قسم التقنيات الاحيائية

مادة : الانسجة و التحضيرات المجهرية

المرحلة الثانية

الكورس الاول

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Lecture 1..... Micro-technique

Definitions:

- **Micro-technique: The art of preparing objects for examination under the microscope and of preserving objects so prepared.**
- **Microscopy: is the technical field of using microscopes to view samples and objects that cannot be seen with the unaided eye. There are two well-known branches of microscopy: Optical and Electron microscopy.**
- **Microscope: (from the Ancient Greek: *mikrós*, "small" and *skopeîn*, "to look" or "see") is an instrument used to see objects that are too small for the naked eye. The science of investigating small objects using such an instrument is called microscopy.**

Types of microscopes:

Microscopes can be separated into several different classes. One grouping is based on what interacts with the sample to generate the image, i.e., light or photons (optical microscopes), electrons (electron microscopes).

A- Optical microscope (LIGHT MICROSCOPY), the most common and first to be invented, uses light to image the sample. All types based on the interaction of light with tissue components and are used to study tissue features in different ways. Many wavelengths of light, ranging from the ultraviolet to the visible can be used to cause samples to fluoresce to allow viewing by eye or with the use of specifically sensitive cameras.

Types of Optical microscope:

1-Bright-Field Microscopy (Conventional)

Widely used by students of histology, stained preparations are examined by means of ordinary light that passes through the specimen. The microscope includes an optical system and mechanisms to move and focus the specimen (Figure 1).

The optical components consist of three lenses. The condenser collects and focuses a cone of light that illuminates the object to be observed. The objective lens enlarges and projects the image of the object in the direction of the eyepiece. The eyepiece or ocular lens further magnifies this image and projects it onto the viewer's retina or a charge-coupled device (CCD) highly sensitive to low light levels with a monitor and camera. The total magnification is obtained by multiplying the magnifying power of the objective and ocular lenses.

2-Fluorescence Microscopy

When certain cellular substances are irradiated by light of a proper wavelength, they emit light with a longer wavelength—a phenomenon called fluorescence.

Fluorescent compounds with affinity for specific cell macromolecules may be used as fluorescent stains. For examples: Alcridine orange, which binds both DNA and RNA. Under light microscope give orange fluorescent emit). Other compounds such as DAPI and Hoechst stain specifically bind DNA and are used to stain cell nuclei, emitting a characteristic blue fluorescence under UV. Another important

application of fluorescence microscopy, is when Antibodies labeled with fluorescent compounds are extremely important in immunohistologic staining.

In fluorescence microscopy, tissue sections are usually irradiated with ultraviolet (UV) light, the fluorescent substances appear brilliant on a dark background. For this method, the microscope has a strong UV light source and special filters that select rays of different wavelengths emitted by the substances.

3-Phase-contrast microscopy

Is based on the principle that light changes its speed when passing through cellular and extracellular structures. These changes are used by the phase-contrast system to cause the structures to appear lighter or darker in relation to each other. Because they allow the examination of cells without fixation or staining, so, the use of phase contrast does not require staining to view the slide. Phase-contrast microscopes are prominent tools in all cell culture laboratories. This microscope technique used to study the cell cycle in live cells.

B-Electron microscope :

Are based on the interaction of tissue components with beams of electrons. The wavelength in the electron beam is much shorter than that of light, allowing a 1000-fold increase in resolution.

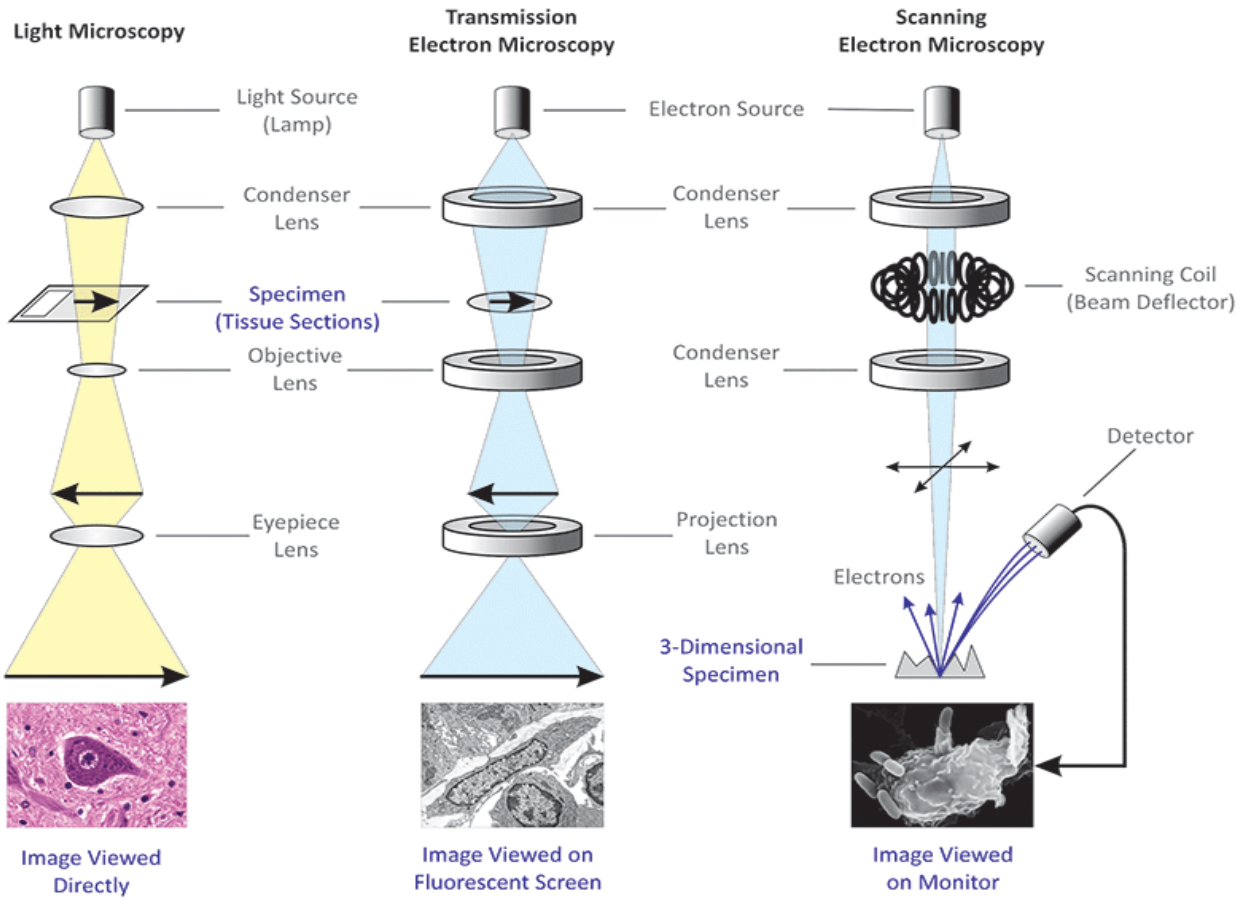
1-Transmission Electron Microscopy (TEM):

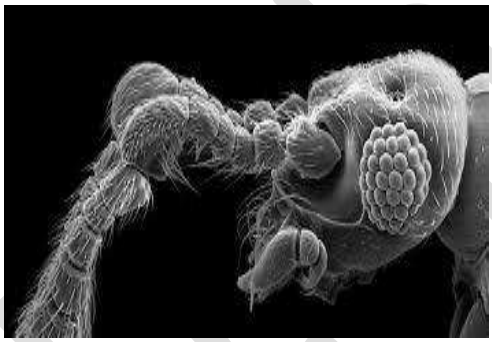
Is an imaging system that permits resolution around 3 nm. This high resolution allows magnifications of up to 400,000 times to be viewed in detail. Unfortunately, this level of magnification applies only to isolated macromolecules or particles. Very thin tissue sections can be observed with details at magnifications of up to about 120,000 times.

In the TEM a metallic filament cathode emits electrons that move toward an anode, a metal plate with a central hole that forms a beam of electrons passing through it. The voltage difference between cathode and anode can be varied between roughly 60 and 120 kV, producing electron beams of different wavelengths. The beam is focused by passing through electromagnets whose strength is also variable.

2-Scanning Electron Microscopy (SEM):

Is provides a high resolution view of the surfaces of cells, tissues, and organs. Like the TEM, this microscope produces and focuses a very narrow beam of electrons, but in this instrument the beam does not pass through the specimen. Instead, the surface of the specimen is first dried and spray-coated with a very thin layer of heavy metal (often gold) through which electrons do not pass readily. When the beam is scanned from point to point across the specimen, it interacts with the metal atoms and produces reflected electrons or secondary electrons emitted from the metal. These are captured by a detector, and the resulting signal is processed to produce a black-and-white image on a monitor.





General methods in microscopic techniques

A. **<u>Non-sectioning methods</u>: In this method ,the samples do not require sectioning ,instead its treated in different ways according to the type of the sample ,which is include the following methods:**
   1. **Smear method / المسحة**
   2. **Squash method /الهرس**
   3. **Maceration method / النقع**
   4. **Printing method / الطبع**
   5. **Spreading method / النشر**
   6. **Whole mount method / العينة الكاملة**
   7. **Dry mount method / العينة الجافة**
   8. **Wet mount method / العينة الرطبة**

Smearing:

Applicate on liquid tissues as in: Blood, seminal fluid, bacterial cultures. The sample spread as a thin or thick layer on a clean glass slide, fixed, stained and mounted. Thin smear used in the case of differential count of white blood cells .Thick smear used in the case of malaria diagnosis in the blood.

In brief, the steps necessary in the preparation of fluid specimen smears include the following:

1. **Smearing the material itself into a layer of the required thickness.**
2. **Fixing the layer to ensure its adherence to the slide and to make sure that the contained cells remain in their normal shape.**
3. **The staining and mounting of the fixed smears.**

Fixing process achieved through drying by air or head or by alcohol or in one of the conventional fixatives (For example: 2% of osmic acid solution).

Squashing:

Squash is prepared through pressing the sample piece by a cover glass on a clean glass slide. A drop of water or stain solution mixed with the sample piece before squashing it.

The squash preparations are temporary .It is not easy to make them permanent slides because of the improper dehydration or clearing for the sample tissue under the cover slide. Also, removing the cover cause loosing most of the sample parts and this will lead to bad preparations.

Squash method used to study chromosomes, study parts of mitosis in plants as in radical tips of onion or in animal cells or to study giant chromosomes in salivary gland of fruit fly (Drosophila).

Maceration:

A chemical method used to disassemble the tissue or separate tissue components which are tightly bind to each other, so we can study the shape of the cells in a particular tissue. For example, the study of muscle fibers and bone preparation technique whereby a clean skeleton is obtained from a vertebrate carcass by leaving it to decompose inside a closed container at near-constant temperature. This may be done as part of a forensic investigation, as a recovered body is too badly decomposed for a meaningful autopsy.

For this purpose, special solutions used and followed by a fixative, ex.:

1. **Alcohol 30% for 24 hr. or more.**
2. **One part formalin in 100 parts of 10% NaCl solution for 24 hr. or more.**
3. **NaCl 1% for 24 hr. or more.**
4. **Aquatic solution of chromic acid 0.2 % for 24 hr.**
5. **Nitric acid 20% for 24 hr. (usually used for smooth muscle in urine bladder).**
6. **Saturated solution of boric acid in saline with 2 drops of iodide for each 25 ml, soak the sample for 2-3 days.**
7. **Soaking with enzymes (usually used for connective tissue).and the tissue easily separated by a needle in a process known as teasing.**

Printing:

Tissue printing is a method by which a piece of tissue is placed on an adhesive substrate ,and then removed ,leaving behind a layer of isolated cells ,usually used to study the intracellular parasites as in *Leishmania* –amastigote stage ,which infect the spleen and liver macrophages.

Dry mount:

The simplest kind of mounting, the object is merely placed on the slide. A cover slip may be placed on top to protect the specimen and the microscope's objective and to keep the specimen still and pressed flat. This mounting can be successfully used for viewing specimens like pollen, feathers, hairs, etc.

Wet mount:

Or temporary mount, the specimen is placed in a drop of water or other liquid held between the slide and the cover slip by surface tension. This method is commonly used, for example, to view microscopic organisms that grow in pond water or other liquid media, especially when studying their movement and behavior. Care must be taken to exclude air bubbles that would interfere with the viewing and hamper the organisms' movements.

Preservation:

the process in which the sample preserved in a solution known as preservatives that protect the sample and prevent dehydration, shrinkage, swelling, petrification by bacteria or fungi and autolysis by enzymes. It includes 3 types:

1. **Preservation in alcohol (70-80)% alcohol**
2. **Preservation in fixatives for example (Formalin –acetic acid alcohol –F.A.A, 10% neutral formalin, Buins solution).**
3. **Preservation in paraffin wax: used in the step of embedding, it is considered the best preservatives for a long time (in low temperature degree).**

Lecture 2 ..... Microtechnique

Preparation of Tissues for study

The most common procedure used in histologic research is the preparation of tissue slices or "sections" that can be examined visually with transmitted light. Because most tissues and organs are too thick for light to pass through, thin translucent sections are cut from them and placed on glass slides for microscopic examination of the internal structures.

The ideal microscopic preparation is preserved so that the tissue on the slide has the same structural features it had in the body. However, this is often not feasible because the preparation process can remove cellular lipid, with slight distortions of cell structure.

B-Sectioning method (Paraffin method): This method involve preparing sectioning for the sample from different levels (transfer, cross or longitudinal sectioning), either by free hand or by a special instrument (Microtome).

Tissues taken from the body for disease diagnosis must be processed in the histology lab. To produce microscopic slides, that is viewed under the microscope by pathologist. The techniques for processing the tissues, weather biopsies, large specimens removed at surgery, or tissues from autopsy, are described below:

Paraffin method is used in preparing a selected portion of tissue for pathologic examination .the tissue is fixed, dehydrated, and infiltrated and embedded in paraffin wax, forming a block that is cut with a microtome into slices with 3-10 µm thickness for light microscope, but electron microscopy requires sections less than 1 µm thick. In brief the steps for preparing paraffin sections for histology include:

1. **Fixation of the specimen and then washing the fixative.**
2. **Dehydration: in order to remove water from the tissue to impregnate with a fluid capable of dissolving wax.**
3. **Clearing: removing the dehydrating agent, a chemical substance, solvent or miscible with molten wax used for that purpose.**
4. **Infilteration: socking the cleared specimen in molten wax long enough to ensure that it will become completely impregnated.**
5. **Embedding: casting the new impregnated specimen into a rectangular block of wax (paraffin).**
6. **Cutting: into sections by attaching the block of wax to a holder and then inserted into suitable microtome, which cut the block into ribbons of sections.**
7. **Placing the ribbons on a glass slides in such a manner that they will lie flat and that the contained sections will be adherent, when the wax has been dissolved.**
8. **Removal of the wax by heat and filter paper and by washing with clearing agent.**
9. **Rehydration the specimen.**
10. **Staining (Hematoxylin –Eosin stains).**
11. **Mounting by Canada balsam.**

Fixation: Small pieces of tissue are placed in solutions of chemicals that cross-link proteins and inactivate degradative enzymes, which preserves cell and tissue structure from decay, either through autolysis or putrefaction.

The most common fixative for light microscopy is 10% neutral buffered formalin (4% formaldehyde in phosphate buffered saline). For electron microscopy, the most common fixative is gluteraldehyde (2% solution in PBS).

Purpose of fixation:

1. **To preserve the specimen in shape it had before fixation.**
2. **Maintain the structure of the cells and sub-cellular components such as cell organelles (nucleus, endoplasmic reticulum, mitochondria).**
3. **To prepare the specimen to resist many changes that occur during latter treatments (in the embedding process) or shrinkage occur by dehydration.**
4. **To protect the specimen from damage by proteolytic enzyme.**

5. **Fixatives are toxic to most common microorganisms (bacteria) , which might exist in the tissue samples.**
6. **The fixative work as (Mordant) through increasing the specimen affinity to stain.**

Washing: at the end of the fixation process, the specimen should be washed, in order to remove the fixative remains and avoid over-fixing and prevent reaction between unbound component of the fixative solution and other chemical in latter treatments, especially with staining.

Dehydration: (الانكاز-إزالة الماء) mean "removing of water from". It is an important step in the preparation of specimens for microscopic examination. The reason why water should be removed from the specimen includes:

1. **Various types of stains do not mix or dissolved in water.**
2. **No mixing or reaction occurs between water and paraffin wax, which is used in Infiltration and Embedding process.**
3. **Most of the media in which the specimen will be mounted are not miscible with water.**

The commonest reagent used for dehydration is (Ethyl) alcohol, which is available in most labs as: neutral grain spirit (95%) and absolute alcohol (100%).It is conventional to employ the series of 30% ,50%, 70% and 95% and to pass the specimen from one of these strength to the next ,leaving it in each sufficiently long to become impregnated.

(Acetone) is very first, but a fire hazard, so it is only safe for small hand processed sets of tissues. (Dioxan`) can be used without clearing, but has toxic fumes.

Clearing: the process of removing alcohol from dehydrated tissue. It is very important step because the resinous media used for mounting the specimens and waxes used for embedding before cutting sections are not miscible with alcohol than they are with ether.

Many of the reagents used for clearing have a high index of refraction, so that they make objects saturated with them appear more transparent or clearer. The commonest clearing agent is (Xylene). It tend to render objects little brittle. (Toluene) works well, and it's more tolerant to small amounts of water left in the tissue, but is three times more expensive than xylene. (Chloroform), also used for clearing, but is a health hazard, and is slow.

Infiltration: (التشريب) preparing a specimen for examination require its infiltration with an embedding medium that allows it to be thinly sliced. Typically in the range of 5-15 µm (1 µm = 1/1000 mm).

