หนึ่งอาจารย์หนึ่งผลงาน ประจำปีการศึกษา 2550

ภาพเลื่อนประกอบการสอน

เรื่อง เนื้อเยื่อสัตว์ - Animal Tissues

บทที่ 1. เนื้อเยื่อบุผิว – Epithelial Tissue

บทที่ 2. เนื้อเยื่อเกี่ยวพัน - Connective Tissue

บทที่ 3. เนื้อเยื่อกล้ามเนื้อ - Muscular Tissue

บทที่ 4. เนื้อเยื่อประสาท - Nervous Tissue

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เมษายน 2551

Histology

Animal Tissues

1

Histology

- Histology is the study of normal structure and function of cells, tissues, organs, and systems in the body .
- Learning normal tissue architecture and understanding its relation to normal tissue and organ function will provide the student with the foundation for recognizing the hallmarks of pathology and disease.
  - Histology ~ study of animals tissue
  - Plant Anatomy ~ study of plant tissues

2

Tissue

A group of connected cells in an animal or plant that are

- similar to each other,
- have the same purpose and
- form the stated part of the animal or plant

3

4-Basic Animal Tissue Types

1. Epithelial Tissues or Epithlium ~ lining tissues & glands
2. Connective tissues ~ binding tissues
3. Muscular tissues ~ contractile tissues
4. Nervous Tissues ~ conducting tissues

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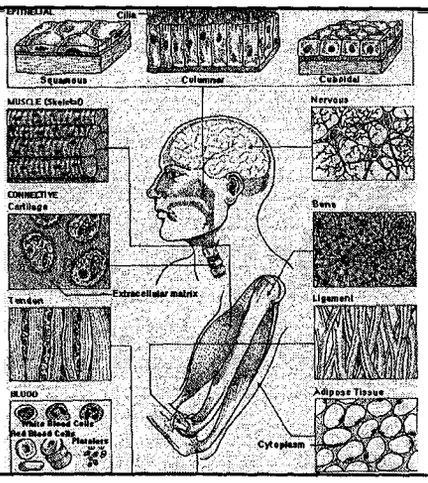

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Epithelium

Epithelium, singular

Epithelia, plural

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The Concept of Epithelium

- The layer of cells near the periphery can be modified for protection or defence and can prevent fluid loss or desiccation.
- These cells can also be modified for metabolic purposes such as control of substances taken up by the organism or excreted and for the collection of information or signals from the external environment.
- These cells at the border between the external and internal environments, the epithelial cells, are extremely important in many aspects of physiological homeostasis.

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Features of Epithelium

- Epithelium lines the surfaces of the body and is mainly located on the borders between the external and internal environments.
- Epithelium also lines all the internal body spaces that have a connection with the external environment at some stage.
- Epithelium plays an important role in homeostasis of the body and in maintaining the physiological parameters of the internal environment different from those outside the body.

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Features of Epithelium (cont.)

- Epithelium develops in the embryo from all the three germ layers (Ectoderm, Mesoderm, Endoderm).
- For example,
  - Ectodermal origin: Epidermis of the skin
  - Mesodermal origin: Epithelium lining the serous cavities (peritoneum, pleura, pericardium) (and is often referred to as mesothelium)
  - Endodermal origin: Epithelium lining most of the intestinal tract

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Features of Epithelium (cont.)

- Endothelium, lining the blood vessels, is not a true epithelium, as it is derived from mesenchyme (and should be considered as belonging to connective tissue.
- Endothelium has no connection at any stage with the external environment.)

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Proliferation and regeneration of epithelium

- Epithelia are present in vulnerable sites of the body, where they are continually exposed to the hazards of the external environment.
- Epithelial cells are constantly subjected to mechanical damage, destroyed, or sloughed off.
- Epithelia have remarkable proliferative properties and typically show many dividing cells (mitoses) in order to replace the cells lost and maintain the integrity of the tissue.
- In cases of trauma or wounds, the epithelia need to cover the lesion as rapidly as possible, repair the lining tissue and prevent damage to the underlying tissues.
- Most of the cancers of the body are the result of uncontrolled proliferation of epithelial cells.

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Characteristics of Epithelium

1. Epithelial tissue covers surfaces with an uninterrupted layer of cells.
   Epithelium covers nearly all external and internal body surfaces.
2. Epithelial cells are attached to one another.
   Special devices (intercellular junctions, tonofilaments) provide for structural integrity (wholeness) of the epithelium.
   There are several types of cell junctions.
3. Epithelial cells have small intercellular spaces.
   The narrow spaces between cells are sealed off from the external environment by cell junctions near the free surface of the cells. Epithelial tissue has very little interstitial fluid.
   Epithelium is an avascular tissue and has no integral blood supply.

1

Characteristics of Epithelium (cont.)

4. Epithelial cells are polarized.

   An epithelium has a free surface, the apical surface, exposed to the outside, and

   An attached surface, the basal surface, resting on the underlying connective tissue.

5. Epithelial cells are separated from the underlying tissue by a basement membrane. The cell itself lies on a basal lamina.

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Basal Lamina

- All epithelia lie on a basal lamina, separating them from the underlying connective tissue (*lamina propria*).
- The basal lamina provides structural support and acts in part as a selective barrier for the epithelial layer.
- The basal laminae are formed by the epithelial cells themselves.
- In some cases the basal laminae are greatly thickened (as in the glomeruli and filtration system of the kidneys).

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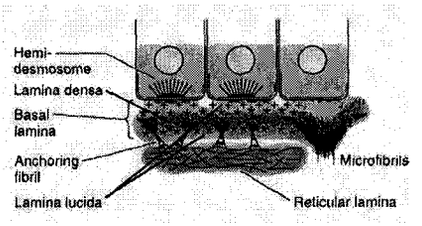
Basal Lamina

The basal laminae, as seen by transmission electron microscopy, are seen to be formed from an electron-dense layer (50-80 nm thick) composed of non-fibrous type IV collagen and the proteoglycan, heparan sulfate, surrounded on both sides by a less-dense layer containing the glycoprotein, laminin.



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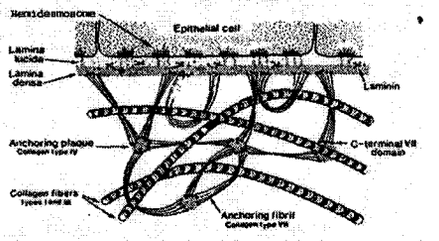
Basement Membrane

- Basement membrane is a structure that supports overlying epithelial cells or endothelial cells.
- Basement membrane is a thin sheet of collagen and glycoproteins produced in part by the epithelial cells themselves and in part by underlying connective tissue cells (specifically, fibroblast).



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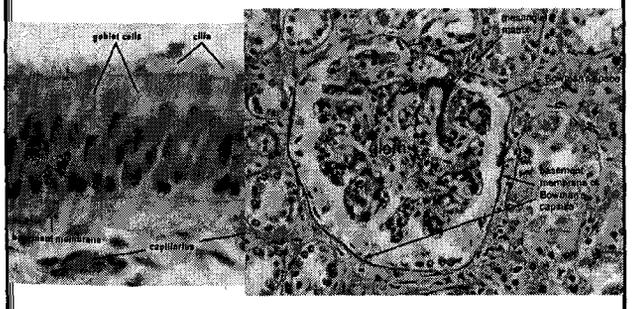
Basement Membrane

a thin sheet of collagen and glycoproteins



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Function and Importance of Basement Membrane

- The primary function of the basement membrane is to anchor down the epithelium to its loose connective tissue underneath. This is achieved by cell-matrix adhesions through cell adhesion molecules (CAMs).
- The basement membrane acts as a mechanical barrier, preventing malignant cells from invading the deeper tissues. Early stages of malignancy that are thus limited to the epithelial layer by the basement membrane are called carcinoma *in situ*.

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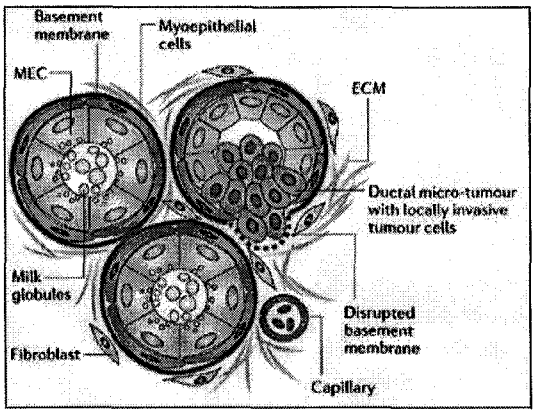

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Function and Importance of Basement Membrane (cont.)

- The basement membrane is also essential for angiogenesis (development of new blood vessels). Basement membrane proteins have been found to accelerate differentation of endothelial cells.
- It also plays an important role in glomerular filtration in the kidney.
- Noncollagenous domain basement membrane collagen type IV is autoantigen (target antigen) of autoantibodies in the autoimmune disease Goodpasture's syndrome.

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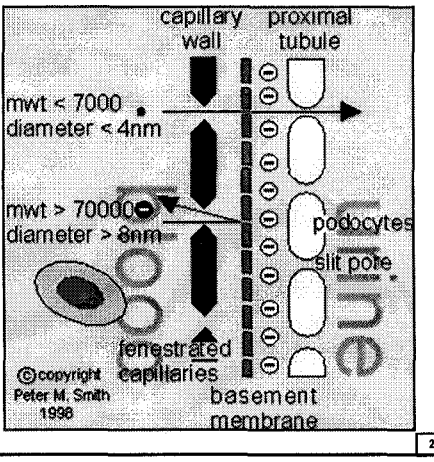
Glomerular Filtration in the Kidney



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Polarity of Epithelial Cells

- Epithelial cells are polarized cells and we can distinguish different areas of the cells (apical, basal, lateral) with specific structural modifications (unlike other tissues, where structural polarity is not found).
- Specific structures found on the apical surface (the free surface facing the lumen or external environment) include : microvilli, stereocilia, cilia or flagella.
- The lateral surfaces form cellular junctions.

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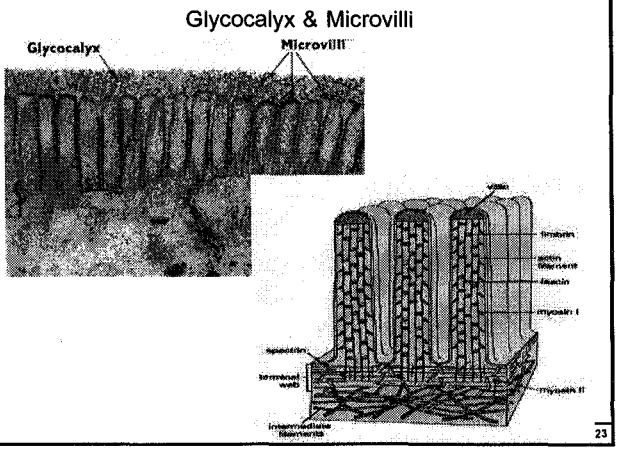
Glycocalyx & Microvilli



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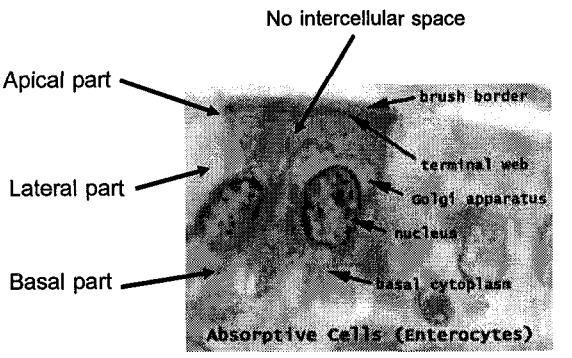

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Types of Cell Junctions of Epithelium

- The lateral surfaces (between adjacent epithelial cells) typically have "junctional complexes" including :
  - Tight junctions : impermeable area, enabling the organism to maintain the integrity of its internal environment
  - Adhering junctions (desmosomes) : adhering junctions, promoting adhesion and reinforcing the structural integrity and sites for stress fibers
  - Communicating junctions (gap junctions or nexuses) : communication, which allow the exchange of nutrients, ions, signals between adjacent cells).

