of membrane for ossification and this results in an increase in the size of bone. The osteoblasts at the periphery arrange themselves in a continuous layer and these also produce parallel plates of bone at the periphery. The mesenchyme in the region forms a fibrous membrane enclosing the bone the periosteum.
- Bone formed in this process has a spongy character and consists of irregular plates of bone, which branch and unite with one another and in the meshes is enclosed embryonic connective tissue rich in blood vessels forming the red marrow.

DEVELOPMENT OF ENCHONDRAL OSSIFICATION

- Most of the bones in the body are preceded by a temporary cartilaginous model of the same shape as the definite bone and the chief peculiarity of the method is the preliminary destruction of the cartilage and its replacement by bone, which develops exactly as in intramembranous ossification. So bones formed by this method are called replacement or substitution bones.The bones of the *appendicular skeleton* are all *substitution bones*.

- In the hyaline cartilage, which is to be substituted by bone, the cartilage cells enlarge in the centre and become arranged in characteristic radial rows and some lime is deposited in their matrix. The cartilage cells and part of the matrix then disintegrate forming primary morrow cavities. This destruction is accompanied by a simultaneous invasion of this region by the vascular connective tissue, rich in cells derived from the perichondrium.
- These cells perform the function of osteoblasts of depositing lime salts in the cartilage matrix and this results in the formation of bars of calcified matrix. Bone thus formed is spongy in nature consists of network of bony plates enclosing the primary marrow spaces containing blood vessels and connective tissue corpuscles and this constitutes the red marrow. In a progressive manner the cartilage undergoes invasion, destruction and replacement by spongy bone.
- This spongy bone at the centre is destroyed and absorbed by giant cells called osteoclasts. Thus a large marrow cavity is created in the centre of the bone. Simultaneously the perichondrium at the periphery functions as periosteum and deposits, by the activity in the centre and periosteal bone at the periphery, its destruction and absorption by osteoclasts at the centre goes on, resulting in increased dimension of the marrow cavity and circumferential growth of bone.
- The centre of ossification appearing in the shaft of a long bone of the foetus in the primary centre of ossification. Sometime between birth and puberty, centres of ossification appear at the epiphyses also. At the junction of the shaft and the epiphyses there are two plates of cartilages, one above and the other below termed the epiphyseal cartilages.
- These supply more and more of cartilage for the shaft and the epiphyses for formation of new bone and this process results in an increase in length of the bone. When the bone has reached its adult, size, both in its length circumference, the epiphyseal cartilages are ossified and further growth stops.
- Reconstruction takes place in periosteal bone to form the Haversian systems and the outer and inner circumferential lamellae. The osteoclasts destroy and remove periosteal bone forming Haversian canals. Osteoblasts arrange themselves around them and deposit their exoplasm in concentric layers which are later ossified by deposition of calcium salts.
- Some of the osteoblasts are enqulfed in the lamellae and occupy lacunae and canaliculi. Others withdraw and arrange themselves at the periphery and deposit periosteal lamellae. The cells towards the medullary cavity form the endosteal lamellae. Thus through reconstruction, compact bone is formed outside enclosing cancellated or spongy bone inside, around the medullary cavity.



DEVELOPMENT OF BONES OF THE SKULL

- The earliest indication of the skull is a mass of dense mensenchyme enveloping the cranial end of the notochord and it extends forwards into the nasal region.
- Laterally it becomes continuous with the neuro-cranium, the mesoderm covering and protecting the brain and interiorly with the mesodermal cores of branchial arches.
- Chondrification sets in during the seventh week and it is confined chiefly to the base of the skull-the basioccipital and sphenoidal cartilages.
- The chondrocranium hence refers to the base and neurocranium to the roof and lateral walls.
- Ossification of chondrocranium begins during the third month and forms the occipital, sphenoid ethmoid and pelorus and mastoid parts of the temporal bone.
- The parietals, quamous and tympanic parts of temporal, vomer nasal, lacrimal, malar are all developed in membrane.
- The first branchial arch divides into an upper maxillary and a lower mandibular process.
- The Meckel's cartilage is the mesenchymal core of the - mandibular process which becomes enveloped by surrounding mesenchyme and finally disappears except at the proximal portion where it is transformed into the sphenomandibular ligaments, malleus and incus. The adult mandible develops in membrane.
- The maxillary process undergoes similar degenerations and the mesoderm surrounding the original cartilage develops into the maxilla and palatine bones.