Infilteration with paraffin wax: the paraffin wax chosen depending on several factors:

1. **Specimen type :**
   - **Solid specimens should be infiltered with paraffin melted between 60-66 ºC.**
   - **Little bit solid specimens should be infiltered with paraffin melted between 56-58 ºC.**
   - **Soft specimens should be infiltered with paraffin melted between 50-55 ºC.**
2. **Section thickness:**
   - **Solid paraffin melted between 60-66 ºC, traditionally used with thin sections (< 5 µm).**

- **Soft paraffin melted between 50-55 ºC, traditionally used with thick sections (> 7 µm).**

3. **Room temperature: Paraffin with high melting point requires high room temperature.**

Other choices:

- **Celloiden (Nitrocellulose): used to get high surface area sections and thickness more than 20 µm and with less shrinkage and rupture.**
- **Gelatin: used when the specimens are loose, friable tissues like embryos and brain.**
- **Plastics: used when the specimen should be examined by electron microscope (EM), and to get sections with thinner thickness (less than 1 µm). For example: Methyl methacrylate, Glycol methacrylate, Araldite, and Epon.**

Embedding: A process in which the infilterated specimens coated and impregnated with an embedding medium. In order to increase their mechanical strength and stability and facilitate sectioning into thin slices. This is achieved by preparing a block. It is necessary to decide what type of vessel will be used to cast the final block. This is depending on the size of the tissue piece. Very large pieces are often embedded with the aid of two thick L shape pieces of metal, which then fitted together, from a rectangular mold of varying dimensions. (As show in the fingers). In other times it is preferred to prepare a paper box, the preparation of a paper box is easy; the method is shown in the figures).

Advantage of embedding with paraffin:

1. **Simple and quick.**
2. **Specimens embedded with paraffin can be preserved in a dry place for a long period.**
3. **Thin sections can be prepared from paraffin blocks.**
4. **Sectioning of paraffin blocks gives ribbon contain a series of sections for the same sample tissue.**
5. **Easily affixing the paraffin ribbon on a glass slide.**
6. **Easily to remove the paraffin.**
7. **Paraffin is available with various melting points.**
8. **The cost is not expensive.**

Sectioning: a section is a thin slice cut from biological materials with a view to study either the cells themselves or their arrangements. Those sections may be cut at any angle. They are usually taken through any one of the three plans, which are known as (Transverse- عرضي, Sagittal- سهمي, Frontal- جبهي).

Once the tissues have been embedded, they must be cut into sections that can be placed on a slide. This is done with a "microtome", which is nothing more than a knife with a mechanism for advancing a paraffin block standard distances across it.

A microtome: is a tool used to cut extremely thin slices of material, known as sections. Important in science, microtomes are used in microscopy, allowing for the preparation of samples for observation under transmitted light or electron radiation. Microtomes use steel, glass, or diamond blades depending upon the specimen being sliced and the desired thickness of the sections being cut. Steel blades are used to prepare sections of animal or plant tissues for light microscopy Glass knives are used to slice sections for light microscopy and to slice very thin sections for electron microscopy. Industrial grade diamond

knives are used to slice hard materials such as bone, teeth and plant matter for both light microscopy and for electron microscopy.

Staining: is an auxiliary technique used in microscopy to enhance contrast in the microscopic image? Stains and dyes are frequently used in biology and medicine to highlight structures in biological tissues for viewing, often with the aid of different microscopes. Biological staining is also used to mark cells in flow cytometry, and to flag proteins or nucleic acids in gel electrophoresis.

Many specimens after being impregnated with mounting media become so transparent that their structure cannot be observed under the microscope to overcome this difficulty, such specimens are commonly stained.

Staining the sections of paraffin methods:

Because paraffin sections are colorless, the specimen is not yet suitable for light microscopic examination. To stain tissue sections, the paraffin must be dissolved out again with xylol, and the slide must then be rehydrated through series of solutions of descending alcohol concentration. The tissue on the slide is then stained with haematoxylin in water and stained with eosin in alcohol.

Haematoxylin and eosin (H&E) staining: is used most commonly. Hematoxylin stains DNA in the cell nucleus, RNA-rich portions of the cytoplasm, and the matrix of cartilage, producing a dark blue or purple colour. In contrast, eosin stains other cytoplasmic structures and collagen pink. Here eosin is considered a counterstain, which is usually a single dye applied separately to distinguish additional features of a tissue.

Staining terms:

Chromophore: is part of a molecule responsible for its color.

Auxochrome: a group of atoms attached to a chromophore which modifies the ability of that chromophore to absorb light, alters both the wavelength and intensity of absorption. (Responsible of binding the stain with the tissue).

Alkaline stains: the stain that contain colorful organic basic group that react with the acidic colorless radical group in the tissue, such as: acetate group –COOH, chloride (CL-),sulphate –SO3--. For example: Safranin O, Haematoxylin.

Acidic stains: the stain that contain colorful organic acidic group that bind with the colorless metabolic base of the tissue, such as: (Na+,K+). Include water or alcoholic soluble stains. Eosin Y.

Neutral stains: the stain that contain alkaline and acidic groups (with +ve and –ve ions) in its chromophore. Mostly those stain which are alcoholic soluble and may form colloidal solutions. For example: Neutral red.

Nuclear stains: a stain for cell nuclei usually based on the binding of a basic dye to DNA. Since the cell nuclear contains the nucleic acid which is tend to be stained with alkaline stains, therefore, nuclear stains are alkaline stains. For example: Haematoxylin.

Cytoplasmic stains: a stain for cell cytoplasm, Since the cell cytoplasm is alkaline ,it tend to be stained with acidic stains, the alkaline components of the cytoplasm that bind with acidic groups of the stain

cause the formation of colorful insoluble salts. Therefore, cytoplasmic stains are acidic stains. For example: Eosin.

Progressive staining: a procedure in which staining is continued until the desired intensity of coloring of tissue elements is attained.

Regressive staining: a type of staining in which tissues are over stained and excess dye then removed selectively until the desired intensity is obtained.

Counter staining: a second stain added to a previously stained tissue sample to make cellular details more distinct.

Mounting: The final mounting of an object or section for microscopic examination consists in cementing it between a slide and cover slip in a medium or mountant that will preserve it permanently and retain it in a sufficiently transparent condition for study.

Types of mounting media include:

1. **Gum media: EX. Gum acacia**
2. **Resinous media: EX. Canada balsam**

*** The last steps for preparing permanent slides: (Cleaning, Labeling, Storage).**

Mordant:

A chemical compound used to set dyes on a fabrics or tissue by reacting with the stain to form an insoluble, colored precipitate. When excess dye solution is washed away, the mordating stain remains.

Mordant include tannic acid, alum, Na-chloride, and certain salts of aluminum, chromium, copper, iron, iodine, potassium. Iodine is used as a mordant to set the first dye in gram stains. The three methods used for mordating are:

1. **Pre-mordating: the substrate is treated with the mordant and then dyed.**
2. **Meta-mordating: the mordant is added in the dye both themselves.**
3. **Post-mordating: the dyed material is treated with a mordant.**

Metachromasia:

Certain dyes react with tissue components that shift their normal color from blue to red or purple, this absorbance changes is called "Metachromasia ".

The underlying mechanisms for metachromasia are the presence of polyanions within tissue. When those tissues are stained with a concentrated basic dye solution, such as toluidine blue, the dye molecules are sufficiently close to form dimeric and polymeric aggregates. The absorption properties of these aggregations differ from those of the individual non-aggregated dye molecules.

Cell and tissue that have high concentrations of ionized sulfate and phosphate groups, such as the ground substances of cartilage heparin containing granules of mast cells , and rough endoplasmic reticulum of plasma cells , exhibit metachromasia ,therefore toluidine blue will appear purple to red when it stains there components.

Frozen sections: is a rapid way to fix and mount histology sections .it is used in surgical removal of tumors, and allows rapid determination of margin (that the tumor has been completely removed) it can also be used to determine if tumor is malignant when it is found incidentally during surgery on a patient.

There are two circumstances under which paraffin sections cannot be used:

1) **Where it is desired to preserve in the tissues some fatty materials that would be dissolved out by the reagents used prior to impregnate.**
2) **When speed is of primary importance as in the production of quick sections from tumors for diagnostic purpose.**

The main steps are involved in frozen section preparation:

1. **Freezing the tissue sample (Carbone dioxide or isopentane) (Temperature of – 5 ºC.).**
2. **Sectioning the frozen tissues (cryostat –cutting thickness 5-10 µm).**
3. **Staining the cut sections (Haematoxylin and eosin , methylene blue)**

Medical application:

Biopsies are tissue samples removed during surgery or routine medical procedures. In the operating room, biopsies are fixed in vials of formalin for processing and microscopic analysis in a pathology laboratory.

If results of such analyses are required before the medical procedure is completed, for example to know whether a growth is malignant before the patient is closed, a much more rapid processing method is used.

Lecture 3 ..... Histology

Histology is the study of the tissues of the body and how these tissues are arranged to constitute organs. It involves all aspects of tissue biology, with the focus on how cells' structure and arrangement optimize functions specific to each organ. Organs are formed by an orderly combination of several tissues, and the precise combination of these tissues allows the functioning of each organ and of the organism as a whole.

Despite its complexity, the human body is composed of only four basic types of tissue:

A. **Epithelia tissue**
B. **Connective tissue**
C. **Nerve tissue**
D. **Muscle tissue**

Table: Main characteristics of the four basic types of tissues.

Tissue	Cell	Extracellular Matrix	Main Fonctions
Epithelial	Aggregated polyhedral cells	Small amount	Lining of surface or body cavities; glandular secretion
Connective	Several types of fixed	Abundant amount	Support and protection of

	and wandering cells		**tissues/organs**
Muscle	**Elongated contractile cells**	**Moderate amount**	**Strong contraction; body movements**
Nervous	**Elongated cells with extremely fine processes**	**Very small amount**	**Transmission of nerve impulses**

EPITHELIAL TISSUES

There are two functional types of epithelium:

a) Lining epithelia: cover the free surfaces of the body and its cavities, e.g. epidermis, lining of the gastrointestinal tract and ducts

b) Glandular epithelium: represent all the varieties of epithelia that are specialized for secretion, which is the process by which cells release specific substances onto their apical surfaces.

A-Structural Characterization of Epithelia:

1. **Absence of nerves (except for a few axons in the deeper layers)**
2. **Absence of blood vessels — nutrition is by diffusion from the highly vascular connective tissue (known as the lamina propria).**
3. **Closely attached to each other forming a protective barrier.**
4. **Always has one free (apical) surface open to outside the body or inside cavity).**
5. **Always had one fixed (basal) section attached to underlying connective tissue?**
6. **Very good at regenerating (fixing itself). I.e. sunburn, skinned knee.**

B-Number of layers of cells:

1- Simple: an epithelium with only one layer

2- Stratified: with more layers.

3- Pseudostratified :epithelium appears to be more than one cell thick since the nuclei lie at different heights, but in fact, all the cells are in contact with the basement membrane.

C-Shape of cells at free surface: e.g. Squamous (flattened), Cuboidal, Columnar.

D-Surface specialization (if any) e.g. Keratinised, Ciliated.

Types of lining epithelium:

a) Simple squamous epithelium: a single layer of flattened cells. Ex.: Alveolar lining of the lung, renal corpuscle, Blood vessels.

b) Simple cuboidal epithelium: a single layer of box-shaped (cuboidal) cells. Ex.: Lining of ducts like kidney tubules, thyroid follicles.

c) Simple columnar epithelium: a single layer of tall cells. Ex.: Lining of intestine.

d) Pseudostratified columnar ciliated epithelium: although nuclei lie at different levels, all the cells are attached to the basement membrane and so there is only one layer. Ex.: Lining of trachea.

e) Stratified squamous epithelium (Non-keratinised): Many layers of cells; those at the free surface are flattened. Ex.: Lining of mouth, vagina and rectum.

f) Stratified squamous epithelium (keratinised): Many layers of cells; those at the free surface are flattened; the surface cells are dead and filled with an inert protein, keratin, forming flakes or squares. Ex.: Skin.

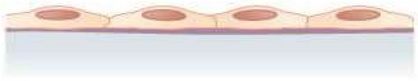
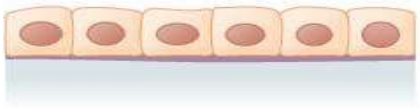
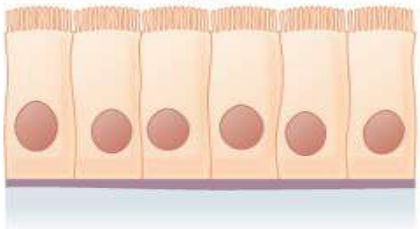
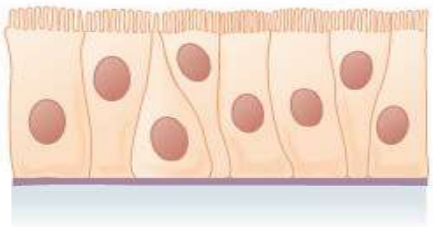
g) Stratified cuboidal epithelium: Many layers of cells; those at the free surface are cuboidal, Ex.: Sweat gland, Salivary gland and Mammary gland.

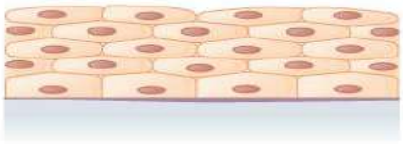
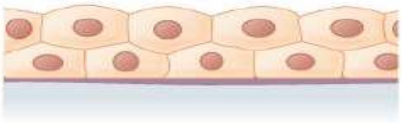
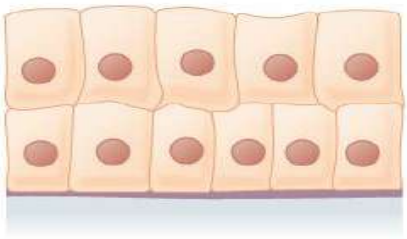
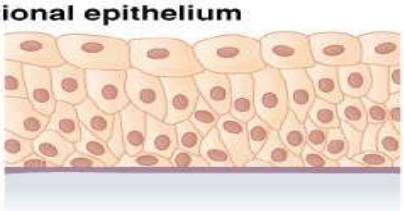
h) Stratified columnar epithelium: Many layers of cells; those at the free surface are columnar, Ex.: Male urethra.

k) Transitional epithelium: there are several layers of cells; those at the free or luminal surface are irregularly polyhedral (like squashed bubbles) and it is called transitional. Ex.: Bladder, ureter.

Specific names are given to epithelium in certain locations:

- **Endothelium: is the epithelial lining of the blood and lymphatic vessels.**
- **Endocardium: is the epithelial lining of ventricles and atria of the heart.**
- **Mesothelium: is the epithelium that lines the walls and covers the contents of the closed cavities of the body. I.e. the abdominal, pericardial, pleural cavities.**

Cells	Location
Simple squamous epithelium 	Air sacs of lungs and the lining of the heart, blood vessels, and lymphatic vessels
Simple cuboidal epithelium 	In ducts and secretory portions of small glands and in kidney tubules
Simple columnar epithelium 	Ciliated tissues are in bronchi, uterine tubes, and uterus; smooth (nonciliated tissues) are in the digestive tract, bladder
Pseudostratified columnar epithelium 	Ciliated tissue lines the trachea and much of the upper respiratory tract

Stratified squamous epithelium 	Lines the esophagus, mouth, and vagina
Stratified cuboidal epithelium 	Sweat glands, salivary glands, and the mammary glands
Stratified columnar epithelium 	The male urethra and the ducts of some glands
Transitional epithelium 	Lines the bladder, uretha, and the ureters

Epithelial Cell polarity

Epithelial cells generally show polarity, with organelles and membrane proteins distributed unevenly within the cell. The region of the cell contacting the ECM and connective tissue is called the **basal pole** and the opposite end, usually facing a space, is the **apical pole**, with the two poles differing significantly in both structure and function. Regions of cuboidal or columnar cells that adjoin neighboring cells comprise the cells' **lateral surfaces**; cell membranes here often have numerous folds which increase the area and functional capacity of that surface.

SPECIALIZATIONS OF THE APICAL CELL SURFACE:

The apical ends of many tall or cuboidal epithelial cells face an organ's lumen and often have specialized projecting structures. These function either to increase the apical surface area for absorption or to move substances along the epithelial surface.

1. **Microvilli** are plasma membrane invagination's of the apical surface that greatly increase the area available for absorption (or secretion). They contain a core of actin microfilaments and are covered by a coat of surface bound carbohydrates, called the **glycocalyx**.

   In kidney found in proximal tubules, known as **Brush border.** At the apices of cells lining the ductus epididymidis and ductus deferens of the male genital tract, its known as **Stereocilia** .

2. **Cilia** are also plasma membrane and cytoplasmic projections from the apical surface. They are specializations for motility and contain a core of microtubules arranged in a specific configuration called the **axoneme**. Cilia are longer and thicker than microvilli. Cilia move back and forth to propel fluid and particles in one direction.