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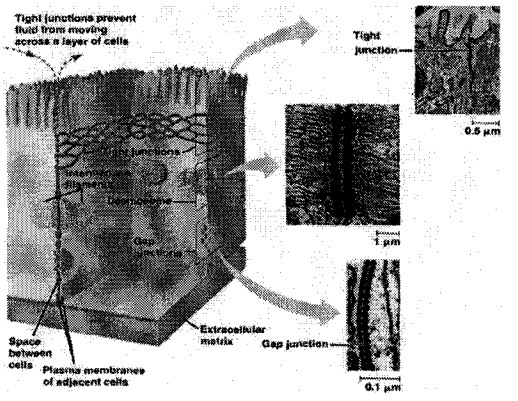
Junctional Complex at the Lateral Surfaces of Epithelial Cells



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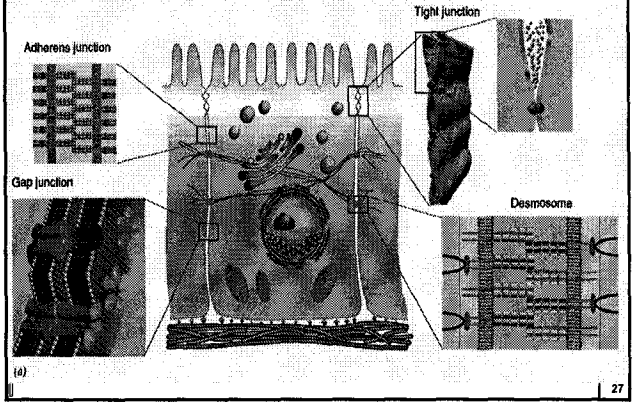
Junctional Complex Components



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Tight junctions [Occludin]

- Tight (occluding) junctions block diffusion; they typically form a seal or gasket around the apical end of cells comprising simple epithelia (i.e., epithelia comprising only a single layer of cells).
- This junction helps assure adequate separation between different fluid compartments (i.e., between the contents of the intestine and the interstitial fluid of the body).

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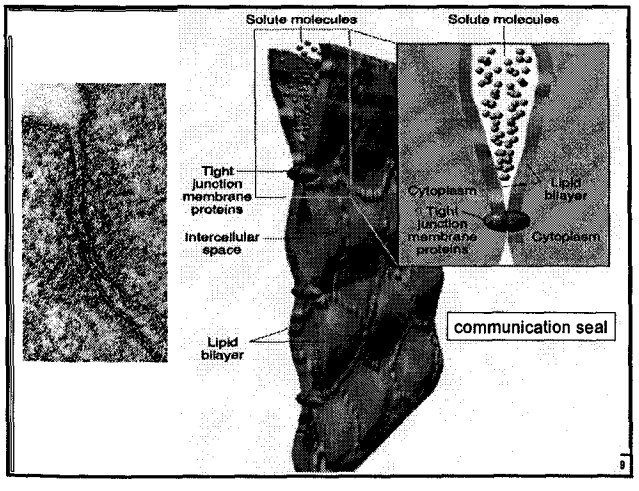

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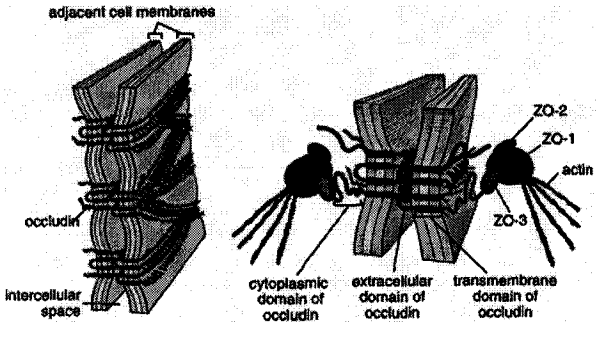
Tight junction [Occludin]



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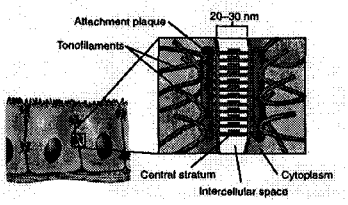
Adhering junctions [Maculae Adherens]

- Adhering junctions (e.g., desmosomes) provide mechanical attachment. Keratinocytes are joined to one another by many adhering junctions.



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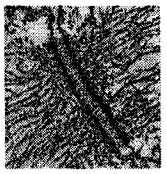
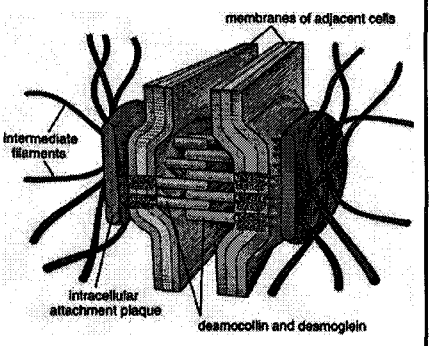
Desmosome [Maculae Adherens]



mechanical stress



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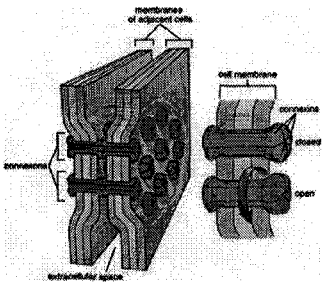
Communicating Junction

- Gap junctions provide direct intercytoplasmic communication between joined cells. That is, ions or small molecules can pass through gap junctions directly from the cytoplasm of one cell into the cytoplasm of an adjacent cell, without passing into intercellular space.



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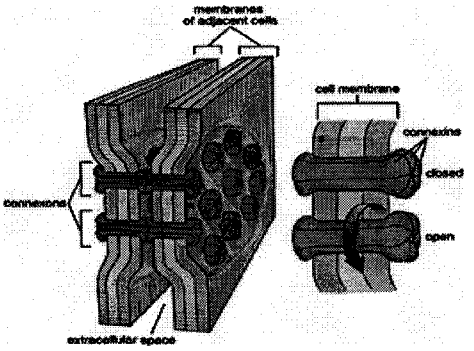
Gap Junction



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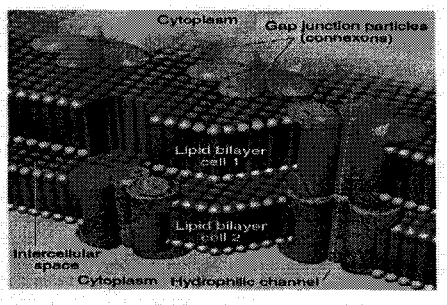
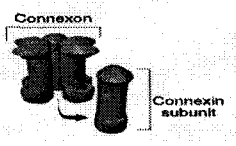
Gap Junction Structure





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Functions of Epithelium

- Epithelium at the border between the internal and external environments
- The functions of epithelium are many and varied, but can be conveniently divided into three major categories:
  1. Protective function,
  2. Metabolic functions,
  3. Sensation

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1. Protective function of epithelium

- Epithelial tissue thus serves both as a protective barrier for the body and as an active interface with the environment.
- The epithelium of the skin protects the underlying tissues from
  - ♦ mechanical injury / reduces friction
  - ♦ harmful chemicals
  - ♦ ultraviolet light
  - ♦ dehydration / waterproof
  - ♦ invasion of foreign bodies / cleaning

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2. Metabolic Functions of Epithelium

2.1 Secretion : In glands, epithelial tissue is specialised to secrete specific chemical substances such as
- ♦ enzymes,
- ♦ hormones and
- ♦ lubricating fluids.

2.2 Absorption : Epithelial lining of the small intestine absorbs nutrients from the digestion of food.

2.3 Excretion : The kidney excretes waste products from the body and reabsorbs needed materials from the urine.
Sweat is also excreted from the body by epithelial cells in the sweat glands.

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Metabolic Functions of Epithelium (cont.)

2.4 Diffusion : A thin lining of simple epithelium promotes the diffusion of gases, liquids and nutrients.

Exchange of metabolites, typically described as ion-transport.

All the substances entering or leaving the body must pass through epithelium and are under its control.

The ion-transporting epithelium may become highly specialized for absorption or excretion.

Example : walls of capillaries and lungs.

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3. Sensation function of epithelium

- Some epithelia are modified for sensory reception. including recognition of sensory stimuli such as pain or as chemoreceptors and photorecptors.
- Sensory stimuli penetrate specialised epithelial cells.
- Specialised epithelial tissue containing sensory nerve endings is found in
  - – skin,
  - – eyes,
  - – ears,
  - – nose and
  - – tongue

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Classification of Epithelium

By Function

1. Covering Epithelium
2. Glandular Epithelium

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Classification of Epithelium

by Morphology

- The number of cell layers and
- The appearance of the cells at the border adjacent to the external environment.
  1. Simple epithelia are composed of a single layer of epithelial cells.
  2. Stratified epithelia are composed of more than one layer of epithelial cells.

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1. Simple Epithelium

- Simple epithelia consist of a single layer of cells.
- When seen in vertical sections the epithelial cells are described as :
  - 1.1 Squamous (flattened)
  - 1.2 Cuboidal (more square or cube-like)
  - 1.3 Columnar (tall and thin)
  - 1.4 Pseudostratified

- ❖ homogeneous : single cell type
- ❖ Heterogeneous : more than one cell ytpe
- ❖ ciliated : cells with cilia on apical surface
- ❖ brush border : cells with microvilli on apical surface
- ❖ pseudostratified : single layer with false impression

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1.1 Simple Squamous Epithelium

- Squamous cells have the appearance of thin, flat plates.
- Squamous cells tend to have horizontall flattened, elliptical nuclei because of the thin flattened form of the cell.
- forms the lining of cavities such as the mouth, blood vessels, heart and lungs and make up the outer layers of the skin.
- lines the serous cavities of the body (peritoneum, pleura, pericardium, mesentery).
- lines cardiovascular system, covers organs and forms glomerular capsules in kidney.

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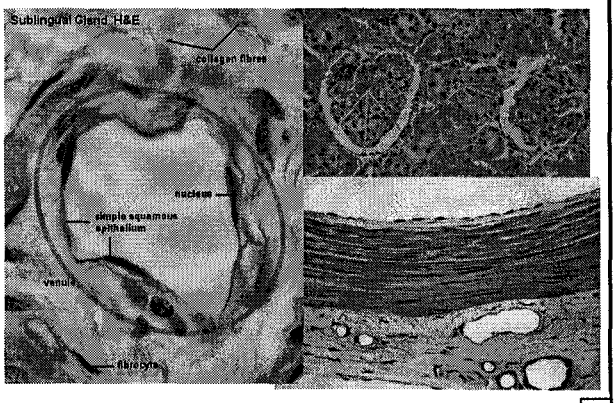
Simple Squamous Epithelium



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1.2 simple Cuboidal Epithelium

- Cuboidal cells are roughly square or cuboidal in shape.
- Each cell has a spherical nucleus in the centre.
- Cuboidal epithelium is found in glands and in the lining of the kidney tubules as well as in the ducts of the glands.
- They also constitute the germinal epithelium which produces the egg cells in the female ovary and the sperm cells in the male testes.

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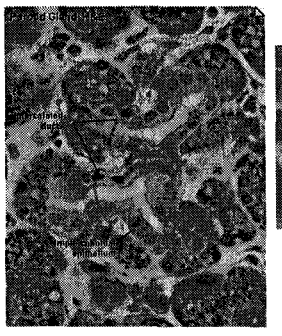
Simple Cuboidal Epithelium



Thyroid gland

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1.3 Simple Columnar Epithelium

- The cells are elongated and column-shaped.
- The nuclei are elongated and are usually located near the base of the cells.
- Columnar epithelium forms the lining of the stomach and intestines.
- Some columnar cells are specialised for sensory reception such as in the nose, ears and the taste buds of the tongue.
- Goblet cells (unicellular glands) are found between the columnar epithelial cells of the duodenum.
- They secrete mucus or slime, a lubricating substance which keeps the surface smooth.