DEVELOPMENT OF VERTEBRAL COLUMN

- The primitive axial support of all vertebrates is the notochord or chordadorsalis. It is a transient structure in mammals and consists of a cylindrical rod of mesodermal cells from the *Sessel's pocket* to the tip of the tail.
- The notochord degenerates soon except at the intervertebral discs within which it persists as the swollen mucoid *nuclei pulposi*.
- The axial skeleton differentiates from the mesenchyme that traces its origin to serially arranged pairs of mesodermal segments - the somites.
- The ventro-medial part of a somite develops into the *sclerotome* and cells proliferate from this mass and migrate towards the notochord. The sclerotomes are destined to from the vertebrae and ribs.
- Each sclerotome presents and anterior loose and a posterior dense part.
- The anterior part of a sclerotome fuses with the posterior part of the sclerotome in front of it, and these reconstituted sclerotomes form the primordia of the definite vertebra.
- From each of these sclerotomes growth takes place in three directions
    - medially to surround the notochord to from the body,
    - above to form the neural arch.
    - ventrolaterally to provide costal processes or primordia of ribs.
- Following this blastemal stage, chondrification sets in during the seventh week and ossification during the tenth week. When the atlas forms its body, it is soon appropriated by the axis as the dens.
- In the thoracic region, the costal processes enlarge and from the ribs. Here the original union of costal process with the vertebrae is replaced by joints (costo-central and costotransverse articulations). Chondrification and ossification follow to form the ribs. The costal processes remain diminutive and are fused with the transverse processes in the cervical and lumbar regions.
- The sternum arises from a pair of mesenchymal bands on the ventrolateral aspects of the body wall. These unite progressively from before backwards and obtain connection with the ribs and cartilages.

- The mesenchyme of the sternum undergoes chondrification at nine weeks and ossification at about five months. The segmentation of the sternum is a feature secondarily acquired.

DEVELOPMENT OF LIMB BUDS AND TAIL BUD

- The limbs are outgrowths from somatopleure.
- Fore limb bud forms very early in development.
- After some time, the hind limb bud and tail bud form.

MODULE-37: DEVELOPMENT OF SENSE ORGANS

Learning outcomes

- At the end of this module the learner will be able to know about the development of
  - eye,
  - ear and
  - skin.

DEVELOPMENT OF SENSE ORGANS

- Lamellated corpuscles are differentiated from a mass of mesenchymal cells clustering around a nerve termination. These multiply, flatten and give rise to concentric fibrous lamellae, the Pacinian corpuscles. A tactile corpuscle originates with a looping plexus of terminal nerve fibres located just beneath the epidermis and this plexus becomes encapsulated along with a cluster of mesenchymal cells.
- Local thickenings of lingual epithelium present taste buds. The basal cells gets elongated and extend towards the surface and specialized into taste cells ending in hair like tips, while others become columnar supporting cells. The gustatory cells are connected to the nerve terminations.
- The first indication of the olfactory epithelium is the thickening of ectoderm of the ventro-lateral surfaces of the head olfactory placodes. These are concerned into olfactory pits which elongate and from the nasal cavities. Rupture of the plate at the deep end of the olfactory sac produces the primitive choanae or posterior nares.

DEVELOPMENT OF EYE

- The eye is derived from three sources
  - The optic nerves and retina from the forebrain
  - The lens from the ectoderm of the head and
  - The accessory tunics from the adjacent mesenchyme.
- From the floor of the forebrain on each side, a diverticulum develops as the optic vesicle. This vesicle elongates to from the optic stalk and it terminates by widening out to form the optic cup. The optic cup is formed by indentation of its distal wall brought about by rapid marginal growth. The optic stalk forms optic nerve and the cup forms the anterior wall forming the nervous portion and the posterior wall, pigmentary layer.

- Meanwhile the surface ectoderm overlying the optic vesicle thickens into a lens placode and this pockets inwards to produce a lens vesicle, which occupies the cavity of the optic cup. The lens vesicle has a layer of cubical cells in front forming the epithelium of the lens and the cells of the back wall from elongated lens fibres.

- The mesoderm surrounding the optic cup forms the sclera, cornea and the chorioid. The vitreous humour is a secretory body from both retina and lens. Later probably and invading mesenchyme also contributes to its structure.

DEVELOPMENT OF EAR

- The ***external ear*** is derived from ectoderm. A series of small swellings develop around the first two branchial grooves called the *auricular hillocks* give rise to the *external*.

- The ***middle ear*** is derived from endoderm. The dorsal projection of the first pharyngeal pouch retains its proximity to the otocyst and becomes the lining of the *eustachian tube* and the *middle ear cavity*.
- The ***internal ear*** is derived from ectoderm. A thickened ectodermal plate, the *auditory placode* located on each side of the hindbrain becomes the auditory pit, which soon close into the *otocyst*. These sink into the mesoderm and get detached from the ectoderm. From the otocyst, the membranous labyrinth and neuroepithelium are developed.

DEVELOPMENT OF SKIN

- The integument has a double origin.
- The epidermis is derived from ectoderm and the dermis or corium from the mesoderm.
- From the ectoderm, nails, hoof, horn, hair, sebaceous glands, sweet glands, mammary glands and arrector pili muscle are developed.