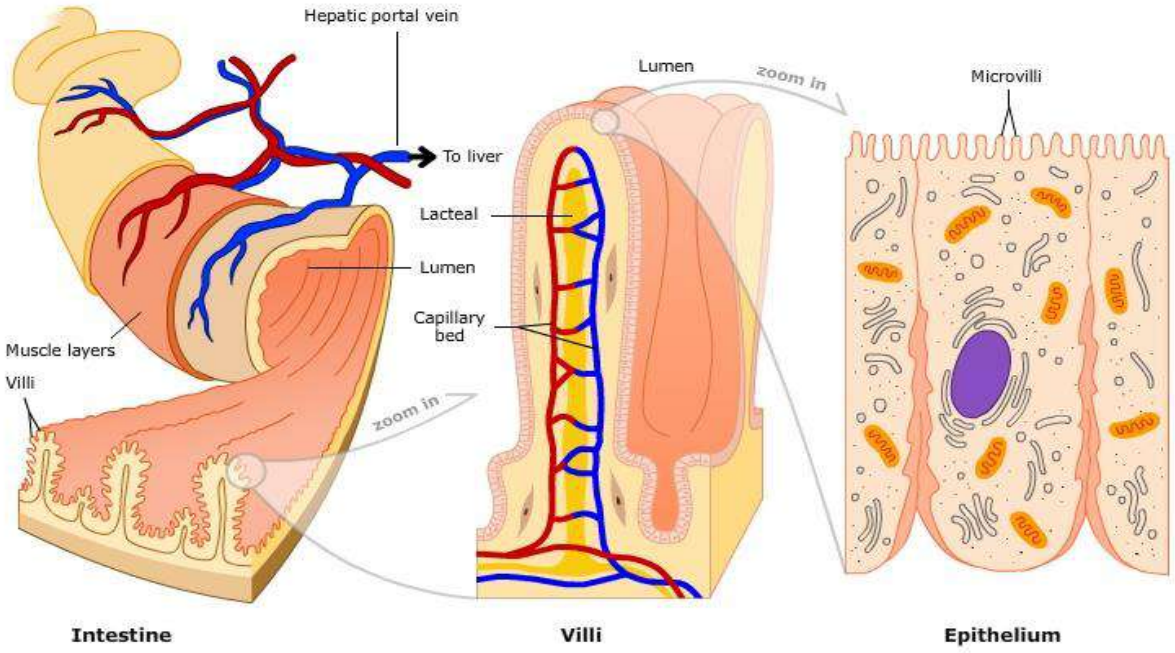


Figure: apical cell surface specializations, cilia on the respiratory epithelial cells.

3. **Flagella**, which have the same microstructure as cilia, occur singly and are much longer in length. They provide motility for spermatozoa.

Lecture 4..... Histology

Glandular (Secretary) epithelium:

It is a modified type of epithelial tissue specialized in production of secretions. Secretion is one major function of epithelial cells.

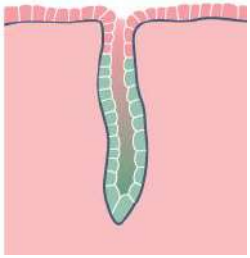
There are two major classifications of glands: (Endocrine glands) and (Exocrine glands). Endocrine glands secrete their product into the extracellular space where it is rapidly taken up by the blood vascular system. The exocrine glands secrete their products into a duct that then delivers the product to the lumen of an organ or onto the free surface of the epithelium.

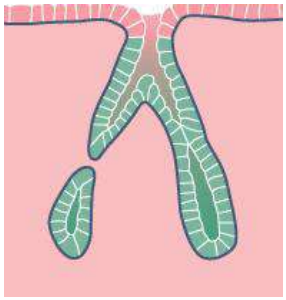
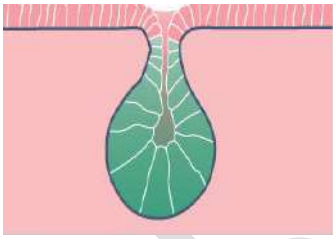
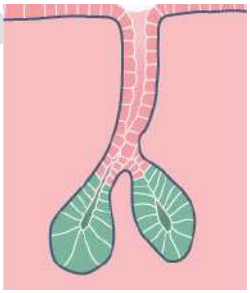
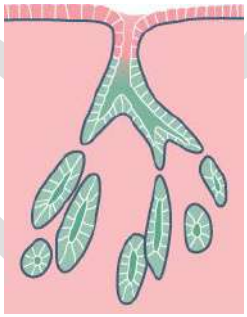
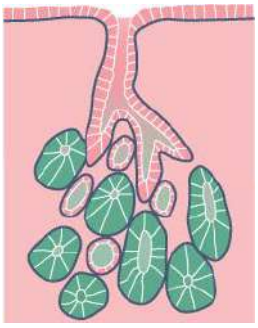
According to the number of cells, glands classified in 2 types:

Glands classification: It is classified according to:

A. **Unicellular gland: consist of single, isolated glandular cells such as the goblet cells which are modified columnar epithelial cells that synthesize and secrete mucus .Scattered among cells of many simple epithelia, especially respiratory and Gastrointestinal tracts. Apical cytoplasm contains mucigen granules. Mucigen is composed of neutral and acidic proteoglycans called mucopolysaccharides.**

B. **Multicellular glands: are composed of clusters of cells and are formed from the invagination / enfolding of epithelial cells and subsequent growth in the underlying connective tissue. It is classified according to the following :**
   1- The duct.
   2- The secretory part (shape).
   3- Nature of secretion.
   4- Mode of secretion.

Simple , Tubular	Simple , coiled , tubular
	
A single, straight tubular lumen into which the secretory products are discharged eg. Intestinal	**A single tube tightly coiled in 3 dimensions eg. Sweat glands.**

gland.	
Simple , branched , tubular  **Several tubular secretory portions (T) converge onto a single unbranched duct (D) eg. Mucus-secreting gland of the stomach (Gastric gland).**	
Simple , single ,Acinar (Alveolar)  **Occur in the form of pockets in epithelial surfaces. Lined by secretory cells eg. penile urethra**	**Simple , Branched , Acinar (Alveolar)**  **Each gland consists of several secretory acini (A) that empty into a single excretory Duct eg. Sebaceous glands, (holocrine).**
Compound , Branched , Tubular  **Secretory portion is branched and coiled and the duct system is also Branched. eg. Brunner's gland of the duodenum.**	**Compound , Acinar (Alveolar)**  **Secretory units are acinar and drain into a branched duct system eg. Pancreas. Mammary gland.**

<u>Types of the Secretion (mucous, serous, mixed)</u>

1. Mucous glands are characterized by their viscous secretions which contain a variety of mucins consisting of carbohydrate- rich glycoproteins. When mucins combine with water, they form the viscous solution known as mucus that has important protective and lubricating functions at epithelial surfaces. Secretory units are mostly tubular and composed of tall pyramidal to columnar secretory cells. Their staining with standard dyes (e.g., H&E) is poor and renders the cytoplasm quite pale in sections.
2. Serous glands are characterized by their watery, protein-containing secretions which are made up of a watery fluid, which contains proteins and other components, including zymogens, bactericidal compounds, and ions. Secretory units are acinar and composed of shorter pyramidal cells arranged around a small lumen.

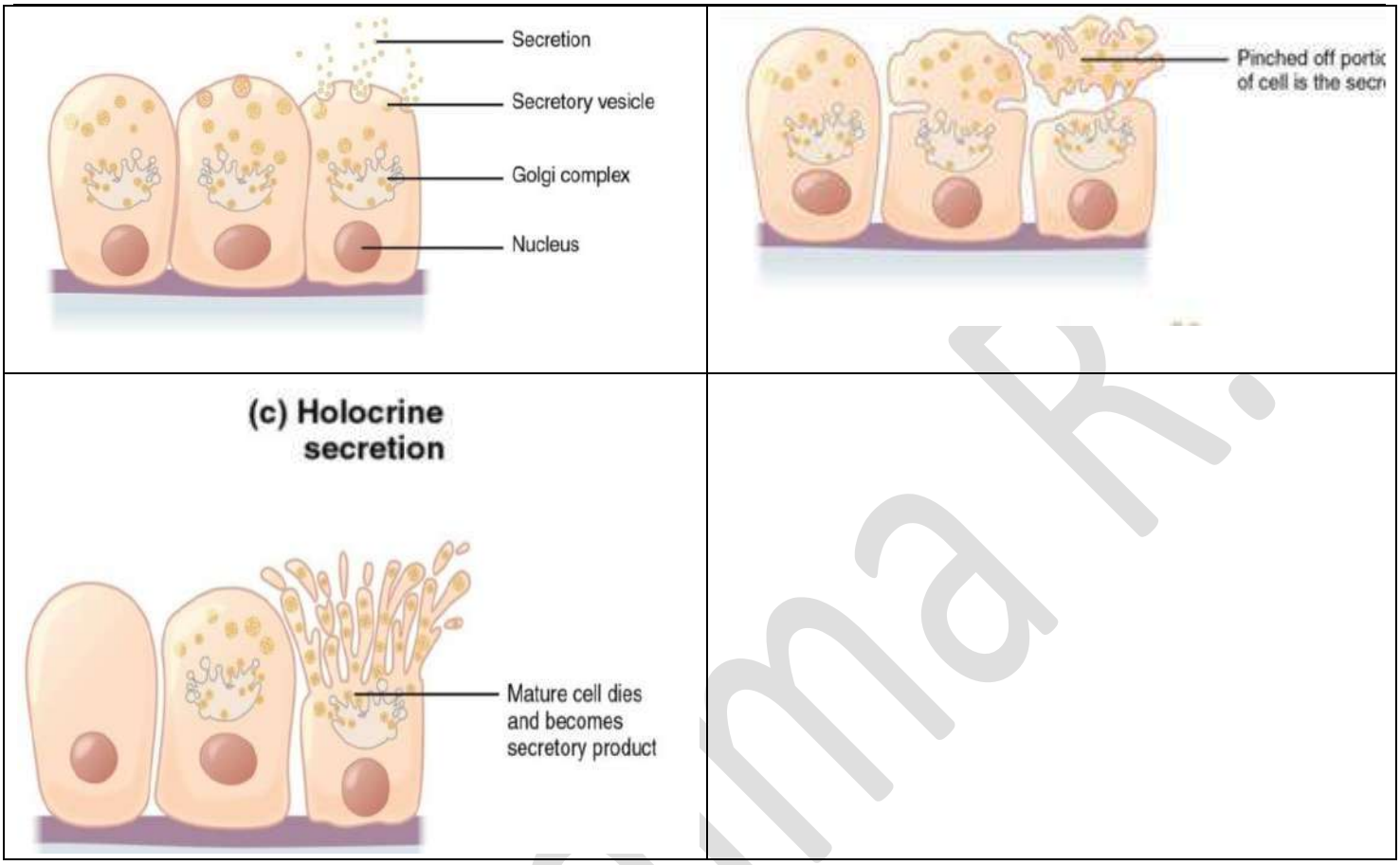
3. Mixed glands contain both mucous and serous secretory units, either separate or as mixed units.
a.Serous demilunes are crescent shaped groups of serous cells that appear to cap the distal ends of mucous secretory units in mixed units (also called crescents of Giannuzzi).
b. Intercellular canaliculi, located between mucous cells in mixed glands, have been described as delicate secretory channels that connect serous cells of demilunes with the central lumen.

Mechanisms of the Secretion
1. Merocrine secretion is the method of exocytosis; the membrane of the secretory granule fuses with the plasma membrane to release the contents of the granule. Most exocrine glands secrete by this mechanism, including salivary glands and pancreas.

2. Apocrine secretion is the mechanism whereby both the secretory product and a portion of the apical secretory cell cytoplasm are pinched off and released. This process has been described as decapitation secretion. Examples of this mechanism apparently occur in all apocrine glands and have been clearly demonstrated in apocrine sweat glands, mammary glands .Apocrine secretion has also been described in non-ciliated bronchiolar epithelial (Clara) cells of lung).

3. Holocrine secretion is the method involving the release of entire cells and their contained secretory product. This process is apparently the result of apoptosis which is programmed secretary cell death. Sebaceous glands, which secrete a lipid-rich sebum into hair follicles, are the classic examples of secretion by this mechanism.

(a) Merocrine secretion	(b) Apocrine secretion



CONECTIVE TISSUES

Connective tissue (CT) is a kind of animal tissue that supports, connects, or separates different types of tissues and organs of the body. All CT has three main components: cells, fibers, and extracellular matrices, all immersed in the body fluids.

Characteristics of CT:

1. **Cells are spread through an extracellular fluid.**
2. **Ground substance - A clear, colorless, and viscous fluid containing glycosaminoglycans and proteoglycans to fix the body water and the collagen fibers in the intercellular spaces. Ground substance slows the spread of pathogens.**
3. **Fibers. Not all types of CT are fibrous. Examples of non-fibrous CT include adipose tissue and blood.**
4. **Both the ground substance and proteins (fibers) create the matrix for CT.**
5. **Not adjacent to other cells**
6. **Vary in degrees of vascularity**

- **Extracellular matrix (ECM) :**

Is a complex structural entity surrounding and supporting cells that are found within mammalian tissues. The ECM is often referred to as the connective tissue. The ECM is composed of 3 major classes of biomolecules:

1. Structural proteins: collagen and elastin.

2. Specialized proteins: e.g. fibrillin, fibronectin, and laminin.

3.Proteoglycans:these are composed of a protein core to which is attached long chains of repeating disaccharide units termed of glycosaminoglycans (GAGs) forming extremely complex high molecular weight components of the ECM.

- **Connective tissue cells:**

1. **Fibroblasts: Spindle shaped cells with big ER and Golgi Synthesize most of complex carbohydrate of extracellular matrix and fibrous molecules (especially collagen) Proliferate and migrate in response to tissue injury.**

2. **Macrophages are a type of white blood cell, of the immune system, that engulfs and digests cellular debris, foreign substances, microbes, cancer cells, and anything else that does not have the type of proteins specific to healthy body cells on its surface[2] in a process called phagocytosis. These large phagocytes are found in essentially all tissues,[3] where they patrol for potential pathogens by amoeboid movement. They take various forms (with various names) throughout the body (e.g., histiocytes, Kupffer cells, alveolar macrophages, microglia, and others).**

3. **Mast cells: Immune Cells, Mediate immediate hypersensitivity reactions .Secrete histamine and Proteases. Cause plasma extravasation (oedema), itching, Activated by IgE receptors cross-linked by antigen.**

4. **Plasma cells: also called plasma B cells, are white blood cells that originate in the bone marrow and secrete large quantities of proteins called antibodies in response to being presented specific substances called antigens. These antibodies are transported from the plasma cells by the blood plasma and the lymphatic system to the site of the target antigen (foreign substance), where they initiate**

its neutralization or destruction. B cells differentiate into plasma cells that produce antibody molecules closely modeled after the receptors of the precursor B cell.

5. **Adipose cells (white fat cells): Mostly just under the skin Store lipids in the form of single droplet Effectors cells for insulin, Take up glucose and synthesize triglycerides for storage in the lipid droplet. Also endocrine organ – secrete leptin, a hormone responsible for appetite regulation .Different from brown fat cells that oxidize lipids to produce heat.**

6. **Leukocytes (Lymphocyte , Monocyte , Neutrophil , Eosinophil , Basophil)**

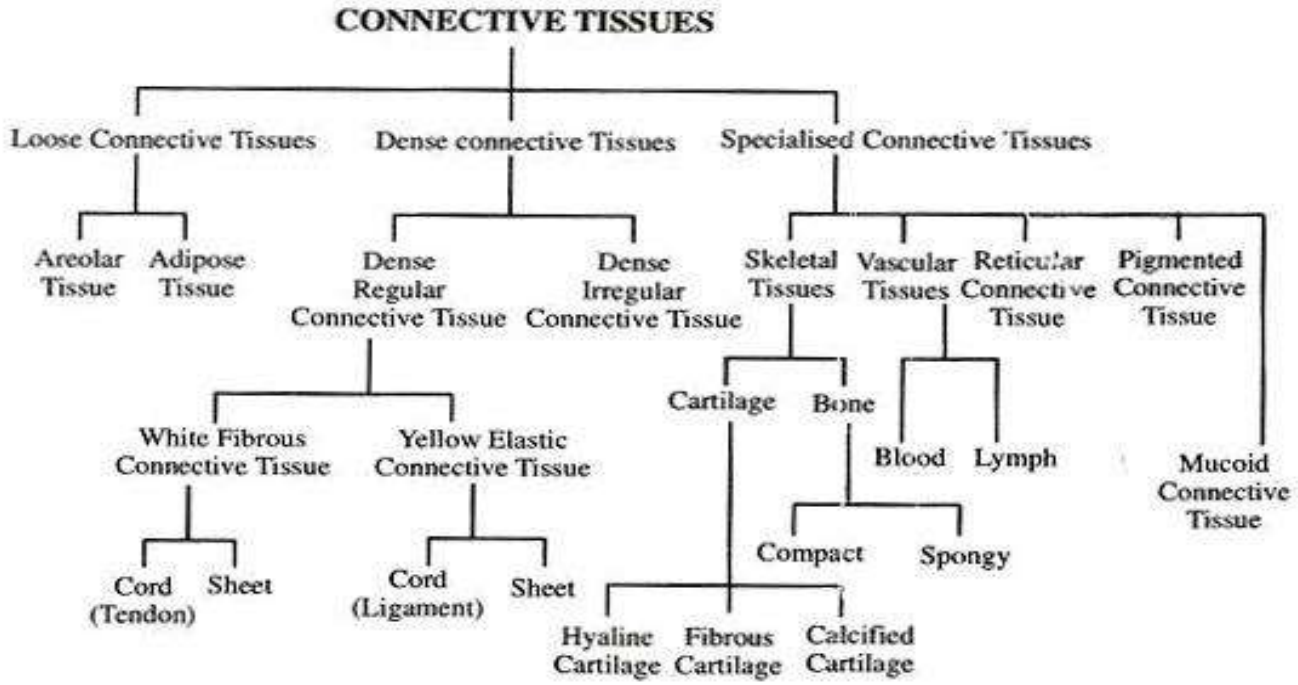
7. **Mesenchymal stem cells: Undifferentiated cells, proliferate and differentiate into fibroblasts, fat cells, and chondrocytes.**

❖ **Connective tissue fibers:**

1. **Collagenous fibers: consist of Alpha polypeptide chains (Type-I) , provide strength, Example location : tendon, ligament, skin, cornea, cartilage, bone, blood vessels, gut, and intervertebral disc. Example location : extracellular matrix**
2. **Elastic fibers: consist of elastic microfibril and elastin , can stretch and recoil,**
3. **Reticular fibers: consist of Type-III collagen, may help connect the tissue to organs or other types of tissue. Example location : liver, bone marrow, lymphatic organs**

Lecture 5..... Histology

Classification of connective tissues



Connective tissue proper:

1-Loose connective tissue:

Is the most common type of connective tissue in vertebrates?

a) Areolar Connective Tissue

b) Reticular Connective Tissue

Cells called Fibroblasts are widely dispersed in this tissue; they are irregular branching cells that secretes strong fibrous proteins and proteoglycans as an extracellular matrix. The cells of this type of tissue are generally separated by quite some distance by a gel-like gelatinous substance primarily made up of collagenous and elastic fibers.