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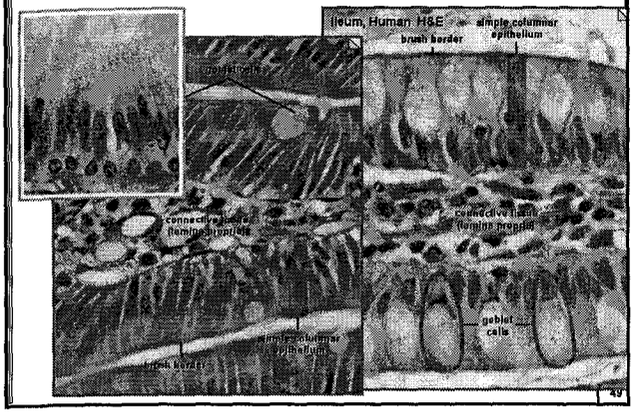
Simple Columnar Epithelium



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1.3.1 Simple Ciliated Columnar Epithelium

- Columnar epithelial cells posses fine hair-like outgrowths, cilia on their free surfaces.
- These cilia are capable of rapid, rhythmic, wavelike beatings in a certain direction.
- This movement of the cilia in a certain direction causes the mucus, which is secreted by the goblet cells, to move (flow or stream) in that direction.
- Ciliated epithelium is usually found in the air passages like the nose.
- It is also found in the uterus and Fallopian tubes of females. The movement of the cilia propel the ovum to the uterus.

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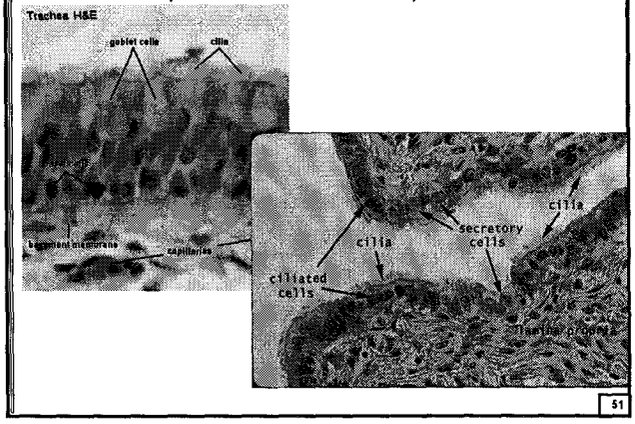
Simple Ciliated Columnar Epithelium



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1.4 Pseudostratified Columnar Epithelium

- Some epithelia consist of a single layer of irregular columnarcells, all in contact with the basal lamina.
- The nuclei of adjacent cells are not orderly arranged but appear at different levels, giving the false appearance of being stratified.
- This epithelium also is ciliated and is an example of a heterogeneous epithelium owing to an additional cell type (mucus-secreting unicellular goblet cells).
- Pseudostratified columnar epithelium is the typical epithelial type of much of the respiratory tract.

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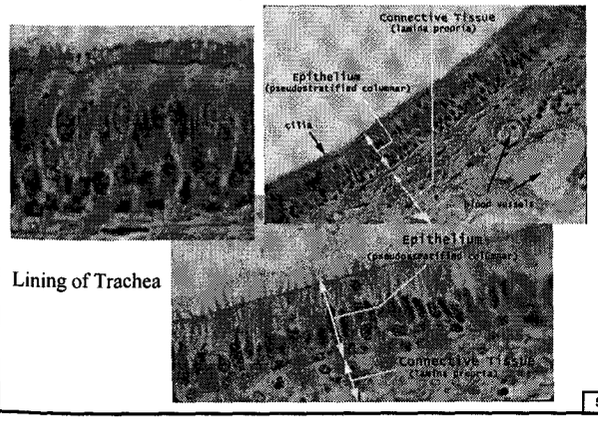
Pseudostratified (ciliated) columnar epithelium



Lining of Trachea

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2. Stratified Epithelium.

- Body linings have to withstand wear and tear, the epithelia are composed of several layers of cells and are then called compound or stratified epithelium.
- The top cells are flat and scaly and it may or may not be keratinised (i.e. containing a tough, resistant protein called keratin).
- The mammalian skin is an example of dry,
  - keratinised, stratified epithelium.
- The lining of the mouth cavity is an example of an
  - unkeratinisied, stratified epithelium.

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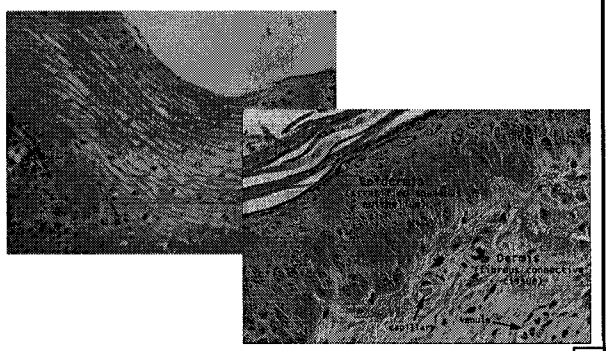
2.1 Stratified Squamous Epithelium

keratinised, stratified epithelium of skin



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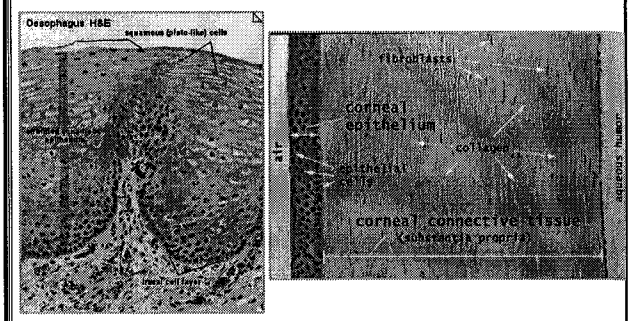
2.1 Stratified Squamous Epithelium

unkeratinisied, stratified epithelium



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Transitional epithelium

- Transitional epithelium is a form of stratified epithelium lining the urinary bladder and part of the urinary tract.
- This epithelium is subjected to large mechanical changes and can adapt accordingly.
- If the bladder is empty, the epithelium appears to be thicker and have more layers, than when the bladder is full and distended, in which case, the cells appear more stretched.
- Transitional epithelium can be recognized by the large rounded epithelial cells lining the lumen (in contrast to other stratified epithelia, where such surface cells are squamous).

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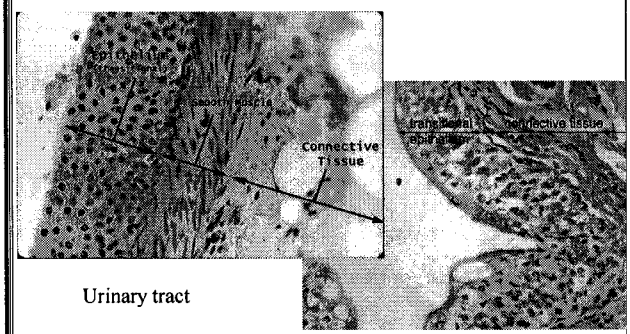
Transitional epithelium



Urinary tract

Urinary bladder

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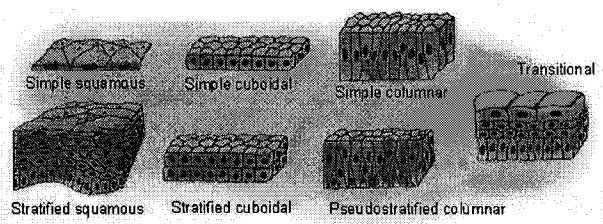
Types of Epithelium



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Glandular Epithelium

Specialization of Epithelium

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5. Shape of Secretory Units
   - 5.1 Tubular - An elongated group of secretory cells with a lumen (which may be small or large) shaped like a tube.
   - 5.2 Acinar or Alveolar - A small grape-like (acinus means "grape") or sac-like (alveolus means "sac") group of secretory cells arranged about a small lumen. These cells are attached to a basement membrane.
   - 5.3 Tubulo-acinar – Lumen of secretory units have both of the above listed shapes

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6. Arrangement (branched or not) and occurrence of Duct System
   - 6.1 Simple glands - Glands of this type have an unbranched duct into which the cells secrete. Each secretory portion empties separately on an epithelial surface.
   - 6.2 Branched glands - Several secretory units empty into an unbranched excretory duct.
   - 6.3 Compound glands - These glands have a highly branched duct system. Secretory portions empty into an elaborate branched duct system, which, in turn, drain into larger ducts.

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Types of exocrine glands in man

1. Simple tubular glands - These glands are epithelial-lined tubules, which open on the apical surface. There are three types.
   - 1.1 Simple straight tubular glands. The long crypts of Lieberkühn, located within the colon with numerous goblet cells.
   - 1.2 Simple coiled tubular glands. Within the dermis, eccrine sweat glands are located. The deeper portion of these simple coiled tubular glands is easily seen. The long unbranched lumen that goes to the apical surface is rarely seen in cross-section.
   - 1.3 Simple branched tubular glands the deeper portion of the tubule branches. These simple branched tubular glands are found primarily in the stomach

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2. Simple alveolar (acinar) glands - glands of this type have many acini emptying into a common duct, and this can be seen with the sebaceous glands that are emptying into the hair follicles located within the dermis of the scalp in this section. Sebaceous glands are also the best representation of secretion by holocrine mechanism.
3. Simple tubulo-alveolar glands - Some of the secretory cells are arranged as acini (alveoli) and others are arranged as tubules. Examples of these include some of the smaller glands of the respiratory tract; minor salivary glands located within the oral cavity are other examples.

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4. Compound tubular glands - These glands have a highly branched duct system. The secretory cells at the ends of the ducts are in the form of tubules. The kidney and testes are examples of a compound tubular gland.
5. Compound alveolar glands - The ducts end in alveoli with dilated sac-like lumina. The lactating mammary gland is a classic example of this type of gland as well as a gland that utilizes the apocrine mechanism of secretion.
6. Compound tubulo-alveolar glands - These glands also have a highly branched duct system, but some of the ducts end as tubules and others end as alveoli. Examples are two of the major salivary glands, the submandibular and the sublingual glands.

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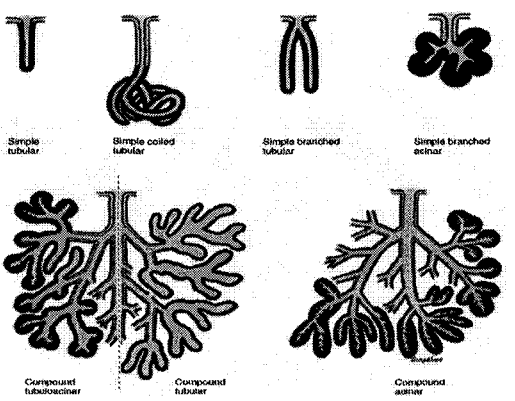
Exocrine Glands in Man



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Endocrine Glands

- Endocrine glands develop initially in the embryo like the multicellular exocrine glands, however their ducts degenerate and disappear (ductless glands) and the glands secrete directly into the blood capillaries.
- Endocrine secretions are known as hormones and the endocrine glands form part of a major regulatory system, known as the endocrine system.

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Endocrine Gland Classification

The secretory cells may be classified into two major groups:

- Polypeptide (or protein)-secreting cells
- Steroid-secreting cells.

1. The endocrine polypeptide (or protein)-secreting cells are typically characterized by well-developed RER (rough endoplasmic reticulum), Golgi bodies and membrane-bound secretory granules. These endocrine cells may be isolated or in small groups (the diffuse endocrine system) and include many of the endocrine cells of the intestine.
2. The endocrine steroid-secreting cells are characterized by well-developed SER (smooth endoplasmic reticulum) and abundant lipid droplets. The mitochondria of these cells have tubular cristae (unlike the typical lamellar cristae of other cell types, e.g. in the testis, ovary, suprarenal cortex.

74

Epithelial tissue Pathology

- The surface location of many epithelial tissues exposes them to a variety of insults, ranging from mechanical damage (cuts, scrapes) and active penetration (mosquitoes, parasites, hypodermics) to bacterial and fungal attack and poisoning by toxic chemicals.
- In simple clean wounds of the skin, one of the earliest healing accomplishments may be proliferation and spread of epithelial keratinocytes, re-establishing epidermal continuity in as little as 24 hours.
- Deep burns are so serious largely because they destroy the many hair follicles and sweat glands that invaginate deep into the dermis and serve as efficient sources of epithelial regrowth after more superficial injury.

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Epithelial tissue Pathology (cont.)

- The importance of epithelial cell regeneration is dramatically illustrated by recovery from cholera.
- A toxin from the cholera vibrio kills the intestinal epithelium.
- Resulting loss of bodily fluid from the uncovered mucosa leads to copious diarrhea, massive dehydration, and death within a few days.
- If, patients can be kept hydrated for those few days, epithelial replacement by stem cell division will restore normal function.

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Epithelial tissue Pathology (cont.)

- When an epithelial cells' ability to divide is stimulated inappropriately, it can result in the formation of a tumor.
- Cells in epithelial tumors often retain their basic epithelial character, remaining attached to one another and differentiating to form layered structures.
- As long as the neoplastic cells respect the basement membrane, the tumor will remain localized.
- But once cells break through this boundary they can enter circulation and metastasize.
- The name carcinoma is applied to any cancer (malignant neoplasm) of epithelial origin; adenocarcinoma names a cancer of glandular origin. (Cancers of mesenchymal origin are called *sarcomas*.)

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End of Epithelial Tissue

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Connective Tissue

1

Connective Tissue

- Connective tissue forms a framework upon which epithelial tissue rests and within which nerve tissue and muscle tissue are embedded. Blood vessels and nerves travel through connective tissue.
- Connective tissue functions not only as a mechanical support for other tissues but also as an avenue for communication and transport among other tissues.
- The principal cell types involved in immunological defense are found within connective tissue

2

Characteristics of Connective Tissue

- Connective tissue typically has many cell types immersed in intercellular material (extracellular matrix) synthezied these cells.
- Connective tissues cells typically account for only a small fraction of the tissue volume.
- The extracellular matrix consists of fibers which are embedded in ground substance containing tissue fluid.

3

Characteristics of Connective Tissue (cont.)

- The role of CT in defense of the organism is related to its content of phagocytic and antibody-producing cells.
- Phagocytic cells engulf inert particles and microorganisms which enter the body as antigens.
- Specific proteins called ~antibodies, produced by CT cells, combine with foreign proteins of bacteria and viruses-or with the toxins produced by bacteria- and combat the biologic activity of theses harmful agents.

4

Characteristics of Connective Tissue (cont.)

- The role of CT in nutrition depends upon its close association with blood vessels. The nutrients carried in the blood and the metabolic wastes transported to the excretory organs diffuse through the CT which surrounds the capillaries.

5

Origin of Connective Tissue

- Connective tissue develops from the embryonic tissue, the mesenchyme (unlike most epithelial tissue which is derived from ectoderm and endoderm).
- The mesenchyme is characterized by branched cells embedded in an abundant amorphous intercellular substance.
- The mesenchyme derives from the middle layers of the embryo, the mesoderm, spread throughout the fetus, surrounding the developing organs and prenetrating into them.

6

Functions of Connective Tissue

- Although many functions are attributed to connective tissue, its primary functions include:
- Providing structural support: bone, cartilage , tendon, ligament, and structural framework
- Serving as a medium for exchange: capsule
- Aiding in the defense and protection of the body: phagocytic cells, antibody producing cells, pharmacological substance producing cells.
- Forming a site for storage of fat

7

Components of Connective Tissue

- Connective tissue consists of cells embedded in an extracellular matrix.
- The matrix, in turn, consists of fibers and ground substance.
  - Connective tissue cells
  - Extracellular matrix
    - Fibers
    - Ground substance

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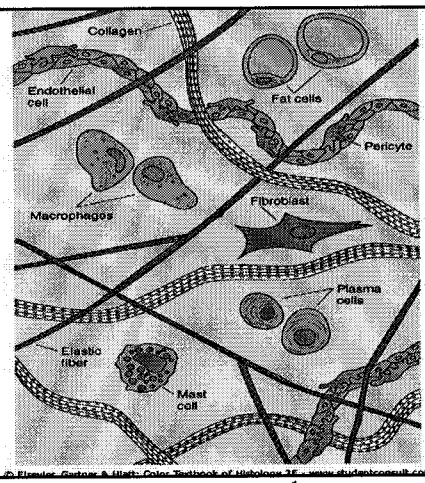
Components of Connective Tissue

Cells	Fibers
Fibroblast	Collagen fibers
Adipocyte	Reticular fibers
Pericyte cells	Elastic fibers
Macrophages	Ground substance
Mast cells	
Lymphocytes, Monocytes, Neotrphiles, ...	
Chondrocyts, Osteocytes & Other cells	

9

Component of connective tissue



10

I. Connective Tissue Matrix (Extracellular matrix)

- Connective tissue matrix is composed of:
  - Ground substance
    - Ground substance is found in all cavities and clefts between the fibres and cells of connective tissues.
    - Ground substance is soluble in most of the solvents used to prepare histological sections and therefore not visible in ordinary sections.
  - Fibers.

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Ground substance

- Ground substance is the background material within which all other connective tissue elements are embedded.
- In ordinary connective tissue, the ground substance consists mainly of water whose major role is to provide a route for communication and transport (by diffusion) between tissues.
- This water is stabilized by a complex of acid mucopolysaccharides [glycosaminoglycans (GAGs), proteoglycans, and glycoproteins], all of which comprise only a small fraction of the weight of the ground substance.
- There is a small quantity of fluid, called Tissue Fluid - that is similar to plasma.

12

Ground substance (cont.)

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

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Acid Mucopolysaccharides	Location
Hyaluronic acis	Skin, umbilical cord, vitreous, synovial fluid. Heart valves, cornea,
Chondroitin	Cornea, embryomic cartilage
Chondroitin-4-sulfate (sulfate of chondroitin A)	Cartilage, bone, skin
Chondroitin-6- sulfate (fulfate of chondroitin C)	Cartilage, tendon, umbilical cord. Intervertebral disk, embryonic cartilage
Dermatan sulfate (chondroitin sulfate B)	Skin, tendon, ligamnets, heartvalves
Keratan sulfate	Cartilage, intervertebral disk, bone, cornea

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Important role of Acid Mucopolysaccharides

- Induction of calcification, control of metabolites, ions, and water, and healing of wounds.
- They are genetically controlled, and disturbances in their metabolism results in pathologic conditions-the so-called Lysosomal diseases.
  - Degradation of dermatan sulfate or heparan sulfate is blocked at the lysosomal level by defective fibroblasts.
  - Lack of hydrolase in lysosomes as the cause of disorders in human- Hurer's syndrome, Hunter's syndrome, Sanfilippo syndrome, and Morquio's syndrome.

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Important role of tissue fluid

- The water, including low molecular weight proteins, in the intercellular substance of CT comes from the blood, passing through the capillary walls into the CT space.
- There are 2 forces acting on the water contained in the capillaries:

1. Hydrostatic pressure of the blood -- from pumping action of the heart.
2. Osmotic pressure of the plasma -- water draws back into the capillaries. The osmotic pressure mainly causes by protein macromolecules – colloid osmotic pressure.

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Important role of tissue fluid (cont.)

- In several pathologic conditions, imbalance of hydostatic pressure and osmotic pressure causes the quantity of tissue fluid may increase considerably - Edema.
- Edema may result from venous obstruction or decrease in venous blood flow – congestive heart failure.
- It may cause by starvation because the consequent protein deficiency results in lack of plasma proteins and in turn a fall in colloid osmotic pressure. Therefore water accumulates in the connective tissue.

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Edema (cont.)

- Edema may be caused by the increased permeability of the blood capillary endothelium due to mechanical injury or to some substance produced in the body – histamine.
- Edema may be caused by the obstruction of lymphatic vessels, eg. by plugs of parasites or tumor cells

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Connective Tissue Fibers

- The **extracellular fibers** of connective tissue are traditionally classified into three types:
  1. Collagen fibers confer main tensile strength, and are the stuff of scars.
  2. Elastic fibers confer elasticity.
  3. Reticular fibers (really, a special form of collagen) provide a delicate supporting framework for loose cells.

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1. Collagen fibers

- Collagen is produced by fibroblasts.
- Collagen is the most common protein in the body. As an essential structural element in the extracellular matrix of most connective tissues, including bone and cartilage, collagen confers toughness and tensile strength to CT. Scars are made of collagen.
- Collagen fiber varies from ~ 1 to 10 μm.
- Longitudinal striations may be visible in thicker fibres.

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Collagen fibers (cont.)

- Collagen is secreted by fibroblasts as procollagen molecules, converted extracellularly into tropocollagen which self-assembles into microscopically visible fibers and grossly evident mechanical structures such as tendons.
- Collagen is a scleroprotein composed of mainly glycine, proline, hydroxyproline, called Tropocollagen.
- The tropocollagen has a head and a tail.

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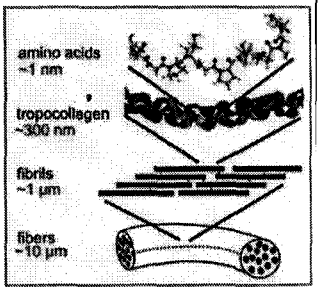
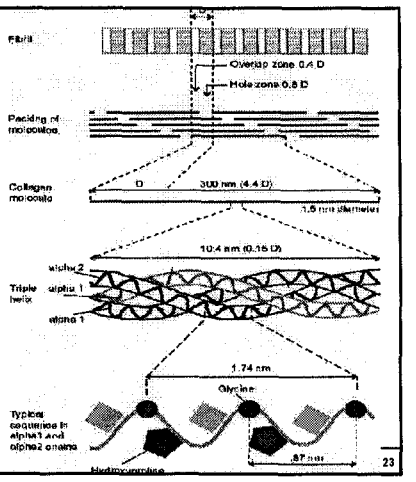
Collagen Fiber Composition

- Tropocollagens become aligned head to tail in overlapping rows with a gap between the molecules within each row.
- The strength of the fibril is due to covalent bonds between collagen molecules of adjacent rows.



22

Collagen fiber.
↑
Fibril
↑
Micrifibril
↑
Tropocollagen
↑
Triplet helix
↑
Polypeptide
(glycine, proline, hydroxyproline)



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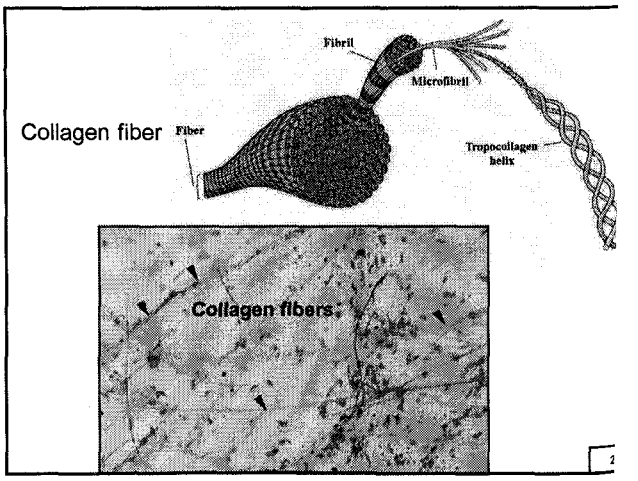
Collagen fiber



Types of Collagen Fibers

- More than a dozen different varieties of collagen exist in the body.
- These varieties are produced by different genes, have somewhat different properties, and occur in different locations.
- The most common forms are
  - Type I collagen forms the familiar eosinophilic collagen fibers of ordinary fibrous connective tissue (e.g., dermis, tendon, organ sheath, fascia).
  - Type II collagen reinforces cartilage.
  - Type III collagen forms reticular fibers and also occurs in basement membrane and bone.
  - Type IV collagen occurs in the basal lamina around smooth and skeletal muscle fibers..
  - Type VII collagen is an interlinking collagen important for formation of basement membrane.