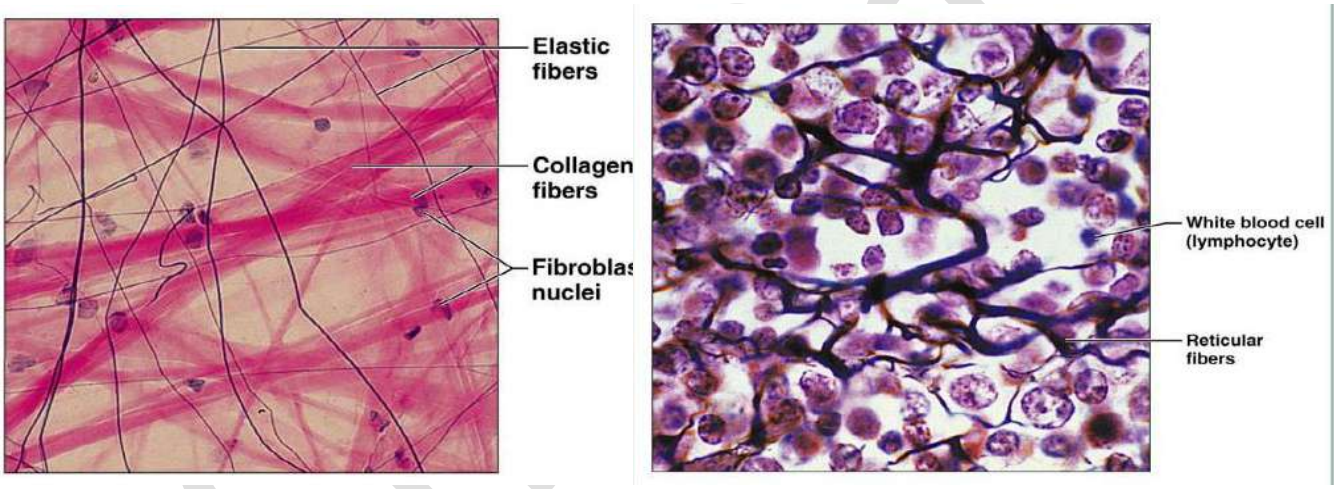
a-Areolar connective tissue:

1. **(Areol) being Latin for a little open space), is a common type of connective tissue.**
2. **It is strong enough to bind different tissue types together, yet soft enough to provide flexibility and cushioning.**
3. **Its fibers run in random directions and are mostly collagenous, but elastic and reticular fibers are also present.**

4. **Location: It surrounds blood vessels and nerves and penetrates with them even into the small spaces of muscles, tendons, and other tissues. It is found beneath the dermis layer and the epithelial tissue of all the body systems.**

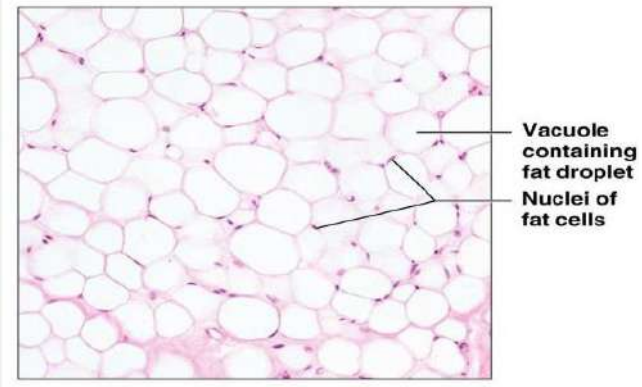
b-Reticular connective tissue:

1. **It has a network of reticular fibers, made of type III collagen. Reticular fibers are not unique to reticular connective tissue, but only in this type are they dominant.**
2. **Reticular fibers are synthesized by special fibroblasts called Reticular cells. The fibers are thin branching structures.**
3. **Location: Is found around the liver, the kidney, the spleen, and lymph nodes, as well as in bone marrow. Adipose tissue is held together by reticular fibers.**



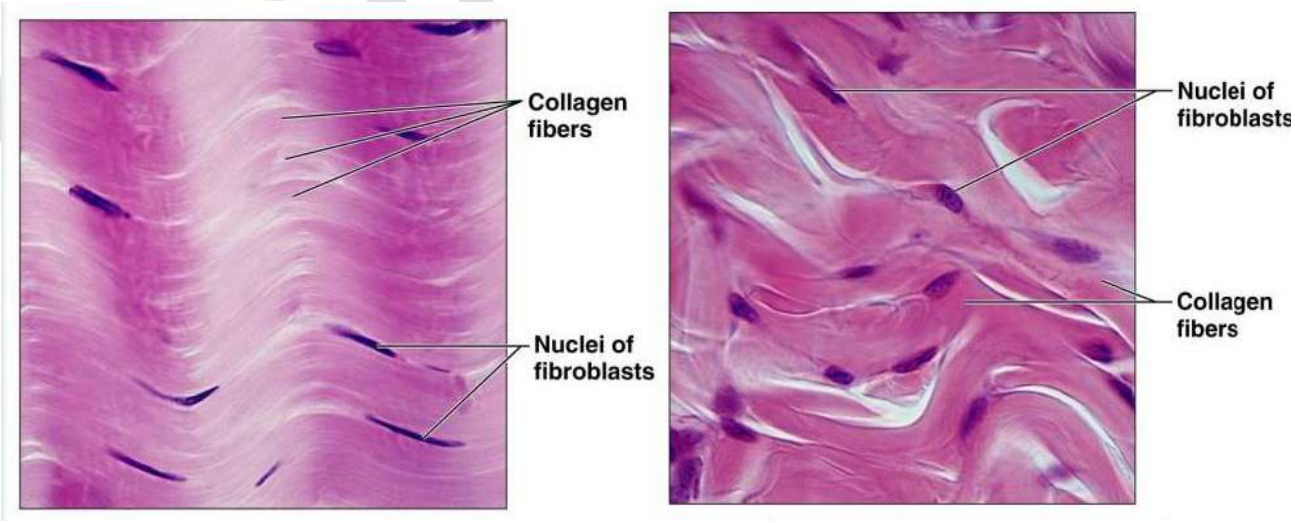
c-Adipose tissue (body fat)

1. **Mainly composed of Adipocytes (Have nucleus pushed to the side of the cell by large fat droplet).**
2. **Other cells called Stromal vascular fraction (SVF) which includes (Pre-adipocytes, Fibroblasts, Vascular endothelial cells and a variety of immune cells (i.e. Macrophages).**
3. **There are two types of adipose tissue: White adipose tissue (WAT) and Brown adipose tissue (BAT).**
4. **Is located beneath the skin (Subcutaneous fat), around internal organs (Visceral fat), in bone marrow (yellow bone marrow) and in the breast tissue.**
5. **Adipose tissue contains many small blood vessels.**
6. **Function includes providing the body with reserve food fuel .insulates against heat loss , supports and protects organs.**



2-Dense connective tissue:

1. **Also called dense fibrous tissue, has fibers as its main matrix element, mainly composed of collagen type I.**
2. **Rows of Fibroblasts, fiber-forming cells, that manufacture the fibers, Crowded between the collagen fibers**
3. **Location: Tendons , Ligaments and the lower layers of the skin (dermis), where it is arranged in sheets.**
4. **Types:**
   a) **Dense Regular Connective Tissue: regularly arranged bundles packed with fibers running same way for strength in one direction (Parallel to each other), Major cell type is the Fibroblast. Found in: Tendon (strong, rope-like structures connect skeletal muscles to bones) and Ligaments (connect bones to bones at joints, are stretcher and contain more elastic fibers than tendons).**
   b) **Dense Irregular Connective Tissue: Primarily irregularly arranged collagen fibers (bundles of packed fibers in all directions for strength). Major cell type is the Fibroblast. Found in: Dermis of the skin, organ capsules, submucosa of digestive tract**



Special connective tissue:

1-Fluid connective tissue

a-Blood

b-Lymph

Spleen:

1. **Located in the abdomen, directly beneath the diaphragm, and connected to the stomach.**
2. **Is the body's largest filter of the blood?**
3. **In essence, the spleen is organized as a 'tree' of branching arterial vessels, in which the smaller arterioles end in a (Venous sinusoidal system).**
4. **The organ is surrounded by a fibrous capsule of connective tissue, stemming from which are (Trabeculae) that support the larger vasculature.**
5. **The smaller branches of the arterial supply are sheathed by lymphoid tissue, which forms the (White pulp) of the spleen.**
6. **The organ parenchyma is divided into two large compartments, the White pulp and the Red pulp, which are distinguished by color in fresh organ sections at low magnification.**
7. **The white pulp harbors dense and highly organized accumulations of B and T lymphocytes around arterioles.**
8. **Most of the red pulp consists of blood-filled spaces. These red pulp spaces are composed of two different structures: First, the splenic sinuses represent a specialized part of the vasculature connecting arterioles and veins. Second, the splenic cords are strands of loose connective tissue without endothelium filled with all types of blood cells, macrophages and plasma cells.**

Lecture 6 ..... Histology

2-Supporting connective tissue

1-Cartilage

1. **Is a flexible connective tissue found in many areas in the bodies of humans and other animals, including the joints between bones, the rib cage, the ear, the nose, the bronchial tubes and the intervertebral discs? It is not as hard and rigid as bone but is stiffer and less flexible than muscle.**
2. **Cartilage is composed of specialized cells called Chondrocytes (1) that produce a large amount of extracellular matrix (2) composed of collagen fibers (3), abundant ground substance rich in proteoglycan, and elastin fibers.**

3. **Cartilage is classified in three types (differ in the relative amounts of these three main components): Elastic cartilage, Hyaline cartilage, Fibrocartilage.**
4. **Chondroblasts that get caught in the matrix are called chondrocytes. They lie in spaces called lacunae with up to eight chondrocytes per lacuna.**
5. **Unlike other connective tissues, cartilage does not contain blood vessels (Avascular). The chondrocytes are supplied by diffusion.**

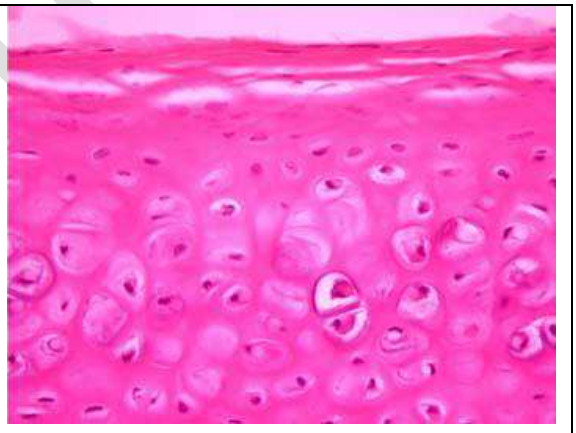
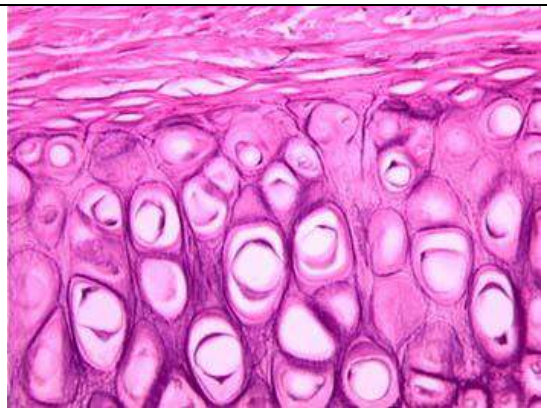
Repair

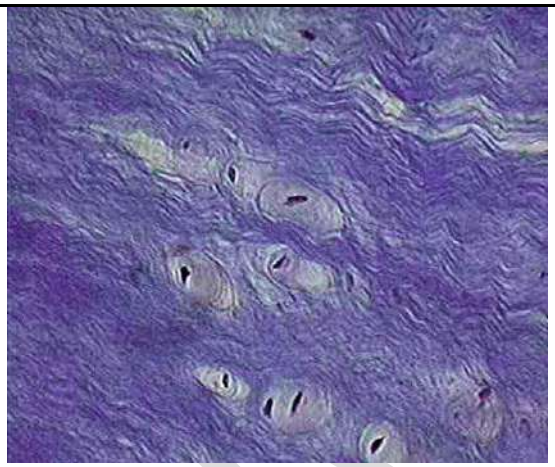
Cartilage has limited repair capabilities: Because:

a- Chondrocytes are bound in lacunae; they cannot migrate to damaged areas. Therefore cartilage damage is difficult to heal.

b- Also, because hyaline cartilage does not have a blood supply, the deposition of new matrix is slow. Damaged hyaline cartilage is usually replaced by fibrocartilage scar tissue.

Types of cartilage

Hyaline Cartilage **Chondrocytes located in lacunae .Extensive extra-cellular matrix contain (Fibers, ground substance, collagen, hyaluronic acid, proteoglycans, glycoproteins, Macromolecules, water, fibers bind together and give firm, flexible properties to tissue. Found at ends of bones, nose, trachea, larynx.**		
Elastic Cartilage **Similar to hyaline cartilage but has elastic fibers running in all directions in addition to collagen. Found in auricle of ear, walls of external auditory canals, eustachian tubes, epiglottis, and larynx. Maintains shape, deforms but returns to shape; flexibility of organ; strengths and supports structures.**		

Fibrocartilage **Fibrous Cartilage is a form of connective tissue transitional between dense connective tissue and hyaline cartilage. Chondrocytes may lie singly or in pairs, but most often they form short rows between dense bundles of collagen fibers. In contrast to other cartilage types, collagen type I is dominant in fibrous cartilage. Is typically found in relation to joints (forming intra-articular lips, disks and menisci) and is the main component of the intervertebral disks, symphysis pubis.**		

2-Bone

Structure and Histology of a Long bone.

A-Diaphysis: Shaft of bone cross section shows from outside toward inside the following layers:

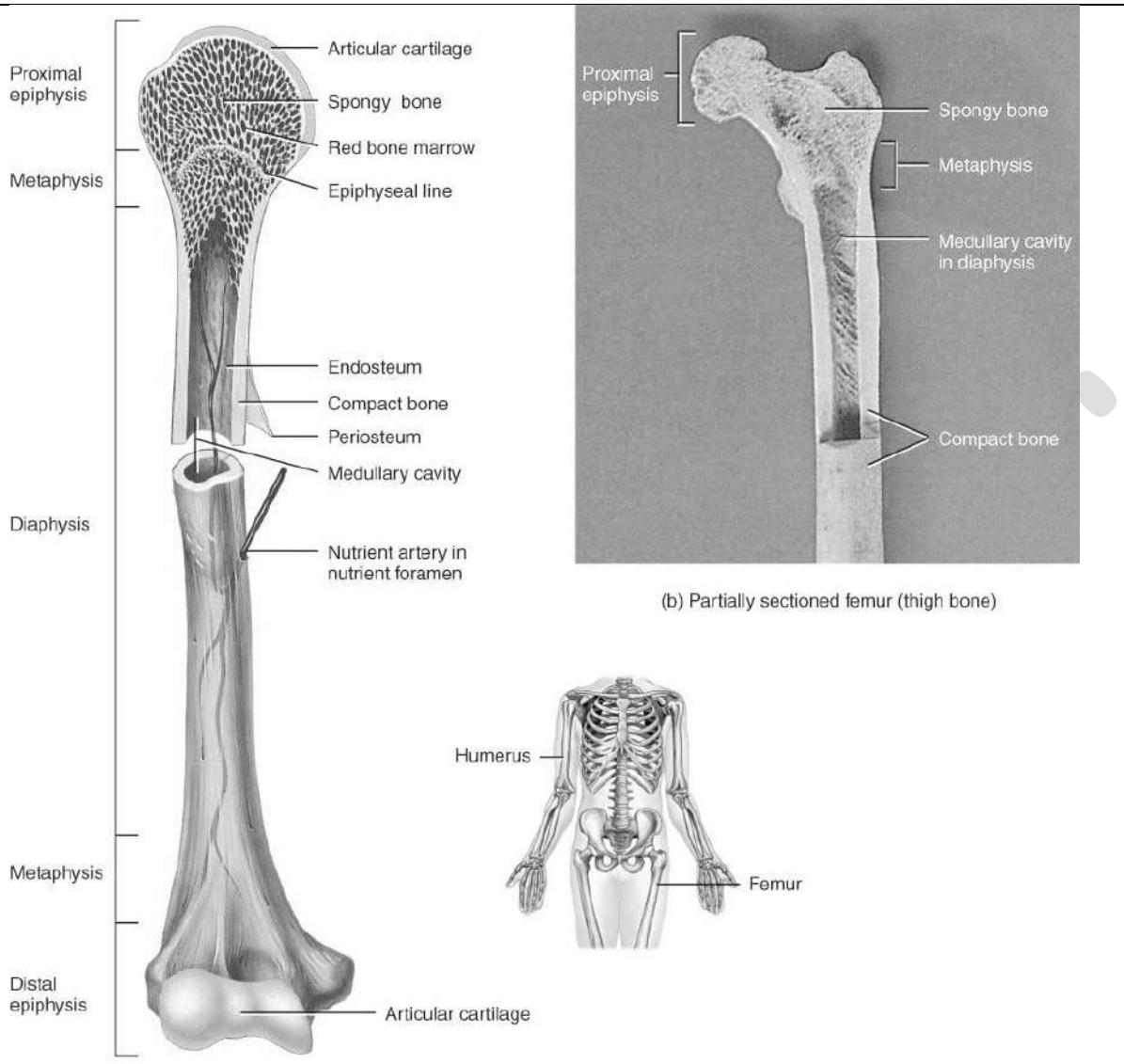
1. **Periosteum:** outer wrapping of bone made up of collagen (dense irregular connective tissue).
2. Compact bone:
3. **Endosteum** : inner layers are osteogenic and contain **Osteoblasts** (bone forming cells), **Osteoclasts** (bone destroying cells; this layer is richly supplied by blood vessels, nerves and lymphatic vessels.
4. **Medullary cavity for marrow**: that contains blood forming tissue (red marrow) or yellow or fat marrow; lined with an endosteal membrane.

B-Epiphyses: ends of bones that form articular surfaces; Epiphyseal line and spongy bone.

• Articular cartilage: covers joint surfaces of epiphyses; made up of hyaline cartilage; acts to cushion stresses during joint movement.

• Epiphyseal line: Remnants of epiphyseal growth plate, a band of actively dividing hyaline cartilage that acts to lengthen bone.

• **Histology:**



(a) Partially sectioned humerus (arm bone)

(b) Partially sectioned femur (thigh bone)

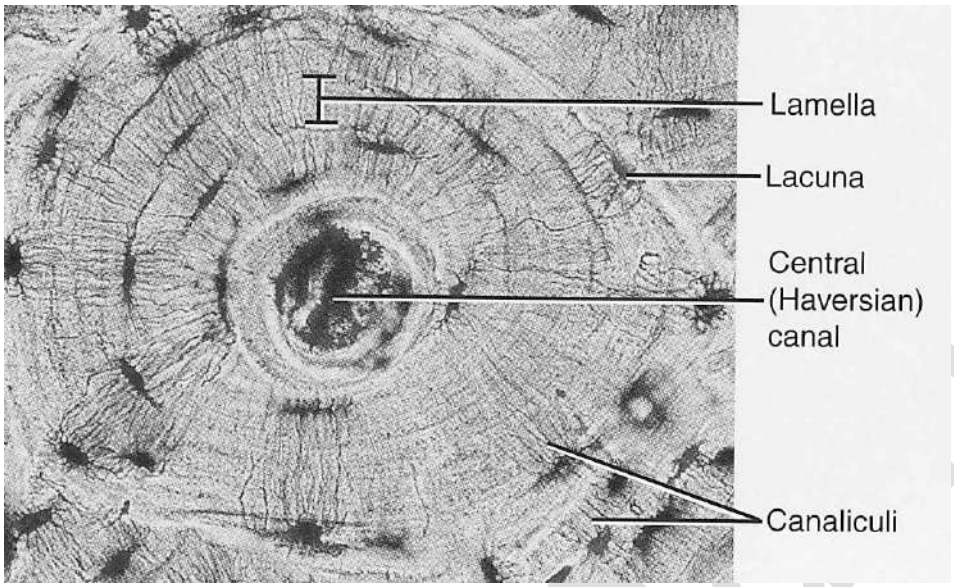
Microscopic Anatomy of Bone Tissue

The structural layout of bone can be classified in one of the following groups: either trabecular (cancellous or spongy) or compact.

1. Compact bone composed of lamellar and Haversian bone:

- **Osteon:** concentric cylinders of bone that usually run in the long axis of bone and support stress and weight of bone.
- **Osteocyt:** amoeboid bone cells that maintain bone matrix.
- **Lacunae:** small cavities in which bones cells reside.
- **Lamella:** each layer of concentric tube of an osteon (Haversian system).
- **Haversian canal:** central canal of Haverian system that contains blood vessels and nerves.
- **Canaliculi:** canals of radiating out from lacunae and housing pseudopods of osteocytes; mechanism of nutrient transfer from one osteocyte to another.

- **Volkmann's canal:** transversely arranged canals that bring blood vessels into the Haversian canals.

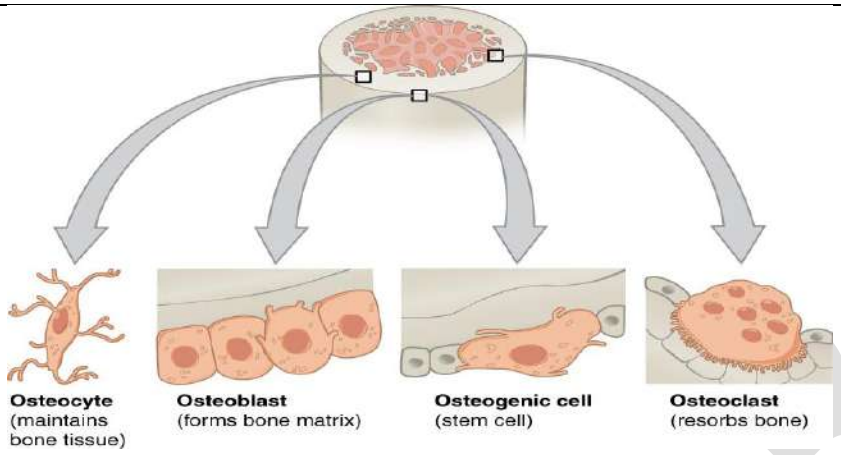


2-Trabecular (cancellous or spongy bone:

Histologically, spongy bone is comprised of anastomosing strips of slender bone known as trabeculae that enclose marrow and blood vessels. It forms the relatively softer core of the bones that is filled with marrow. The less densely arranged trabeculae also contribute to making the bones lighter (as opposed to the heavier compact bone). Communication between adjacent cavities is achieved by canaliculi.

2-Types of Bone Cells:

- **Osteoblasts:** embryonic bone cells that lay down bone matrix.
- **Osteocytes:** mature bone cells that are derived from osteoblasts and are trapped in bony matrix.
- **Osteoclasts:** bone cells that break down and remodel bone; derived from hemopoietic stem cells.
- **Macrophages:** use acids to destroy bone; are able to phagocytize demineralized and dead osteocytes.



Lecture 7 ..... Histology

Bone formation (osteogenesis or ossification)

Bone develops by replacement of a preexisting connective tissue. The two processes of bone formation or osteogenesis observed in the embryo are: (1) intramembranous bone formation, in which bone tissue is laid down directly in primitive connective tissue or mesenchyme (Figures 5-1 and 5-2), and (2) endochondral bone formation, in which bone tissue replaces a preexisting hyaline cartilage, the template or anlage of the future bone (Figures 5-3 to 5-5).

Figure 5-1 Intramembranous ossification

Figure 5-2 Intramembranous ossification

Figure 5-3 Endochondral ossification: Primary ossification center

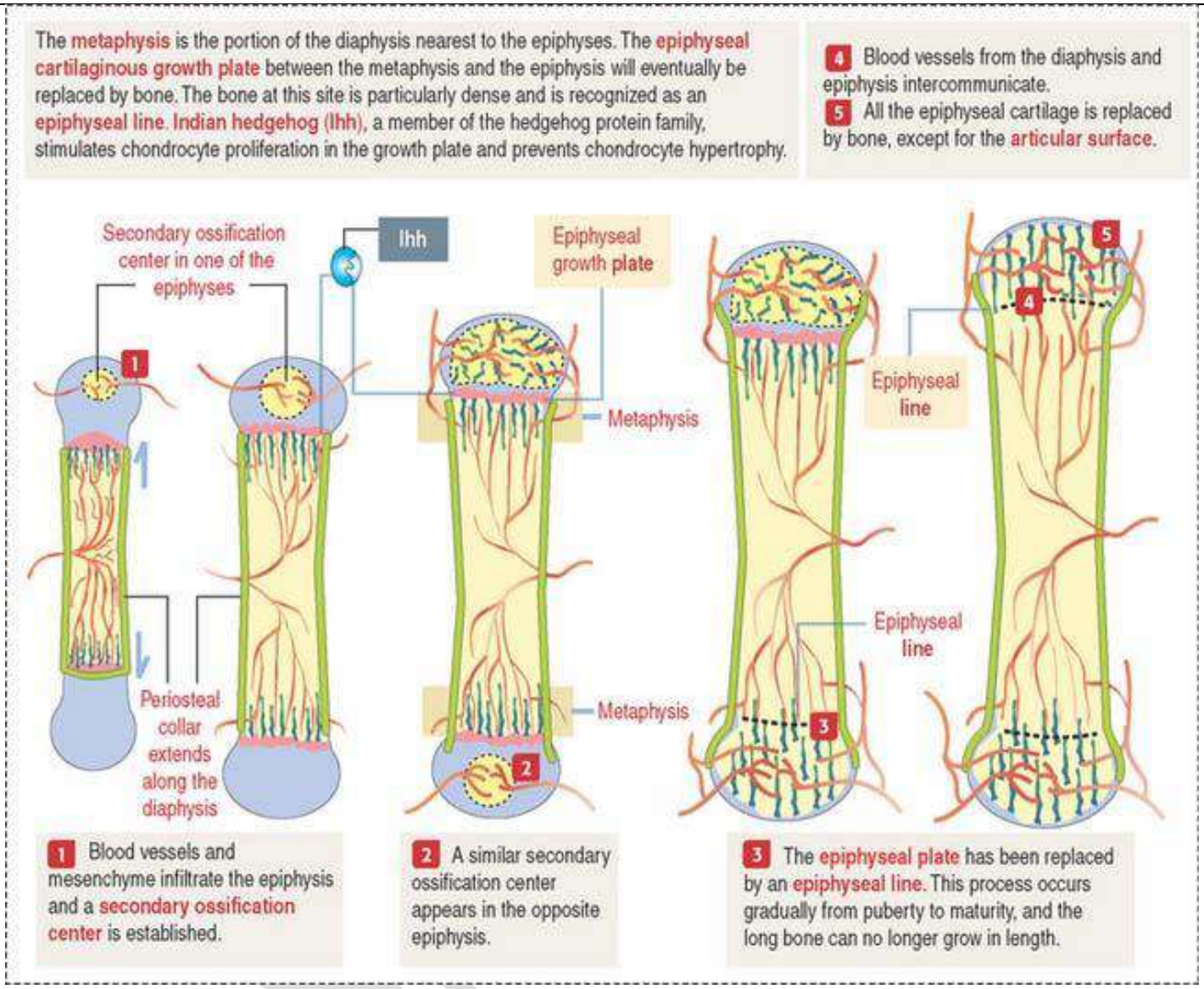


Figure 5-4 Endochondral ossification: Secondary ossification centers

Figure 5-5 Endochondral ossification: Four major zones

The mechanism of bone matrix deposition during intramembranous and endochondral ossification is essentially the same: A primary trabecular network or primary spongiosa is first laid down and then transformed into mature bone. But there is a difference: In endochondral ossification, cartilage is replaced by bone matrix.

The integumentary system:

Includes the skin and all its appendages, namely the nails, hair and sweat glands.

Skin histology:

The largest bodily organ that covers and protects the external surface of the body. Its function includes (Protection, thermoregulation, detecting sensory stimuli) . There are three general layers of the skin, and from superficial to deep, they are the epidermis, dermis and hypodermis. Each layer can be further subdivided into their own constituent regions.

1-Epidermi: most superficial
2-Dermis: deep layer
3- Hypodermis: deepest layer with loose connective and adipose tissue.

The fine structure of the skin shows considerable regional variations in epidermal and dermal thickness, distribution of epidermal appendages, and melanocyte content. Skin is glabrous or non–hair bearing on the palms and soles, whereas hair-bearing skin covers the rest of the body.

The Epidermis

The normal epidermis is a stratified squamous epithelium undergoing continuous renewal. The major cell in the epidermis is the ectodermally derived keratinocyte, making up approximately 95% of the epidermal cells. As the keratinocyte progressively moves from its attachment to the basement membrane to the skin surface, it forms several morphologically distinct epidermal layers: stratum basale or stratum germinativum, stratum spinosum, stratum granulosum, and stratum corneum . Other cell types found in the epidermis include melanocytes, Langerhans cells, and Merkel cells.

Layers of the epidermis:

The epidermis is significantly thicker in the regions of the palms and soles, when compared to other areas of the body. Furthermore, there are no sebaceous glands or hair follicles located in the skin in the palms and soles, while those structures are found in other areas of the body. The thick, hairless skin in the palms and soles are therefore called glabrous skin, while skin elsewhere is referred to as hirsute (hairy) skin. Of note, the stratum lucidum is absent from hirsute skin but present in glabrous skin.

Cell types:

1. **Keratinocytes**: squamous epithelial cells that originate from basal stem cells; continuously mature from basal to corneum layer and desquamate.
2. **Melanocytes**: synthesize melanin that gives color to the skin and protects it from ultraviolet radiation.
3. **Langerhans cells**: antigen presenting cells.
4. **Merkel cells**: (mechanoreceptors), also known as Merkel-Ranvier cells or tactile epithelial cells are oval-shaped mechanoreceptors essential for light touch sensation and found in the skin of vertebrates.

Layers:

The epidermis is the uppermost layer of the skin. Going from superficial to deep, it consists of five layers:

1. Cornified layer (stratum corneum) :(الطبقة المتقرنة) - dead, polyhedral and non-nucleated cells filled with keratine filaments. Composed of 10 to 30 layers.

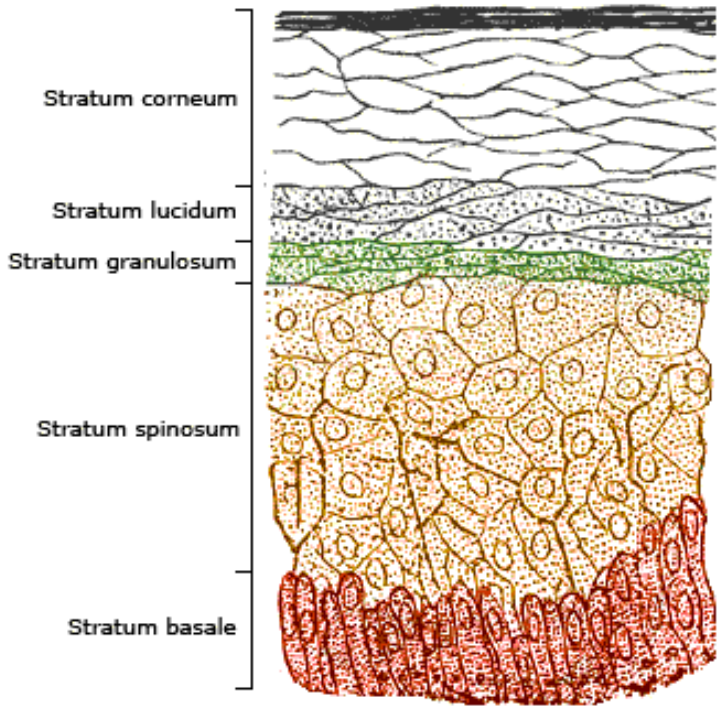
2. Translucent layer (stratum lucidum): (الطبقة الشفافة)- present only in palms and soles; translucent cells filled with keratine filaments.

   The epidermises of these two areas are known as "thick skin" because with this extra layer, the skin has 5 epidermal layers instead of 4

3. Granular layer (stratum granulosum): (الطبقة الحبيبية)- flattened, polygonal pycnotic cells that contain keratohyaline granules, from two to three layers . Keratinocytes lose their nuclei and their cytoplasm appears granular.

4. Spinous layer (stratum spinosum): (الطبقة الشوكية)- contains post-mitotic cells from stratum basale that contain keratine fibrils; melanosomes, Langerhans cells, immunologically active cells, are located in the middle of this layer.

5. Basal/germinal layer (stratum basale/germinativum): (الطبقة الجرثومية)- stem cells constantly undergoing mitosis (proliferating and non-proliferating keratinocytes), regenerate other layers. They are closely associated with cutaneous nerves and seem to be involved in light touch sensation.

Schematic image showing a section of epidermis, with epidermal layers labeled	

Dermis

This region is irregularly arranged and filled mostly with connective tissue. It lies deep to the basement membrane of the stratum basale.

Cell types:

The dermis also contains two general types of cells. There are **permanent cells**, which are part of other fixtures in the dermis (i.e. arrector pili muscles, vessels, and nerves) and **migratory cells** (i.e. lymphocytes and other leukocytes) that carry out an immune function.

Layers:

There are two definitive layers of the dermis

1. **Papillary layer (Stratum papillare) (الطبقة الحليمية)**

It is characterized by dermal papillae, which are raised irregular projections that interlace with the epidermal ridges of the epidermis. Apically, the papillae are blunted and can be separated into cusps. They are less abundant and smaller in thin skin that has minimal mechanical stress, when compared to in areas of thicker skin (i.e. palms and soles), where they tend to form curved parallel lines.

Overall, the papillary layer not only gives mechanical support to the epidermis, but it also provides metabolic sustenance as well.

2. **Reticular layer (Stratum reticulare) (الطبقة الشبكية)**

Deep to the papillary layer is the reticular layer of the dermis. There is no clear demarcation between the two structures. Unlike the papillary layer, the reticular layer contains mostly coarse type I fibers with variable number of elastic fibers. There is significant interaction between the type I and type III fibres in both layers to the point where a sturdy, yet malleable, lattice is formed.

Hypodermis

Subcutaneous tissue (Tela subcutanea)

Finally, the dermis rests on a layer of loose connective tissue known as the hypodermis. It is a superficial fascial sheath with interspersed adipose tissue (panniculus adiposus). The fascia reduces the friction between the dermis and deeper musculature, while the adipose tissue participates in thermoregulatory mechanisms as well as disperses forces generated from direct impact.