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2. Elastic fibres

- Elastic fibers are thinner and do not have striations.
- They branch and unite with one another, forming an irregular network.
- Elastic fibers are colored in fresh tissues - they are light yellow , eg. in the elastic ligaments of the vertebral column.
- Elastic fibers can be stretched to about 150% of their original length. They resume their original length if the tensile forces applied to the elastic fibers are relaxed - in blood vessels contribute to the efficiency of the blood circulation and important component of the skin.

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3. Elastic fibres (cont.)

- Elastin is a somewhat odd protein – elastin- in that its amino acid sequence does not determine a specific three-dimensional structure of the molecule. Instead, elastin remains unfolded as a random coil.
- Elastin molecules are cross-linked to each other by desmosin and isodesmosin links, producing elastin coils.
- Elastic fibres consist of individual microfibrils, which are embedded in an amorphous matrix.

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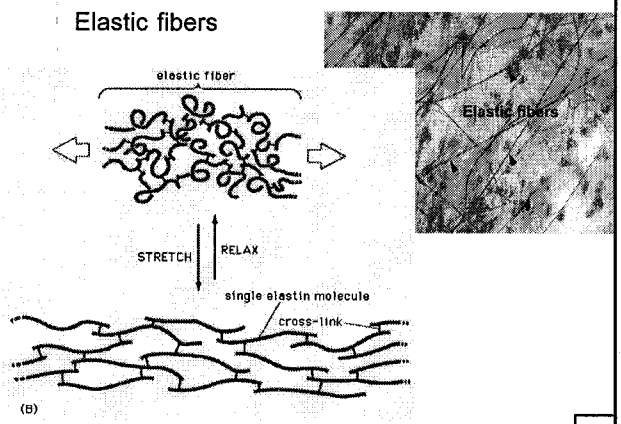
Elastic fibers



28

3. Reticular Fibers

- Reticular fibers are very delicate and form fine networks instead of thick bundles. They are usually not visible in histological sections but can be demonstrated by using special stains. For example, in silver stained sections reticular fibers look like fine, black threads
- reticular fibers consist of collagen - although the main type of tropocollagen found in reticular fibers, type III, is different from that of the coarse collagen fibers.
- Reticular fibers give support to individual cells, for example, in muscle and adipose tissue.

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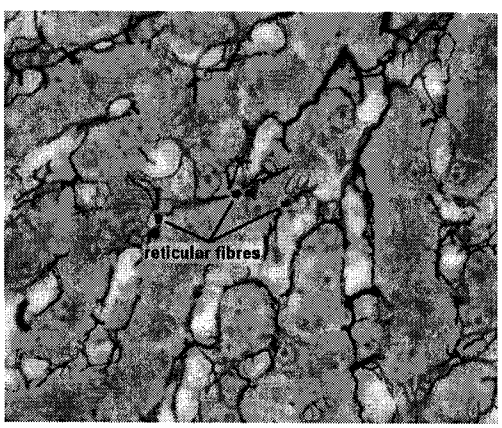

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II. Cellular Components of CT

- The cells in connective tissues are grouped into two categories:
  - fixed cells (stable in place) and
  - transient cells (migrating cells)

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Fixed cells

- Fixed cells are a resident population of cells that have developed and remain in place within the connective tissue,
- The fixed cells are a stable and long-lived population that includes:
  - Fibroblasts
  - Adipose cells
  - Pericytes
  - Mast cells
  - Macrophages ; certain cells of the macrophages (e.g., Kupffer cells of the liver) to be fixed connective tissue cells.

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Transient cells

- Transient cells - free or wandering cells - originate mainly in the bone marrow and circulate in the bloodstream.
- Upon receiving the proper stimulus or signal, these cells leave the bloodstream and migrate into the connective tissue to perform their specific functions

- Transient cells include:
  - Plasma cells
  - Lymphocytes
  - Neutrophils
  - Eosinophils
  - Basophils
  - Monocytes
  - Macrophages

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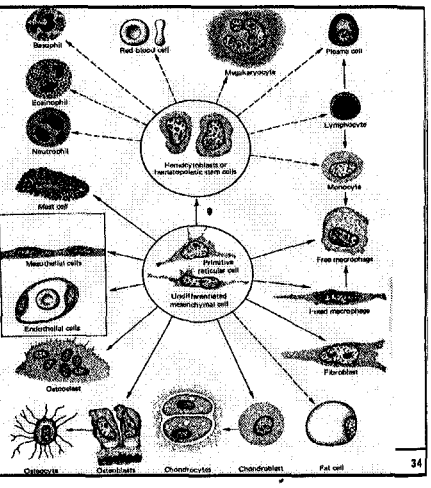
Connective Tissue Cells



34

1. Fibroblasts

- Fibroblasts, the most abundant cell type in the connective tissue, are responsible for the synthesis of almost all of the extracellular matrix.
- Fibroblasts are the least specialized of the cells making up connective tissue and may even be represented by several different functioning populations within certain areas of the body.
- Fibroblasts may occur in either an active state or a quiescent state. Some histologists differentiate between them, calling the quiescent cells fibrocytes; however, because the two states are transitory,

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Fibroblasts (cont.)

- Fibroblasts are capable of some movement.
- Fibroblasts seldom unergo cell division but may do so during wound healing.
- These cells, however, may differentiate into adipose cells, chondrocytes (during formation of fibrocartilage), and osteoblasts (under pathological conditions).

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Active fibroblasts

- Active fibroblasts often reside in close association with collagen bundles, where they lie parallel to the long axis of the fiber.
- The fibroblasts are elongated, fusiform, darker-stained, large, granular, ovoid nucleus containing a well-defined nucleolus.
- Electron microscopy reveals a prominent Golgi apparatus and abundant rough endoplasmic reticulum (RER) in the fibroblast, especially when the cell is actively manufacturing matrix, as in wound healing.
- Actin and α-actinin are localized at the periphery of the cell, whereas myosin is present throughout the cytoplasm.

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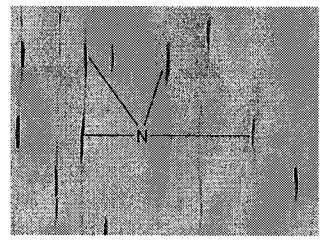
Inactive fibroblasts

- Inactive fibroblasts are smaller, more ovoid, and possess an acidophilic cytoplasm.
- Their nucleus is smaller, elongated, and more deeply stained.
- Electron microscopy reveals sparse amounts of RER but an abundance of free ribosomes.



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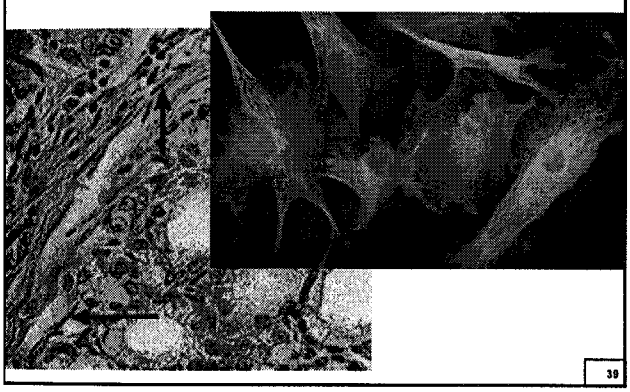
Fibroblasts labeled with fluorescent dyes FITC, Rhodamine, and Dapi



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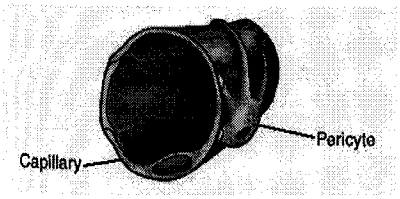
3. Pericytes

- Pericytes derived from undifferentiated mesenchymal cells, partly surround the endothelial cells of capillaries and small venules
- Pericytes are surrounded by their own basal lamina, which may be fused with that of the endothelial cells
- Pericytes possess characteristics of endothelial cells and smooth muscle cells in that they contain actin, myosin, and tropomyosin, suggesting that they may function in contraction.
- Under certain conditions, pericytes may differentiate into other cells.

40

pericyte



A slender, relatively undifferentiated, connective tissue cell that occurs about capillaries or other small blood vessels. Also called adventitial cell.

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2. Adipose Cells

- Fat cells are found throughout the body in loose connective tissue and are concentrated along blood vessels. They may also accumulate into masses, forming adipose tissue.
- Adipose cells are fully differentiated cells that function in the synthesis, storage, and release of triglycerides.
- There are two types of fat cells, which constitute two types of adipose tissue.
- Unilocular fat cells. Cells with a single, large lipid droplet, called, form white adipose tissue.
- Multilocular fat cells. Cells with multiple, small lipid droplets, called, form brown adipose tissue.

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White fat cells

- Unilocular fat cells are large spherical cells, up to 120 μm in diameter, that become polyhedral
- Unilocular fat cells continuously store fat in the form of a single droplet, which enlarges so much that the cytoplasm and nucleus are displaced peripherally against the plasma membrane, giving these cells a "signet ring" profile , small Golgi complex situated adjacent to the nucleus, only a few mitochondria, and sparse RER, but an abundance of free ribosomes.
- The fat droplet is not bounded by a membrane.

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Brown fat cells

- Brown fat cells are smaller and more polygonal than white fat cells. Moreover, because the brown fat cell stores fat in several small droplets rather than a single droplet, the spherical nucleus is not squeezed up against the plasma membrane.
- Multilocular fat cells contain many more mitochondria but fewer free ribosomes than unilocular fat cells.
- Brown fat cells lack RER, they do have smooth endoplasmic reticulum (SER).

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Storage and Release of Fat by Adipose Cells

- During digestion, fats are broken down in the duodenum by pancreatic lipase into fatty acids and glycerol. The intestinal epithelium absorbs these substances and reesterifies them in the smooth endoplasmic reticulum to triglycerides, which then are surrounded by proteins to form chylomicrons.
- Chylomicrons are released into the extracellular space at the basolateral membranes of the surface absorptive cells, enter the lacteals of the villus, and are carried by the lymph to the bloodstream. Additionally, very-low-density lipoprotein (VLDL), which is synthesized by the liver, and albumin-bound fatty acids are present in the bloodstream.

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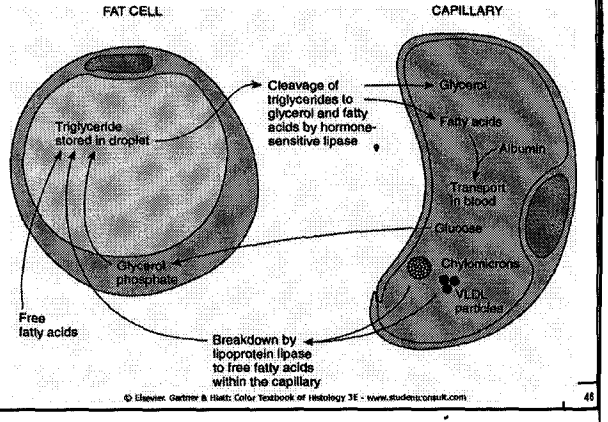
Transport of lipid between a capillary and an adipose cell



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Storage and Release of Fat by Adipose Cells (cont.)

- In the capillaries of adipose tissue, VLDL, fatty acids, and chylomicrons are exposed to lipoprotein lipase from fat cells, which breaks them down into free fatty acids and glycerol.
- The fatty acids enter the connective tissue and diffuse through the cell membranes of adipocytes. These cells then combine their own glycerol phosphate with the imported fatty acids to form triglycerides, which are added to the forming lipid droplets within the adipocytes until needed.
- Adipose cells can convert glucose and amino acids into fatty acids when stimulated by insulin.

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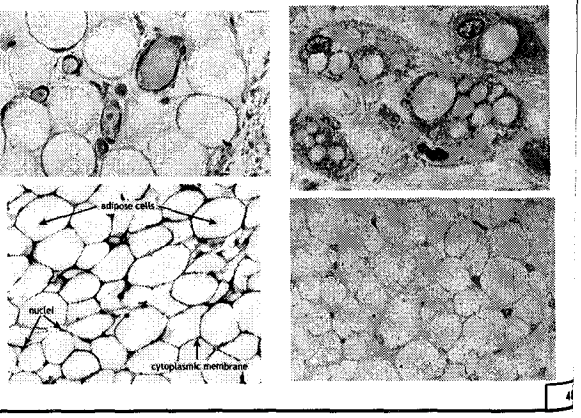
Uniloculat Adipos Cells **Multilocular Adipose cells**



4. Mast Cells

- Mast cells probably derive from precursors in the bone marrow, located throughout the body in the connective tissue proper and along small blood vessels
- They are ovoid and possess a centrally placed, spherical nucleus, numerous membrane-bound granules containing primary and secondary mediators and released during immediate hypersensitivity reactions.
- These mediators initiate the inflammatory response, activate the body's defense system by attracting leukocytes to the site of inflammation.
- Mast cells possess high-affinity cell-surface Fc receptors (FceRI) for immunoglobulin E (IgE), function in the immune system known as immediate hypersensitivity reaction (anaphylactic reaction) which may have lethal consequences).

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The primary mediators in inflammatory response

- The gents present in the granules are referred to as the primary mediators (also known as preformed mediators), containing
  - heparin,
  - histamine
  - neutral proteases
    (tryptase, chymase, and carboxypeptidases),
  - aryl sulfatase , such as peroxidase, and superoxide dismutase,
  - eosinophil chemotactic factor (ECF) and
  - neutrophil chemotactic factor (NCF).

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The secondary mediators in inflammatory response

- Mast cells synthesize a number of secondary mediators at the time of their release, *not* stored in granules.
  - leukotrienes (C4, D4, and E4),
  - thromboxanes (TXA2 and TXB2),
  - prostaglandins (PGD2).
  - platelet-activating factor (PAF),
  - bradykinins,
  - Interleukins (IL-4, IL-5, IL-6), and
  - tumor necrosis factor-alpha (TNF-α).

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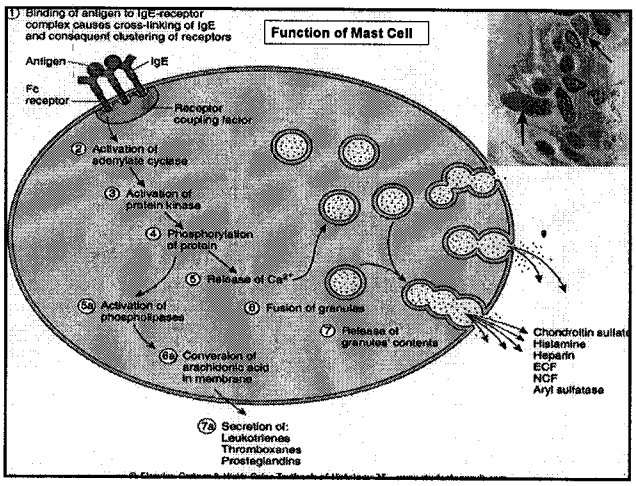

5. Macrophages

- Macrophages belong to the mononuclear phagocytic system and are subdivided into two groups of cells, phagocytes and antigen-presenting cells.
- Macrophages are irregularly shaped, varying from short, blunt projections to finger-like filopodia.
- More active macrophages have pleats well-developed Golgi apparatus, prominent RER, and an abundance of lysosomes and folds in their plasma membranes as a consequence of cell movement and phagocytosis.
- Their cytoplasm is basophilic and contains many small vacuoles and small dense granules.
- The eccentric nucleus is somewhat distinctive in that it is ovoid and usually indented on one side, so that it resembles a kidney

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- Macrophages localized in certain regions of the body were given specific names;
  - Kupffer cells of the liver
  - Dust cells of the lung
  - Langerhans cells of the skin
  - Monocytes of the blood
  - Macrophages of the connective tissue, spleen, lymph nodes, thymus, and bone marrow
  - Osteoclasts of bone
  - Microglia of the brain
- Under chronic inflammatory conditions, macrophages congregate, greatly enlarge, and become polygonal epithelioid cells
- When the particulate matter to be removed is excessively large, several to many macrophages may fuse to form a foreign-body giant cell, a giant multinucleated macrophage

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Macrophage Function

- Macrophages phagocytose senescent, damaged, and dead cells and cellular debris and digest the ingested material through the action of hydrolytic enzymes in their lysosomes
- Macrophages assist in defense of the body by phagocytosing and destroying foreign substances, including microorganisms.
- Macrophages also play a key role in presenting antigens to lymphocytes.

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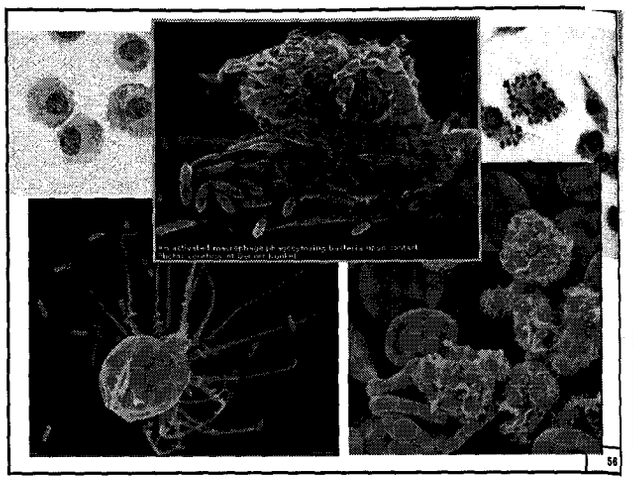

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6. Plasma Cells

- Plasma cells derived from B lymphocytes that have interacted with antigen, produce and secrete antibodies and are responsible for humorally mediated immunity.
- Plasma cells are large, ovoid cells with an eccentrically placed nucleus, intensely basophilic as a result of a well-developed RER, a few mitochondria are scattered.
- The spherical nucleus possesses heterochromatin radiating out from the center, giving it a characteristic "clock face" or "spoked" appearance.

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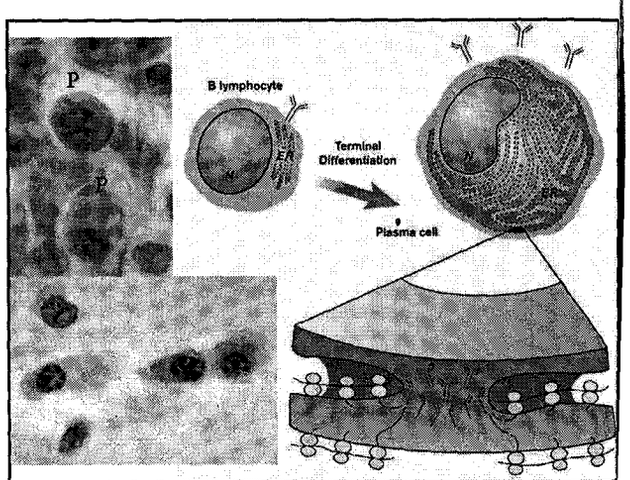

7. Leukocytes

- Monocytes have been discussed under "Macrophages."
- Neutrophils phagocytose and digest bacteria in areas of acute inflammation, resulting in formation of pus, an accumulation of dead neutrophils and debris.
- Eosinophils, like neutrophils, are attracted to areas of inflammation by leukocyte chemotactic factors. Eosinophils combat parasites by releasing cytotoxins. They also are attracted to sites of allergic inflammation, where they moderate the allergic reaction and phagocytose antibody-antigen complexes.
- Basophils (similar to mast cells) release preformed and newly synthesized pharmacological agents that initiate, maintain, and control the inflammatory process.
- Lymphocytes are present only in small numbers in most connective tissue, except at sites of chronic inflammation, where they are abundant.

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Classification of Connective Tissue

Classification of connective tissue

I. Connective tissue proper
   1. Loose Ct
   2. Dense Ct -- 2.1 Regular dense CT
      2.2 Irregular dense CT

II. Connective tissue with special properties
   1. Adipose tissue
   2. Elastic tissue
   3. Hematopoietic tissue (Reticular tissue)
   4. Mucous tissue

III. Supporting connective tissue
   1. Cartilage
   2. Bone

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Loose (Areolar) Connective Tissue

- Loose connective tissue is characterized by abundant ground substance and tissue fluid (extracellular fluid) housing the fixed connective tissue cells: fibroblasts, adipose cells, macrophages, and mast cells as well as some undifferentiated cells.
- The ground substance are loosely woven collagen, reticular, and elastic fibers.
- Coursing in this amorphous tissue are small nerve fibers as well as blood vessels that supply the cells with oxygen and nutrients.

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Dense regular connective tissue

- Compose of coarse collagen bundles densely packed and oriented into parallel cylinders or sheets that resist tensile forces.
- Because of the tight packing of the collagen fibers, little space can be occupied by ground substance and cells.
- Thin, sheet-like fibroblasts are located between bundles of collagen with their long axes parallel to the bundles.
- Tendons, ligaments, and aponeuroses are examples of dense regular collagenous connective tissue.

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Dense irregular connective tissue

- contains mostly coarse collagen fibers interwoven into a meshwork that resists stress from all directions.
- The collagen bundles are packed so tightly that space is limited for ground substance and cells.
- Fine networks of elastic fibers are often scattered about the collagen bundles.
- Fibroblasts, the most abundant cells of this tissue, are located in the interstices between collagen bundles.
- Dense irregular connective tissue constitutes the dermis of skin, the sheaths of nerves, and the capsules of the spleen, testes, ovary, kidney, and lymph nodes.

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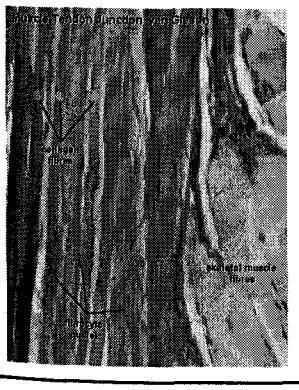
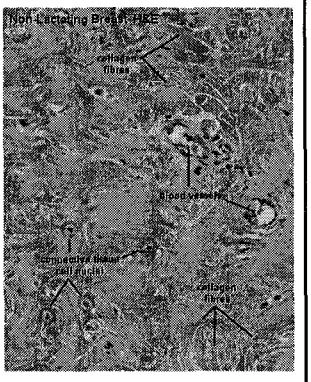
Dense irregular connective tissue

Dense regular connective tissue





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Adipose Tissue

- Adipose tissue is classified into two types according to whether it is composed of unilocular or multilocular adipocytes.
- Other differences between the two types of adipose tissue are color, vascularity, and metabolic activity.
  - White adipose tissue (Unilocular adipose tissue)
  - Brown adipose tissue (Multilocular adipose tissue)

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White (Unilocular) Adipose Tissue

- Each unilocular fat cell contains a single lipid droplet, giving the adipose tissue composed of such cells a white color.
- White adipose tissue is heavily supplied with blood vessels, which form capillary networks throughout the tissue.
- The plasma membranes of the unilocular adipose cells contain receptors for several substances, including insulin, growth hormone, norepinephrine, and glucocorticoids, that facilitate the uptake and release of free fatty acids and glycerol.

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Brown (Multilocular) Adipose Tissue

- Brown adipose tissue (brown fat) is composed of multilocular fat cells, which store fat in multiple droplets.
- This tissue may appear tan to reddish brown because of its extensive vascularity and the chytochromes present in its abundant mitochondria
- Multilocular adipose tissue has a lobular organization and vascular supply similar to those of a gland.
- Brown fat tissue is very vascular because the vessels are located near the adipocytes.
- Brown adipose tissue is associated with production of body heat because of the large number of mitochondria in the multilocular adipocytes composing this tissue.

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Brown (Multilocular) Adipose Tissue (cont.)

- These adipose cells can oxidize fatty acids at up to 20 times the rate of white fat, increasing body heat production three-fold in cold environments.
- The neurotransmitter norepinephrine activates the enzyme that cleaves triglycerides into fatty acids and glycerol, initiating heat production by oxidation of fatty acids in the mitochondria.
- Thermogenin, a transmembrane protein located on the inner membrane of mitochondria, permits backflow of protons instead of utilizing them for synthesis of adenosine triphosphate (ATP); as a result of uncoupling oxidation from phosphorylation, the proton flow generates energy that is dispersed as heat.