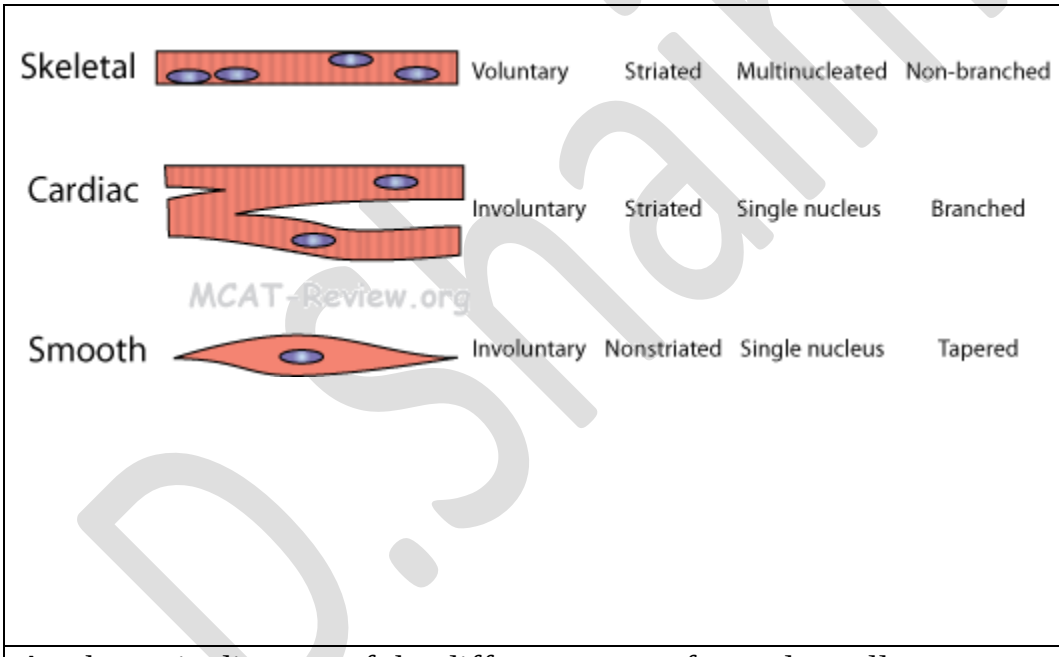
Lecture 8 ..... Histology

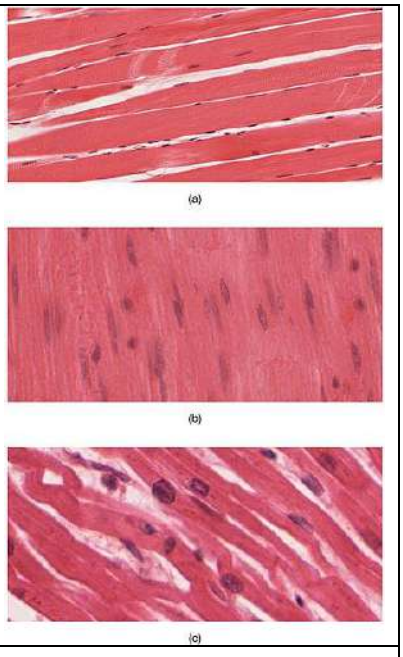
Muscle tissue

Muscle tissue is a basic biological tissues present in animals. It is a soft tissue that composes muscles, and gives rise to the muscles ability to contract. Muscle tissue comes in different types, depending on function and location in the body. In humans and mammals the three types are:

1. Skeletal Muscle: or striated muscle found in the large body muscles, voluntary, packed in bundles and attached to bones for movement.
2. Smooth Muscle or non-striated muscle, found in organ walls and blood vessel walls, involuntary, spindle-shaped cells for pushing things through organs
3. Cardiac Muscle: found in heart wall, involuntary, striated muscle with intercalated discs connecting cells for synchronized contractions during heartbeat.

Functions:
1) Responsible for body movement
2) Moves blood, food, waste through body's organs
3) Responsible for mechanical digestion





A schematic diagram of the different types of muscles cells

1) Skeletal muscle cells are long tubular cells with striations (3) and multiple nuclei (4). The nuclei are embedded in the cell membrane (5) so that they are just inside the cell. This type of tissue occurs in the muscles that are attached to the skeleton. Skeletal muscles function in voluntary movements of the body.
2) Smooth muscle cells are spindle shaped (6), and each cell has a single nucleus (7). Unlike skeletal muscle, there are no striations. Smooth muscle acts involuntarily and functions in the

movement of substances in the lumens. They are primarily found in blood vessel walls and walls along the digestive tract.

3) Cardiac muscle cells branch off from each other, rather than remaining along each other like the cells in the skeletal and smooth muscle tissues. Because of this, there are junctions between adjacent cells (9). The cells have striations (8), and each cell has a single nucleus (10). This type of tissue occurs in the wall of the heart and its primary function is for pumping blood. This is an involuntary action.

Structure: Muscle cells (**Myocytes**) are elongated and classified and or compatible as either striated muscle cells or smooth muscle cells depending on the presence or absence, respectively, of organized, regularly repeated arrangements of myofibrillar contractile proteins called **myofilaments**.

Skeletal striated muscle

Skeletal muscle is a form of striated muscle tissue which is under the control of the somatic nervous system; that is to say, it is voluntarily controlled. As their name suggests, most skeletal muscles are attached to bones by bundles of collagen fibers known as tendons.

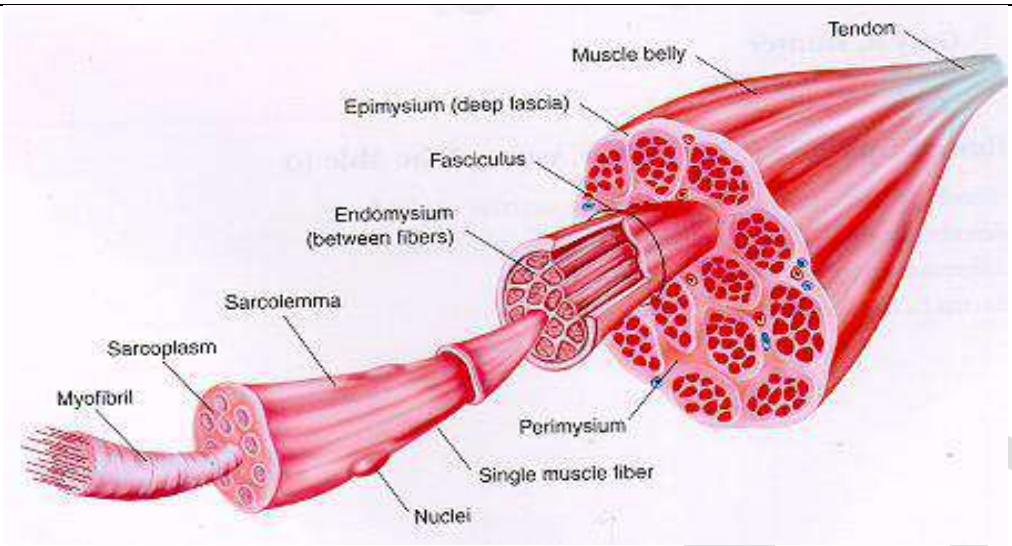
Skeletal muscle is made up of individual components known as myocytes, or "muscle cells", sometimes colloquially called "muscle fibers". They are formed from the fusion of developmental myoblasts (a type of embryonic progenitor cell that gives rise to a muscle cell) in a process known as myogenesis. These long, cylindrical, multinucleated cells are also called myofibers.

The myofibers are in turn composed of myofibrils. The myofibrils are composed of actin and myosin filaments repeated in units called a sarcomere, the basic functional unit of the muscle fiber. The sarcomere is responsible for skeletal muscle's striated appearance and forms the basic machinery necessary for muscle contraction. The term muscle refers to multiple bundles of muscle fibers held together by connective tissue.

Epimysium :is the fibrous tissue envelope that surrounds skeletal muscle. It is a layer of dense irregular connective tissue which ensheaths the entire muscle and protects muscles from friction against other muscles and bones

Perimysium is a sheath of connective tissue that groups muscle fibers into bundles (anywhere between 10 and 100 or more) or fascicles.

Endomysium, meaning *within the muscle*, is a wispy layer of areolar connective tissue that ensheaths each individual myocyte (muscle fiber, or muscle cell)



Structure of muscle fibers

Individual muscle fibers are formed during development from the fusion of several undifferentiated immature cells known as myoblasts into long, cylindrical, multi-nucleated cells. Differentiation into this state is primarily completed before birth with the cells continuing to grow in size thereafter. The principal cytoplasmic proteins are myosin and actin (also known as "thick" and "thin" filaments, respectively) which are arranged in a repeating unit called a sarcomere. The interaction of myosin and actin is responsible for muscle contraction.

The plasma membrane is called the sarcolemma with the cytoplasm known as the **sarcoplasm**. In the sarcoplasm are the myofibrils. The myofibrils are long protein bundles about 1 micrometer in diameter each containing myofilaments. Pressed against the inside of the sarcolemma are the unusual flattened nuclei between the myofibrils are the mitochondria.

While the muscle fiber does not have a smooth endoplasmic reticulum, it contains a sarcoplasmic reticulum. The sarcoplasmic reticulum surrounds the myofibrils and holds a reserve of the calcium ions needed to cause a muscle contraction. Periodically, it has dilated end sacs known as terminal cisternae. These cross the muscle fiber from one side to the other. In between two terminal cisternae is a tubular infolding called a transverse tubule (T tubule). T tubules are the pathways for action potentials to signal the sarcoplasmic reticulum to release calcium, causing a muscle contraction. Together, two terminal cisternae and a transverse tubule form a triad.

Blood vessels

Vessels in the body transport fluids, either blood or lymphatic fluid, which allows for distribution of nutrients, waste products, hormones, etc. throughout the body. There are two components of the vascular system:

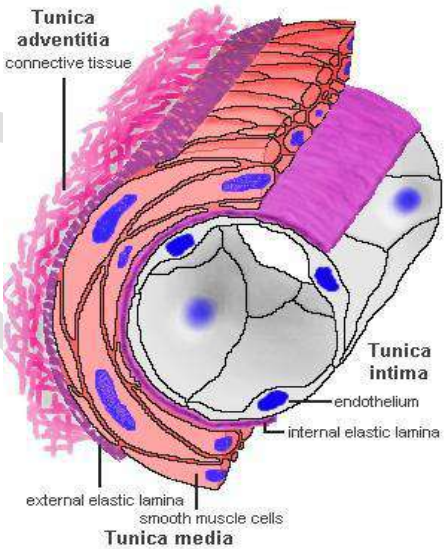
1. Cardiovascular system – transports blood, and includes the heart, arteries, capillaries, and veins
2. Lymphatic system – which returns tissue fluid (lymph) from the tissues back to the cardiovascular system

Both of these systems are essentially a set of tubes, with different characteristics. Here, we focus on the arteries, capillaries, veins. That vessels have three basic components (from inside to outside):

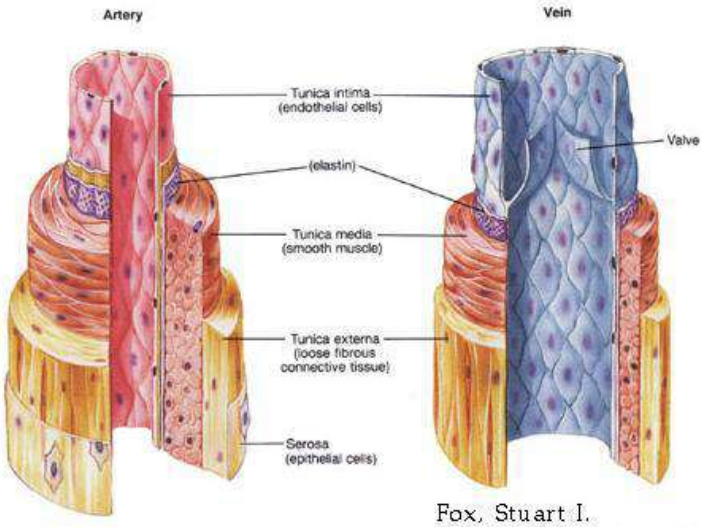
1.Tunica intima – a simple squamous epithelium, called the endothelium, with underlying loose connective tissue

2.Tunica media – a thicker layer with smooth muscle and elastic fibers

3.Tunica externa (adventitia) – dense connective tissue

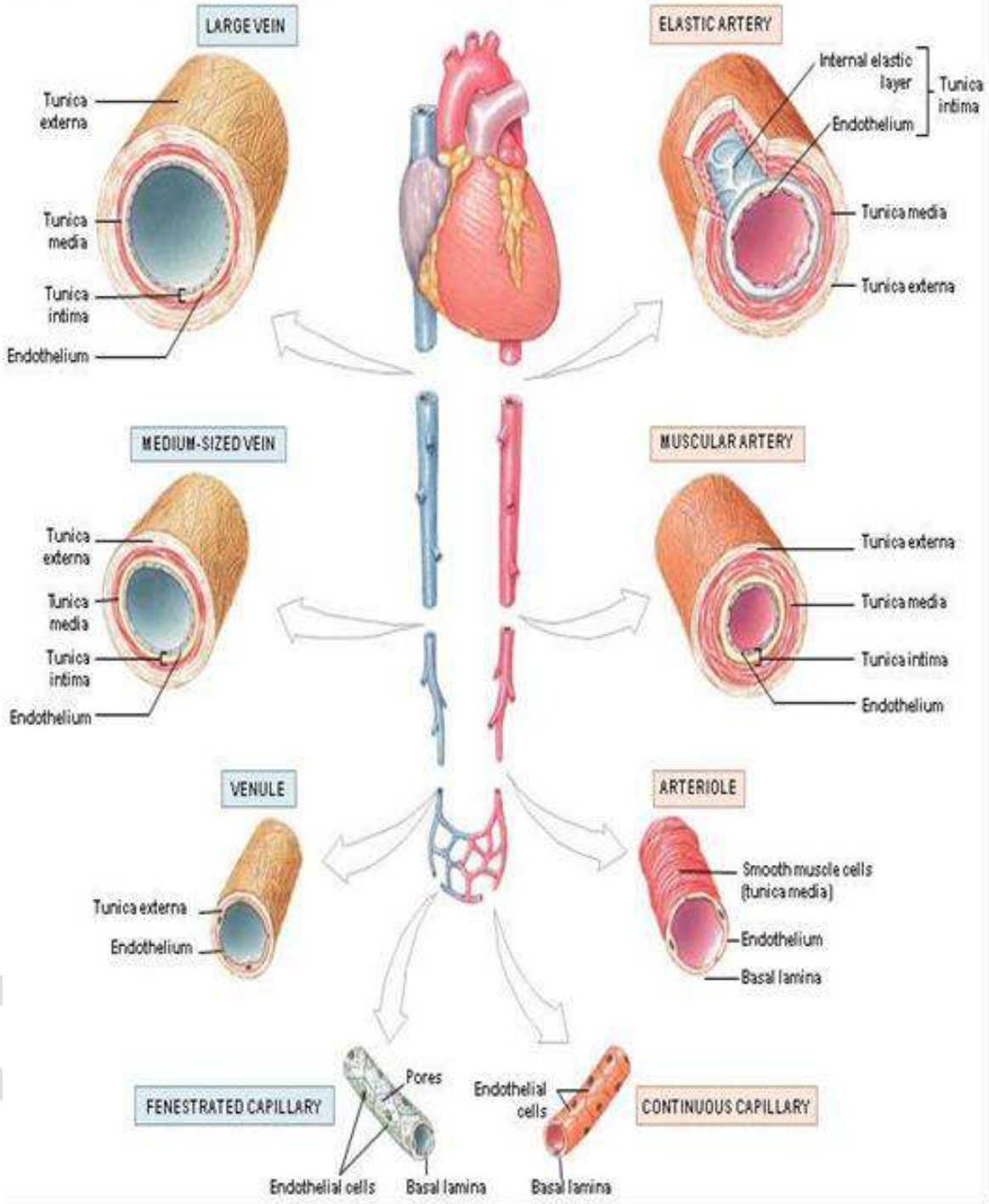


In the higher-powered image, it is easier to see the tunica intima (green double-arrow), tunica media (black double-arrow) and adventitia (blue double arrow). Arrows indicate nuclei of endothelial cells that form the inner lining of vessels.



Fox, Stuart I.
Human Physiology 4th
Brown Publishers

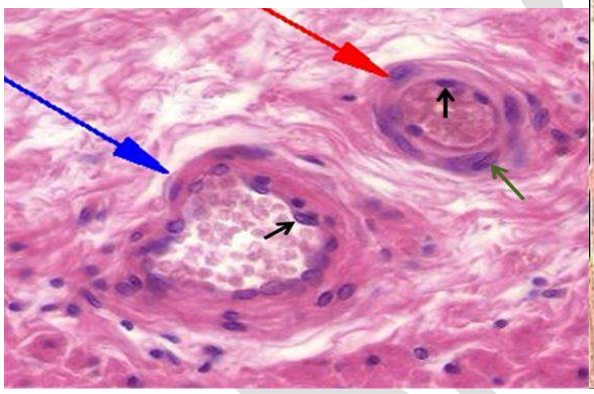
Figure 21-2: Histological Structure of Blood Vessels

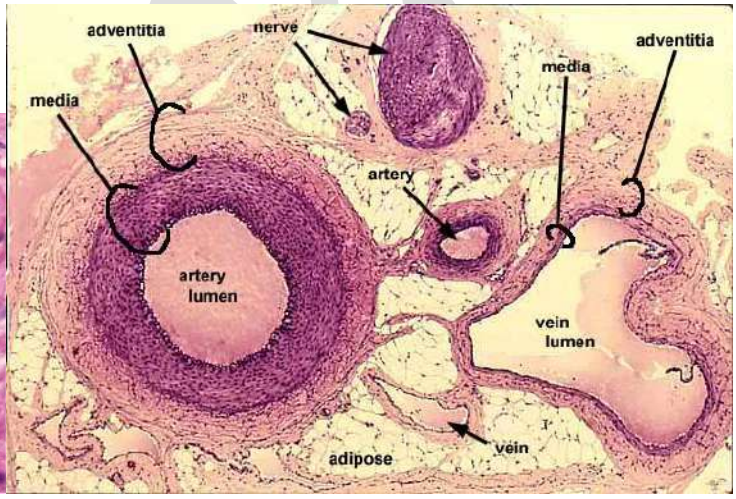


In this overview, we will focus on a few key differentiating features of vessels:

1. The major histological difference between arteries and veins lies in the thickness and muscularity of the tunica media; arteries have a thicker, more muscular tunica media
2. Capillaries are composed simply of endothelial cells, without a tunica media or adventitia

Histologically, differentiating between arteries/arterioles (red arrow) and veins/venules (blue arrow) is best done by comparing vessels of approximately the same size. Arteries have a thicker smooth muscle layer in their wall; therefore, their wall is relatively thicker compared to the size of the vessel itself, with a narrower lumen. In addition, arteries tend to be rounder. Both will typically contain blood cells in their lumen, though during tissue preparation they can be washed away (see vessel toward the left) and become trapped in inappropriate locations.