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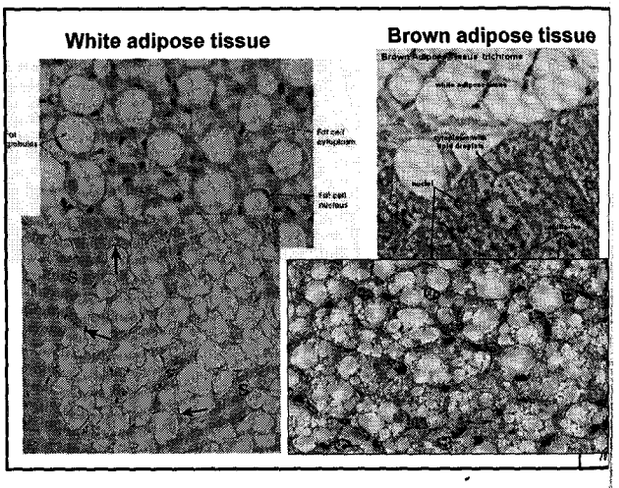

Elastic connective tissue

- Dense regular elastic connective tissue possesses coarse branching elastic fibers with only a few collagen fibers forming networks.
- Scattered throughout the interstitial spaces are fibroblasts.
- The elastic fibers are arranged parallel to one another and form either thin sheets or fenestrated membranes.
- The latter are present in large blood vessels, ligamenta flava of the vertebral column, and the suspensory ligament of the penis.

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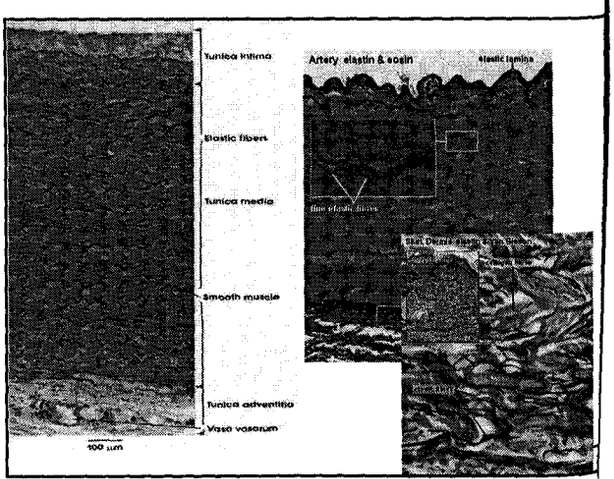

Reticular Tissue

- Type III collagen is the major fiber component of reticular tissue.
- The collagen fibers form mesh-like networks interspersed with fibroblasts and macrophages.
- It is the fibroblasts that synthesize the type III collagen.
- Reticular tissue forms the architectural framework of liver sinusoids, adipose tissue, bone marrow, lymph nodes, spleen, smooth muscle, and the islets of Langerhans.

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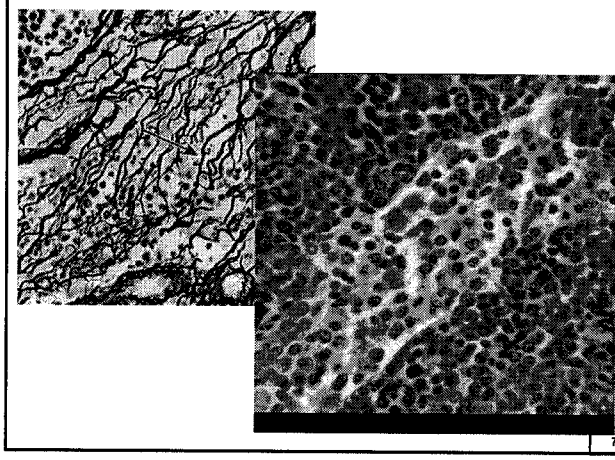

74

Mucous tissue

- Mucous tissue is a loose, amorphous connective tissue exhibiting a jelly-like matrix primarily composed of hyaluronic acid and sparsely populated with type I and type III collagen fibers and fibroblasts.
- This tissue, also known as Wharton's jelly, is found only in the umbilical cord and subdermal connective tissue of the embryo.

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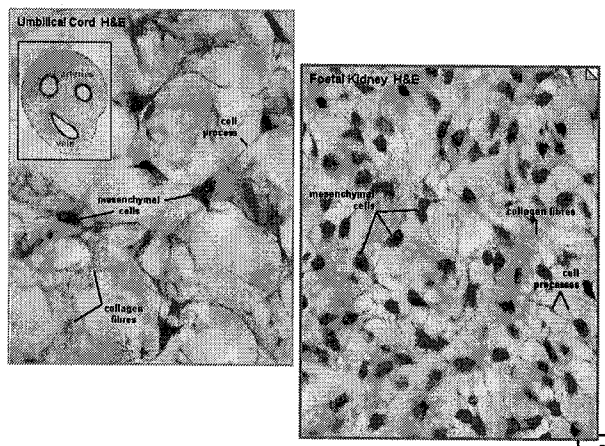

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Cartilage

- Cartilage cells are called chondrocytes, which occupy small cavities called lacunae within the extracellular matrix they secreted.
- The cartilage is neither vascularized nor supplied with nerves or lymphatic vessels
- The extracellular matrix is composed of glycosaminoglycans and proteoglycans, collagen and elastic fibers.
- The flexibility and resistance of cartilage to compression permit it to function as a shock absorber, and its smooth surface permits almost friction-free movement of the joints of the body as it covers the articulating surfaces of the bones.

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Perichondrium

- The perichondrium is a connective tissue sheath covering that overlies most cartilage.
- It has an outer fibrous layer and inner cellular layer whose cells secrete cartilage matrix.
- The perichondrium is vascular, and its vessels supply nutrients to the cells of cartilage.
- In areas where the cartilage has no perichondrium (e.g., the articular surfaces of the bones forming a joint), the cartilage cells receive their nourishment from the synovial fluid that bathes the joint surfaces.
- Perichondria are present in elastic and most hyaline cartilages, but absent in fibrocartilage.

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3-Type cartilage

- There are three types of cartilage according to the fibers present in the matrix.

1. Hyaline cartilage
2. Elastic cartilage
3. Fibrocartilage

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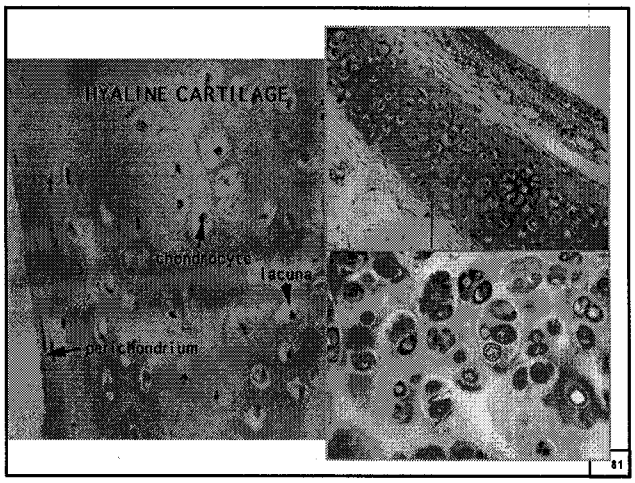
Hyaline cartilage

- Hyaline cartilage contains type II collagen in its matrix; it is the most abundant cartilage in the body and serves many functions.
- Chondrocytes are spindle-shaped, narrow cells that are derived from mesenchymal cells. They possess an ovoid nucleus with one or two nucleoli.
- It is located in the nose and larynx ventral ends of the ribs ventral ends of the ribs articulating surfaces of the movable joints of the body.
- It is this cartilage that forms the cartilage template of many of the bones during embryonic development and constitutes the epiphyseal plates of growing bones



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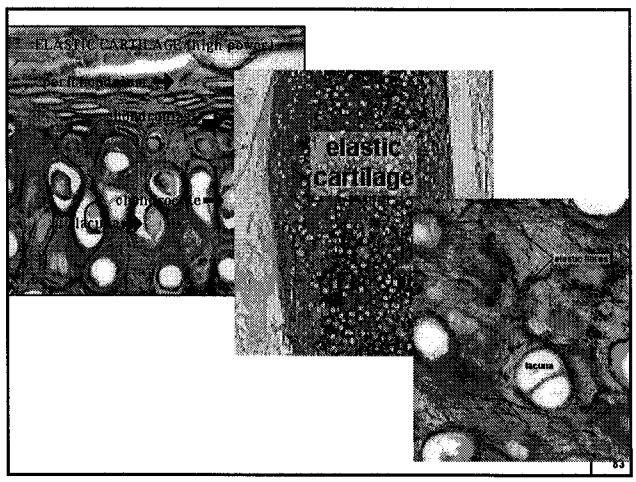
Elastic cartilage

- Elastic cartilage greatly resembles hyaline cartilage, except that its matrix and perichondrium possess elastic fibers.
- The matrix of elastic cartilage possesses abundant, fine to coarse branching elastic fibers interposed with type II collagen fiber bundles, giving it much more flexibility than the matrix of hyaline cartilage
- The chondrocytes of elastic cartilage are more abundant and larger than those of hyaline cartilage.
- The elastic fiber bundles of the territorial matrix are larger and coarser than those of the interterritorial matrix.
- It is located in the pinna of the ear, the external and interna auditory tubes, the epiglottis, and the larynx.



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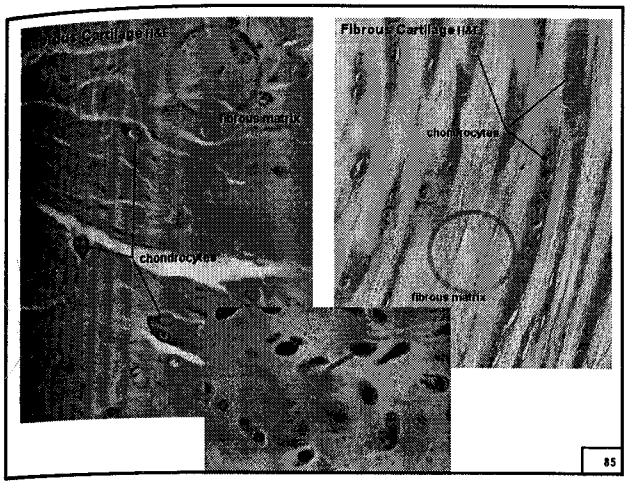
Fibrocartilage

- Fibrocartilage, unlike hyaline and elastic cartilage, possess no perichondrium and its matrix includes type I collagen, allowing it to withstand strong tensile forces.
- Chondrocytes of fibrocartilage usually arise from fibroblasts that begin to manufacture proteoglycans and become incarcerated in their own matrices and differentiate into chondrocytes.
- Chondrocytes are often aligned in alternating parallel rows with the thick, coarse bundles of collagen, which parallel the tensile forces attendant on this tissue
- Fibrocartilage is present in intervertebral disks, in the pubic symphysis, in articular disks, and attached to bone. It is associated with hyaline cartilage and with dense connective tissue.



85

Bone

- Bone extracellular matrix is calcified, incarcerating the cells that secreted it.
- Bone is the primary structural framework for support and protection of the organs of the body, including the brain and spinal cord and the structures within the thoracic cavity, the lungs and heart.
- Bone also serves as levers for the muscles attached to them, thereby multiplying the force of the muscles to attain movement.
- Bone is a reservoir for several minerals of the body; it stores about 99% of the body's calcium.
- Bone contains a central cavity, the marrow cavity, which houses the bone marrow, a hemopoietic organ.

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- Bone is covered on its external surface with periosteum, which consists of an outer layer of dense fibrous connective tissue and an inner cellular layer containing osteoprogenitor (osteogenic) cells.
- Osteoprogenitor cells are derived from embryonic mesenchymal cells and retain their ability to undergo mitosis.
- The central cavity of a bone is lined with endosteum, a specialized thin, connective tissue composed of a monolayer of osteoprogenitor cells and osteoblasts.