Higher-powered view of the same vessels…

All blood vessels are lined by a simple squamous epithelium, referred to as an endothelium. Endothelial cells have flattened nuclei (black arrows). The "fatter" nuclei in the wall of the vessel (green arrow), particularly in the artery, belong to smooth muscle cells.

Lecture 9 ..... Histology

Nervous tissue

Nervous tissue is the main component of the two parts of the nervous system; the brain and spinal cord of the central nervous system (CNS), and the branching peripheral nerves of the peripheral nervous system (PNS),

which regulates and controls body functions and activity. It is composed of neurons, or nerve cells, which receive and transmit impulses, and neuroglia, also known as glial cells or more commonly as just glia (from the Greek, meaning glue), which assist the propagation of the nerve impulse as well as providing nutrients to the neuron.Nervous tissue is made up of different types of nerve cells, all of which having an axon, the long stem-like part of the cell that sends action potential signals to the next cell.

Functions of the nervous system are sensory input, integration, control of muscles and glands, homeostasis, and mental activity.

A nerve is made up of many nerve cell fibers bound together by connective tissue. A sheath of dense connective tissue, the epineurium, surrounds the nerve. This sheath penetrates the nerve to form the perineurium, which surrounds bundles of nerve fibers. Blood vessels of various sizes can be seen in the epineurium. The endoneurium, which consists of a thin layer of loose connective tissue, surrounds the individual nerve fibers.

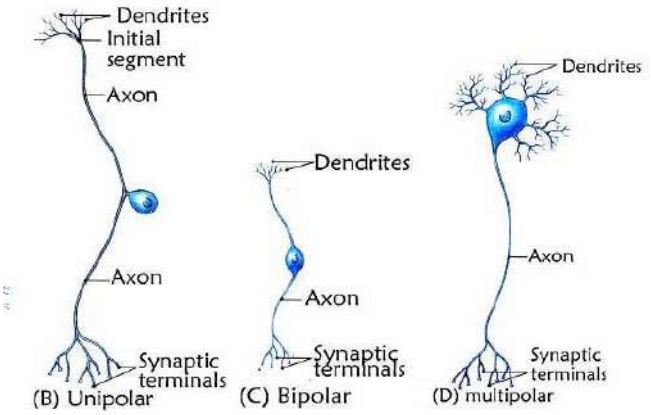
The cell body is enclosed by a cell (plasma) membrane and has a central nucleus. Granules called Nissl bodies are found in the cytoplasm of the cell body. Within the cell body, extremely fine neurofibrils extend from the dendrites into the axon. The axon is surrounded by the myelin sheath, which forms a whitish, non-cellular, fatty layer around the axon. Outside the myelin sheath is a cellular layer called the neurilemma or sheath of Schwann cells. The myelin sheath together with the neurilemma is also known as the medullary sheath. This medullary sheath is interrupted at intervals by the nodes of Ranvier.

Classification of neurons

Neurons are classified both structurally and functionally.

Neurons are grouped structurally according to the number of processes extending from their soma (cell body). Three major neuron groups make up this classification:

1. Multipolar neurons :These are the most common neuron type in humans (more than 99% of neurons belong to this class) and the major neuron type in the central nervous system (CNS).
2. Bipolar neurons: Bipolar neurons are spindle-shaped, with a dendrite at one end and an axon at the other. An example can be found in the light-sensitive retina of the eye. They also rapidly grow.
3. Unipolar neurons: Sensory neurons have only a single process or fiber, which branches close to the cell body into an axon and a dendrite.



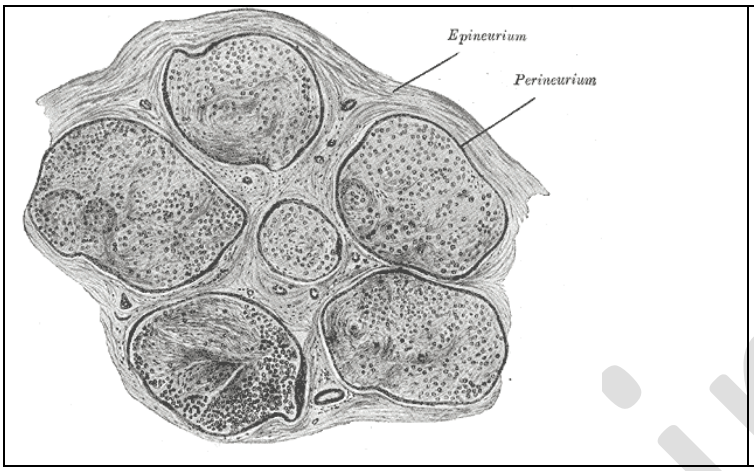
Nervous system divisions:

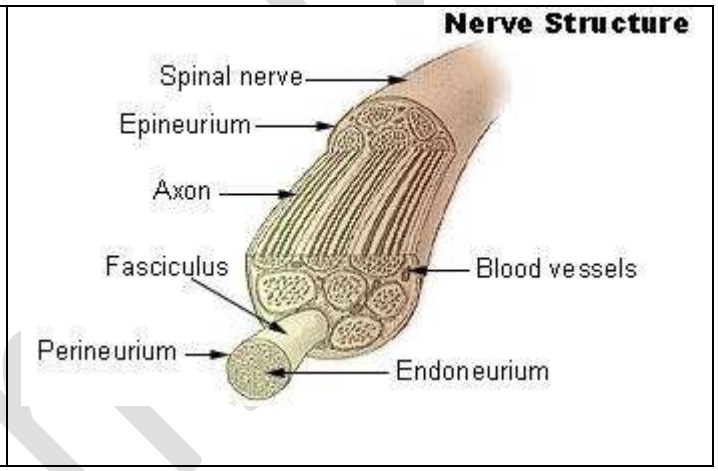
The 3 Elements of Nervous Tissue

1) Brain
2) Spinal cord
3) Nerves

Nerve structure

A nerve fascicle or fasciculus is a small bundle of nerve fibers, enclosed by the perineurium; if the nerve is of small size, it may consist only of a single fasciculus; but if large, the fasciculi are collected together into larger bundles.





In the peripheral nervous system, nerve fibers are each wrapped in a protective sheath known as the endoneurium. These are bundled together into groups known as fascicles, each surrounded by a protective sheath known as the perineurium. Several fascicles may be in turn bundled together with a blood supply and fatty tissue within yet another sheath, the epineurium. This grouping structure is analogous to the muscular organization system of epimysium, perimysium and endomysium.

The perineurium is composed of connective tissue, which has a distinctly lamellar arrangement consisting of roughly 7-8 concentric layers. The perineurium is cellular, and is composed of perineurial cells, which are epithelioid myofibroblasts.

Myelin

Myelin is a dielectric (electrically insulating) material that forms a layer, the myelin sheath, usually around only the axon of a neuron. It is essential for the proper functioning of the nervous system. It is an outgrowth of a type of glial cell. The production of the myelin sheath is called myelination. In humans, the production of myelin begins in the 14th week of fetal development. Schwann cells supply the myelin for peripheral neurons, whereas oligodendrocytes, myelinate the axons of the central nervous system.

Myelin is made up by different cell types, and varies in chemical composition and configuration, but performs the same insulating function. Myelinated axons are white in appearance, hence the "white matter" of the brain. The fat helps to insulate the axons from electrically charged atoms and molecules. These charged particles (ions) are found in the fluid surrounding the entire nervous system. Cholesterol is an essential constituent of myelin. Myelin is about 40% water; the dry mass is about 70–85% lipids and about 15–30% proteins.

Central Nervous System

The central nervous system (CNS) is the part of the nervous system consisting of the brain and spinal cord. It is opposed to the peripheral nervous system (or PNS), which is composed of nerves leading to and from the CNS, often through junctions known as ganglia.

White and gray matter

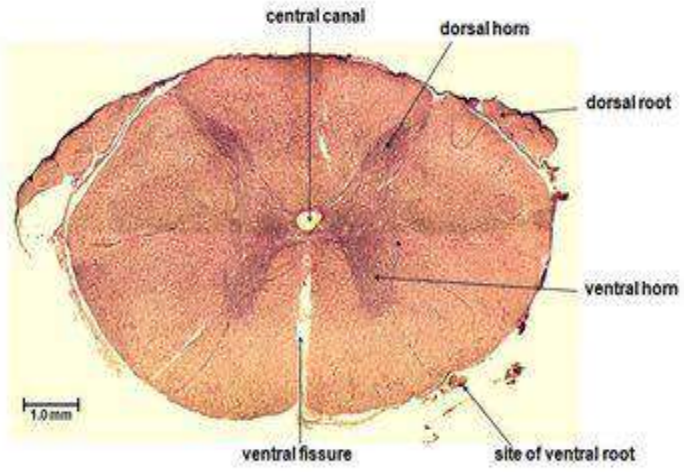
Microscopically, there are differences between the neurons and tissue of the central nervous system and the peripheral nervous system. The central nervous system is divided in white and gray matter. This can also be seen macroscopically on brain tissue. The white matter constitutes of axons and oligodendrocytes, while the gray matter chiefly constitutes of neurons. Both tissues include a number of glial cells (although the white matter contains more), which are often referred to as supporting cells of the central nervous system. Different forms of glial cells have different functions, some acting almost as scaffolding for neuroblasts to climb during neurogenesis such as bergmann glia, while others such as microglia are a specialized form of macrophage, involved in the immune system of the brain as well as the clearance of various metabolites from the brain tissue. Astrocytes may be involved with both clearance of metabolites as well as transport of fuel and various beneficial substances to neurons from the capillaries of the brain. Upon CNS injury astrocytes will proliferate, causing gliosis, a form of neuronal scar tissue, lacking in functional neurons.

Schematic diagram showing the central nervous system in pink, peripheral in yellow.	

Spinal Cord

The spinal cord is composed of two discrete parts; the white matter, which is the outer part of the cord and the grey matter, which is the inner portion of the cord. The white matter is given this name due to its appearance in unfixed histological specimens in which the white nature of the tissue is caused by the myelination of ascending and descending nerve fibres. The grey matter is also named after its unfixed histological appearance and contains the cell bodies of neurons as well as nerve fibres.

Within the spinal cord the grey matter forms an H-shape where the ventral horns of the H are broader than the dorsal horns. The grey matter shape has also been likened to that of a butterfly. The grey matter also has a histologically visible central canal running through it. The ventral horns of the grey matter contain the cell bodies of motor neurones whilst the dorsal horns contain sensory neurons where the cell bodies are found in the dorsal root ganglia.

The above image shows a complete cross-sectional histology of a spinal cord. In this particular stain (H&E) the grey matter can be seen in a slightly darker shade than the white matter. The relative size of the grey matter is small compared to the white matter and therefore the level of the cross-section is unlikely to be around the level of any limbs. The dorsal horns can be seen to extend near to the dorso-lateral surface of the spine. The slide also contains small elements of the dorsal and ventral roots leaving the spinal cord. The connecting element of the grey matter which is immediately ventral to the central canal is called the **grey commissure** (GC). The stained areas found around the edge of the spinal cord are fibrous material that is the pia mater. This pia mater follows the contours of the spinal cord and also folds into the ventral fissure. At the ventral aspect of the ventral fissure some small blood vessels can be seen present in the pia mater.	

Gastrointestinal System,

Include: (mouth , Esophagus, Stomach, Small intestine, Large intestine, anas , Pancreas, Liver)

Histology of the Digestive System

Basic Histological Layers

1. **Mucosa** /The epithelial membrane that lines the GI tract from mouth to anus.
- Secretes mucous, digestive enzymes & hormones
- Absorbs nutrients
- Protects from disease & from the GI contents
- 3 layers:
  - Epidermis/ Lining epithelium/ absorbs nutrients, secretes mucus
  - Lamina propria : Loose connective tissue with nourishing and absorbing capillaries. Contains most of mucosa-associated lymphoid tissue (MALT).
  - Muscularis mucosa /Thin layer of muscle producing only local movements.

2. **Submucosa** / Connective tissue containing major blood and lymphatic vessels and nerves. Many elastic fibers so gut can regain shape after food passes.

3. **Muscularis externa** / Two layers of smooth muscle responsible for peristalsis and segmentation

- Inner circular layer (circumferential) (Squeezes In some places forms sphincters (act as valves)

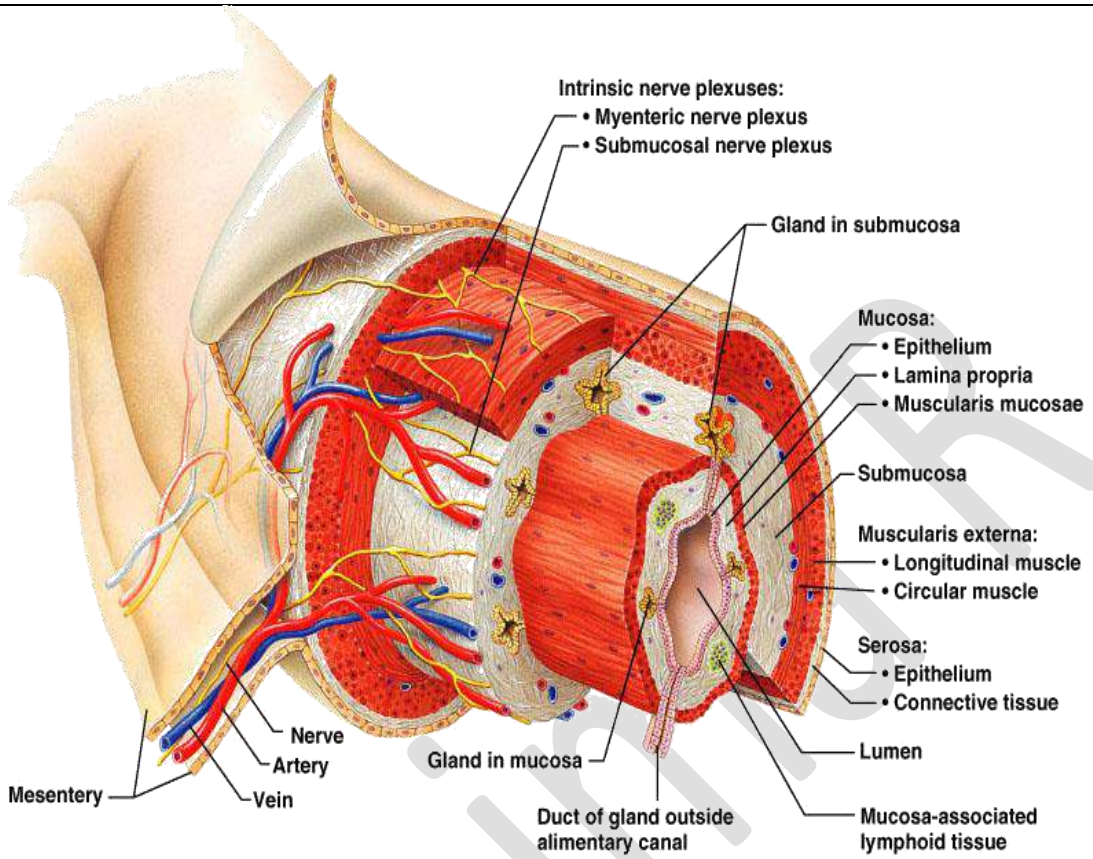
- Outer longitudinal layer: shortens gut

4. **Serosa or Adventitia (the visceral peritoneum)** / Simple squamous epithelium (mesothelium) , Thin layer of areolar connective tissue underbneath

Histology of the Mucosa

Organ	Epithelium
Mouth	Nonkeratinized Stratified Squamous
Pharynx	Nonkeratinized Stratified Squamous
Esophagus	Nonkeratinized Stratified Squamous
Stomach	Simple Columnar
Small Intestine	Simple Columnar
Large Intestine	Simple Columnar
Anus	Nonkeratinized Stratified Squamous

Organ	Folds of the epithelium
Esophagus	none
Stomach	L: Rugae, S: gastric pits
Small Intestine	L: Plicae circulars, Villi S: Crypts of Lieberkuhn, microvilli
Large Intestine	L: Haustra S: Intestinal glands



Histology of the Submucosa

Organ	Specialized structures
Esophagus	Submucosal mucous glands
Stomach	None
Duodenum	Brunner's glands
Ileum	Peyer's Patches
Large Intestine	None

Histology of the Muscularis externa

Organ	Smooth muscle layers
Esophagus	2, circular and longitudinal
Stomach	3, oblique, circular, and longitudinal
Small Intestine	2, circular and longitudinal
Large Intestine	2, circular and longitudinal

Histology of the Serosa

Organ	Serosa
Esophagus	Adventitia due to the fact that the esophagus is not in a cavity
Stomach	Visceral Peritoneum
Small Intestine	Visceral Peritoneum
Large Intestine	Visceral Peritoneum
Anus	Adventitia

Stomach Regions

1. Cardiac region
2. Fundus (dome shaped)
3. Body (Greater curvature , Lesser curvature)
4. Pyloric region (Antrum ,Canal ,Sphincter)

Histology of stomach

1. Simple columnar epithelium: secrete bicarbonate-buffered mucus
2. Gastric pits opening into gastric glands
    - Mucus neck cells
    - Parietal cells : secretes HCL and Intrinsic factor (for B12 absorption)
    - Chief cells : secretes Pepsinogen (activated to pepsin with HCL)
3. Rugae: longitudinal folds on internal surface of the stomach (helps distensibility)
4. Muscularis: additional innermost oblique layer (along with circular and longitudinal layers

Small intestine

- Longest part of alimentary canal (2.7-5 m)
- Most enzymatic digestion occurs here
- Most enzymes secreted by pancreas, not small intestine
- Almost all absorption of nutrients
- Small intestine has 3 subdivisions
    - Duodenum
    - Jejunum
    - Ileum
- Blood supply: superior mesenteric artery; Veins drain into hepatic portal vein

- Small intestine designed for absorption
    - Huge surface area because of great length
    - Structural modifications also increase absorptive area
        - Circular folds (plicae circulares)
        - Villi (fingerlike projections) 1 mm high – simple columnar epithelium: velvety
        - Microvilli
- Intestinal crypts* (of Lieberkuhn) in between villi
    - Cells here divide every 3-6 days to renew epithelium (most rapidly dividing cells of the body)
    - Secrete watery intestinal juice which mixes with chyme (the paste that food becomes after stomach churns it)

Lecture 10 ..... Histology

Liver: The liver is the largest solid organ in the body, weighing about 1.5 kg in the adult. Lies in the right upper quadrant of the abdomen and is completely protected by the thoracic rib cage.. Completely surrounded by a peritoneal membrane, known as Glisson'scapsule.

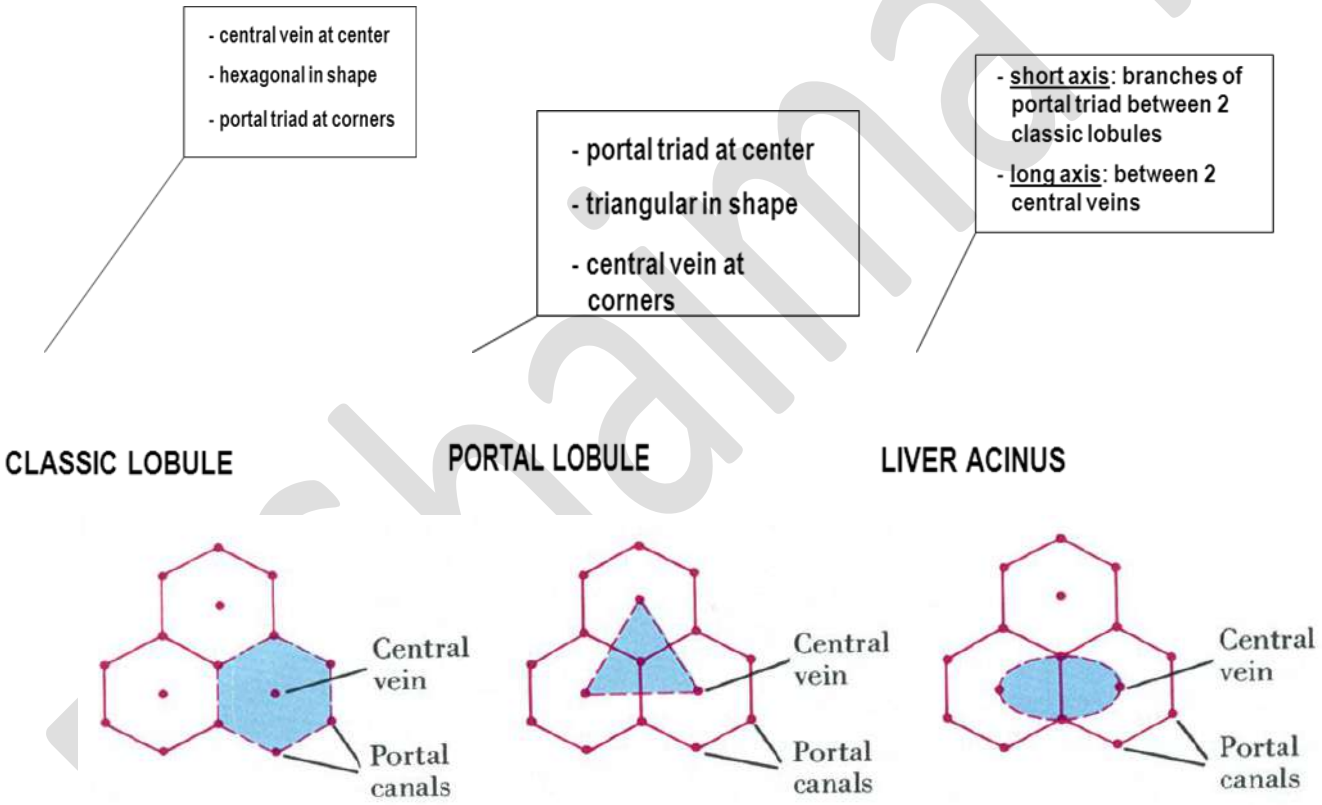
- The liver lobules can be defined in 3 ways:
- 1) **Classic lobule** – centered on the **central vein** with the **portal triads** at each corner. Shown below on the left, the classic lobule may not always be hexagonal in shape.
- 2) **Portal lobule** – centered on the **portal triad**, based on bile secretion, and approximately triangular in shape.
- 3) **Liver acinus of Rappaport** – this is the most functionally important classification. The acinus is roughly oval in shape with 2 central veins and 2 portal triads on opposite ends. Based on the blood flow within hepatic tissue, the acinus is divided into 3 zones. Cells in different zones are specialized for different activity. Zone 1 cells, being closest to the portal triads and hence most oxygenated blood, have the most drug-metabolizing enzymatic activity. Following that same reasoning, zone 3 hepatocytes near the central veins are most susceptible to ischemia.

- As mentioned earlier, the liver has both endocrine and exocrine functions. The various proteins that hepatocytes secrete enter the bloodstream via the liver sinusoids. The liver also secretes bile in the

conventional exocrine fashion. The hepatocytes secrete bile into sealed extracellular spaces called **bile canaliculi**.

EXOCRINE PORTION synthesizes and secretes bile via a system of ducts that is essential for digestion in the intestine

ENDOCRINE PORTION synthesizes and secretes numerous plasma proteins into the bloodstream: (albumin, fibrinogen, prothrombin, lipoproteins, etc.)



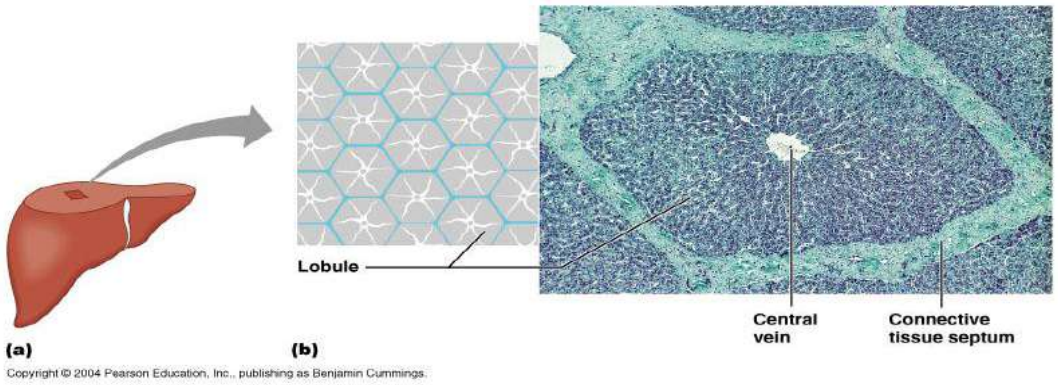
- **Microscopic Anatomy**
  - Liver lobule: hexagonal
  - Central vein: drains the lobule
  - Hepatocytes form plates that radiate from the central vein

- **Portal triad at each corner of the hexagonal system. Consists of branches of:**
  - Hepatic Artery → delivers O_2
  - Hepatic portal vein → delivers nutrients from small intestine

- Bile duct → receives bile from the bile canaliculi that lie between layers of hepatocytes

☐ Liver

- Liver sinusoids → Large leaky capillaries conduct blood from the artery & portal vein to the central vein
- Hepatic macrophages → Kupffer cells lie in sinusoid walls
- Central veins flow into hepatic veins then to the inferior vena cava



PANCREAS

In the adult the average pancreas is about 12-15 cm in length and weighs 60 to 140 g. Histologically, the pancreas has two separate components, exocrine and endocrine glands. The exocrine portion makes up approximately 80% of the organ, and consists of numerous acini aggregated into lobules that can be seen grossly. The endocrine portion cannot be discerned grossly.

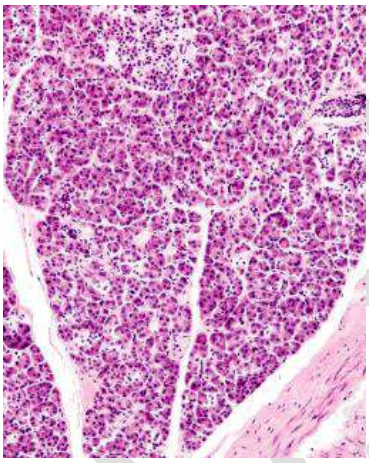
A. Exocrine Pancreas

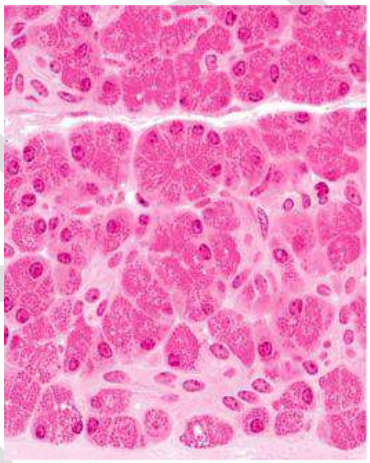
- The pancreas has a poorly defined capsule. It is covered by a thin areolar connective tissue capsule. This capsule gives rise to the connective tissue **septae** that divide the pancreas into lobules. Blood vessels, nerves, lymphatics and ducts traverse through the septae. A principal small artery supplies each lobule.
- Acinar cells constitute the majority of the organ. The cells form rounded or elongated acini usually at the ends of the intercalated ducts.
  - Normal acinar cells are large, pyramidal shaped cells with a single nucleus. The nucleus lies close to the base of the cells that rests on the basal laminae. The nucleus is round with clumped chromatin.

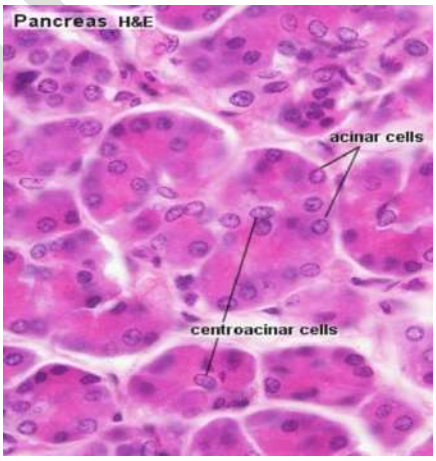
- The apical portion of the cell is filled with eosinophilic zymogen granules. The basal portion is strongly basophilic because the cytoplasm is filled with RER. The cells secrete directly into acinar lumen though the apical surface.

1. The ducts of the exocrine pancreas

- Centroacinar cells, located in the center of the acinus, with a pale nucleus, form the smallest ducts of the gland.
- The intercalated ducts are lined by low cuboidal epithelium. The nucleus is ovoid with inconspicuous nucleoli.
- Intralobular ducts vary in diameter and are lined by simple cuboidal epithelium. A single rounded nucleus appears to fill each cell.
- Interlobular ducts are larger and are lined by simple columnar epithelium. They are located in the septae and are invested by a layer of collagenous tissue.
- Two major ducts are the ducts of Santorini and Wirsung. They have tall columnar epithelium with basal nuclei.







A. B.

A .Pancreas. Human. x 132. H&E. Serous acini only. Note islet of Langerhans below arrow.

B. Pancreas. Monkey. x 540. H&E. . Higher power showing zymogen granules in the acinar cells.

2. Pancreatic exocrine secretion

- Merocrine secretion of proenzymes by the acinar cells is regulated by secretin and cholecystokinin from the enteroendocrine cells of the duodendum and jejunum and nerve stimulation from the vagus.
- Gastric acid in the intestinal lumen stimulates secretin release. Secretin causes acina and ductal cells to add water and bicarbonate to fluid, making it alkaline, rich in electrolytes and poor in enzyme activity. This fluid neutralizes the chyme so that the pancreatic enzymes can function at an optimal neutral pH range.
- Long-chain fatty acids, gastric acid and some essential amino acids in the gut stimulate the release of cholecystokinin. This hormone promotes secretion of an enzyme-rich (but less abundant) fluid.

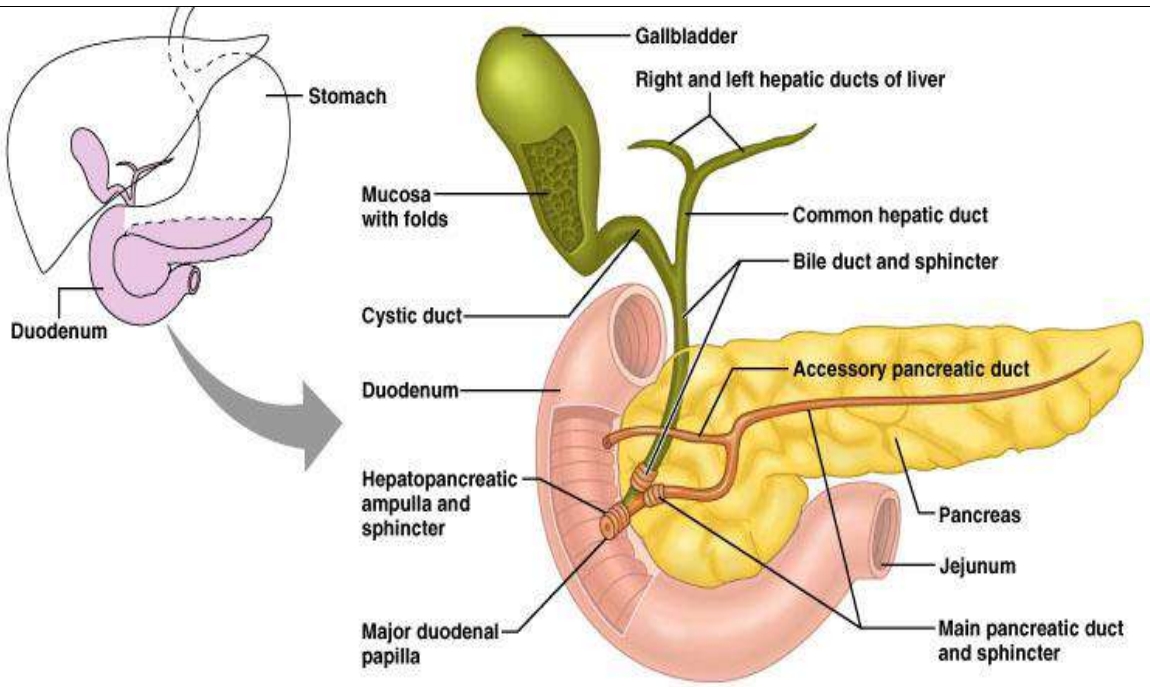
B. The Endocrine Pancreas

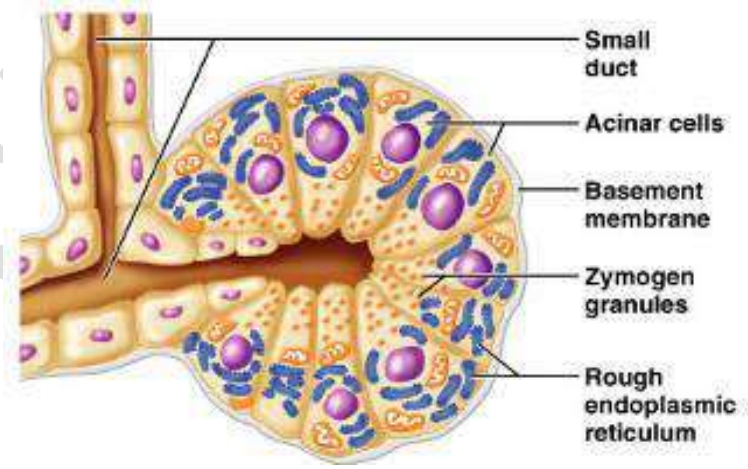
- The endocrine pancreas constitutes 1-2% of the adult pancreas.
- The endocrine cells form scattered aggregates that form the Islets of Langerhans. Each islet is a lightly stained, rounded group which is a multihormonal micro-organ. A small amount of connective tissue accompanies the large capillaries that run though each islet.

A. Islet of Langerhans. Rounded group of endocrine cells surrounded by serous cells. **B.** Islet of Langerhans. Note rich vascularity with red cells in capillaries.

The islet cells are not uniformly distributed in the pancreas with more islets found in the tail. There are four major cell types in the endocrine pancreas that can be recognized by immunohistochemistry:

Cell type	Product	Relative amount	Functions
Alpha (A)	glucagon	15-20%	Increases blood glucose, gluconeogenesis, glycogenolysis
Beta (B)	insulin	60-70%	Promotes decrease of blood glucose, stimulates storage of glucose as glycogen
Delta (D)	somatostatin	5-10%	Inhibits secretion of glucagon and insulin


Stomach
Duodenum
Gallbladder
Right and left hepatic ducts of liver
Mucosa with folds
Common hepatic duct
Bile duct and sphincter
Cystic duct
Accessory pancreatic duct
Duodenum
Hepatopancreatic ampulla and sphincter
Pancreas
Jejunum
Major duodenal papilla
Main pancreatic duct and sphincter


Small duct
Acinar cells
Basement membrane
Zymogen granules
Rough endoplasmic reticulum