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Bone Matrix

- Bone matrix has inorganic and organic constituents.
- The inorganic portion of bone, which constitutes about 65% of its dry weight, is composed mainly of calcium and phosphorus, in the form of hydroxyapatite crystals [Ca10(PO4)6(OH)2].
- The organic component of bone matrix, constituting approximately 35% of the dry weight of bone, includes type I collagen fibers, proteoglycans with chondroitin sulfate and keratan sulfate side chains. In addition, glycoproteins such as osteonectin, osteocalcin, osteopontin, and bone sialoprotein.

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Cells of Bone

- The cells of bone include osteoprogenitor cells, which differentiate into osteoblasts.
- Osteoblasts synthesize the organic matrix of bone and possess receptors for parathyroid hormone.
- When these cells are surrounded by matrix, they become quiescent and are known as osteocytes. The spaces osteocytes occupy are known as lacunae.
- Osteoclasts, multinucleated giant cells derived from fused bone marrow precursors, are responsible for bone resorption and remodeling.

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Osteocytes

- Osteocytes are mature bone cells, derived from osteoblasts, that are housed in lacunae within the calcified bony matrix.
- Radiating out in all directions from the lacunaa are narrow, tunnel-like spaces or canaliculi that house cytoplasmic processes of the osteocyte.
- These processes make contact with similar processes of neighboring osteocytes, forming gap junctions through which ions and small molecules can move between the cells.
- The canaliculi also contain extracellular fluid carrying nutrients and metabolites that nourish the osteocytes.

90

Bone Classification

Bones are classified according to their shape:

1. Long bones display a shaft located between two heads (e.g., tibia).
2. Short bones have more or less the same width and length (e.g., carpal bones of the wrist).
3. Flat bones are flat, thin, and plate-like (e.g., bones forming the brain case of the skull).
4. Irregular bones have an irregular shape that does not fit into the other classes (e.g., sphenoid and ethmoid bones within the skull).
5. Sesamoid bones develop within tendons, where they increase the mechanical advantage for the muscle (e.g., patella) across a joint.

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Structure of Compact Bone

- There are four lamellar systems in compact bone:
  - outer circumferential lamellae,
  - inner circumferential lamellae,
  - osteons, and
  - interstitial lamellae.
- Compact bone is composed of wafer-like thin layers of bone, lamellae, that are arranged in lamellar systems that are especially evident in the diaphyses of long bones.

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Circumferential lamellae

- The outer circumferential lamellae are just deep to the periosteum, forming the outermost region of the diaphysis, and contain Sharpey's fibers anchoring the periosteum to the bone.
- The inner circumferential lamellae, analogous to but not as extensive as outer circumferential lamellae, completely encircle the marrow cavity.
- The interstitial lamellae is irregular arcs of lamellar fragments surrounded by osteons ans cementing lines.
- Trabeculae of spongy bone extend from the inner circumferential lamellae into the marrow cavity, interrupting the endosteal lining of the inner circumferential lamellae.

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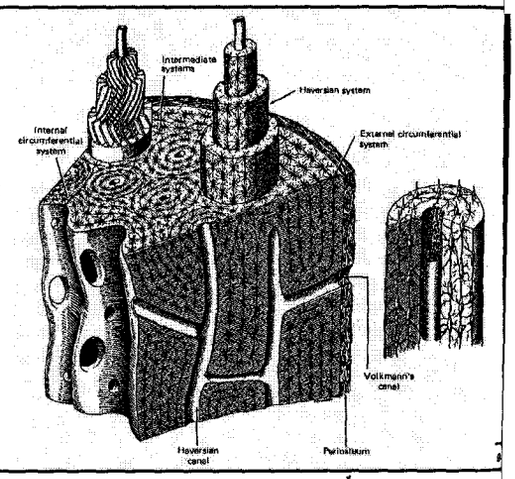
Compact bone structure



Haversian Canal Systems (Osteons)

- Haversian Canal Systems is formed by collagen fibers, oriented almost perpendicular to those of adjacent lamellae.
- Each osteonpossess only 4 to 20 lamellae and is bounded by a thin cementing line.
- Each haversian canal, lined by a layer of osteoblasts and osteoprogenitor cells, houses a neurovascular bundle with its associated connective tissue.
- Haversian canals of adjacent osteons are connected to each other by Volkmann's canals. These vascular spaces are oriented oblique to or perpendicular to haversian canals.

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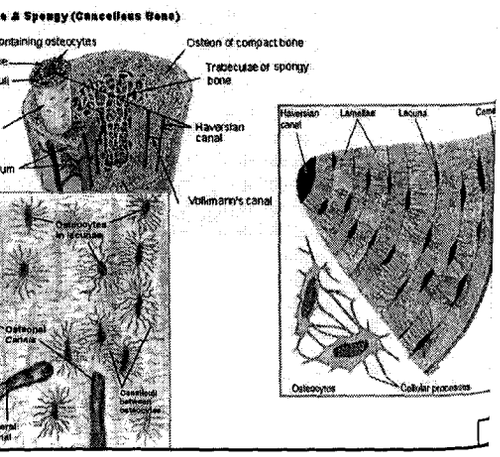

Connective Tissue Diseases

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Connective Tissue Diseases

- Connective tissue diseases can have strong or weak inheritance risks, and can also be caused by environmental factors.
- In patients with connective tissue disease, it is common for collagen and elastin to become injured by inflammation.
- Many connective tissue diseases feature abnormal immune system activity with inflammation in tissues as a result of an immune system that is directed against one's own body tissues, autoimmunity.

98

Heritable Disease Connective Tissues

- Connective tissue is the material between the cells of the body that gives tissues form and strength. This "cellular glue" is also involved in delivering nutrients to the tissue, and in the special functioning of certain tissues.
- Connective tissue is made up of dozens of proteins, including collagens, proteoglycans, and glycoproteins.
- The combination of these proteins can vary between tissues.
- The genes that encode these proteins can harbor defects or mutations, which can affect the functioning of certain properties of connective tissue in selected tissues. T
- his can lead to a HDCT.

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Some Connective Tissue Diseases

- Scurvy - caused by a dietary deficiency in vitamin C, leading to abnormal collagen.
- Rheumatoid Arthritis - Rheumatoid arthritis is a systemic disorder in which immune cells attack and inflame the membrane around joints.
- Scleroderma - Scleroderma is an activation of immune cells which produces scar tissue in the skin, internal organs, and small blood vessels.
- Myositis - Myositis involves inflammation that results in damage to muscle fibers and skin.
- Osteogenesis imperfecta (brittle bone disease) - caused by insufficient production of good quality collagen to produce healthy, strong bones.
- Sarcoma - a neoplastic process originating within connective tissue.

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Heritable Connective Tissue Disorders

- Marfan syndrome - a genetic disease causing abnormal fibrillin.
- Ehlers-Danlos syndrome - causes progressive deterioration of collagens, with different EDS types affecting different sites in the body, such as joints, heart valves, organ walls, arterial walls
- Osteogenesis imperfecta (brittle bone disease) - caused by insufficient production of good quality collagen to produce healthy, strong bones.

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End of Connective Tissue

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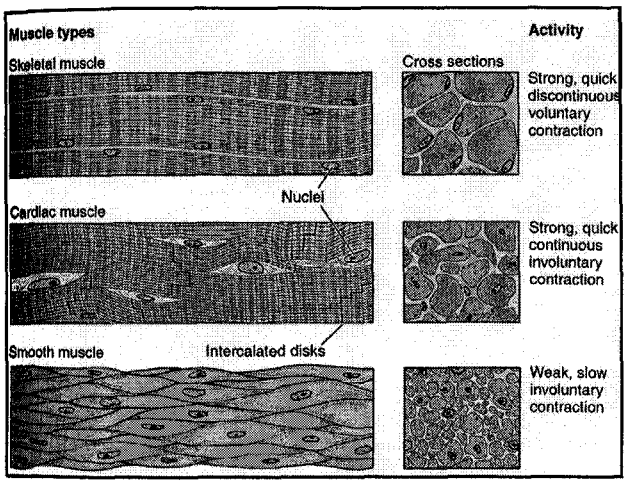
Muscular Tissue

1

Muscular Tissue

* Muscular tissue is composed of differentiated cells containing contractile proteins for cellular contraction that permits locomotion, constriction, pumping, and other propulsive movements.
* There are 3 types of muscles:
  - ♦ skeletal muscle, } Striated Muscle
  - ♦ cardiac muscle }
  - ♦ smooth muscle. Non-striated Muscle
* All three muscle types are derived from mesoderm.

2



* Cells of muscle are elongated and are called either **striated muscle cells** or **smooth muscle cells**, depending on the respective presence or absence of a regularly repeated arrangement of myofibrillar contractile proteins, the **myofilaments**.
* Terms:
  - ⋄ **Sarcolemma** - muscle cell membrane
  - ⋄ **sarcoplasm** - cytoplasm
  - ⋄ **sarcoplasmic reticulum** - smooth endoplasmic reticulum
  - ⋄ **sarcosomes** – mitochondria
  - ⋄ **muscle fibers** - muscle cells

4

Skeletal Muscle

5

Characteristics of Skeletal Muscle

1. **Contractility** - ability to contract (develop tension)
2. **Excitability (Irritability)** - ability to respond to a stimulus
   - ♦ either electrochemical (action potential --> depolarization, etc...) or mechanical (blow to muscle by external force)
3. **Extensibility** - ability to be stretched
   - ♦ **Viscoelastic** - having the ability to stretch or shorten over time (makes an effective stretching program necessary)
   - ♦ **Contractile component (CC)** - actual part of muscle that contracts (actin and myosin)

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Characteristics of Skeletal Muscle (cont.)

3. **Elasticity** - ability to recoil to normal length
   - **Parallel elastic component (PEC)** - passive elastic property of muscle derived from muscle membranes (epimysium, perimysium, endomysium, sarcolemma)
   - **Series elastic component (SEC)** - passive elastic property of muscle derived from the tendons (primarily responsible for elasticity)

7

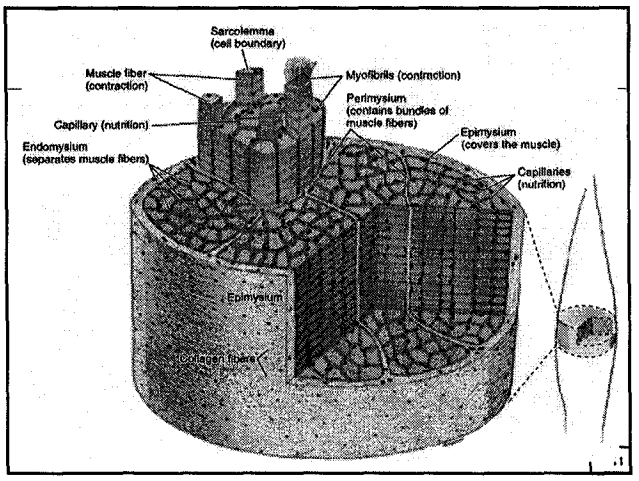
Skeletal Muscle

* Muscle fibers are arranged parallel to one another.
* Skeletal muscle fiber is long, cylindrical, multinucleated, and striated.
* The diameters of the fibers vary, ranging from 10 to 100μm, although hypertrophied fibers may exceed the latter figure.
* The relative strength of a muscle fiber directly depends on its diameter, whereas the strength of the entire muscle is a function of the number and thickness of its component fibers.

Characteristics	Red Muscle Fibers	White Muscle Fibers
Vascularization	Rich vascular supply	Poorer vascular supply
Innervation	Smaller nerve fibers	Larger nerve fibers
Fiber diameter	Smaller	Larger
Contraction	Slow but repetitive; not easily fatigued; weaker contraction	Fast but easily fatigued; stronger contraction
Sarcoplasmic reticulum	Not extensive	Extensive
Mitochondria	Numerous	Few
Myoglobin	Rich	Poor
Enzymes	Rich in oxidative enzymes; triphosphatase	Poor in oxidative enzymes; triphosphatase

Organization of Skeletal Muscle

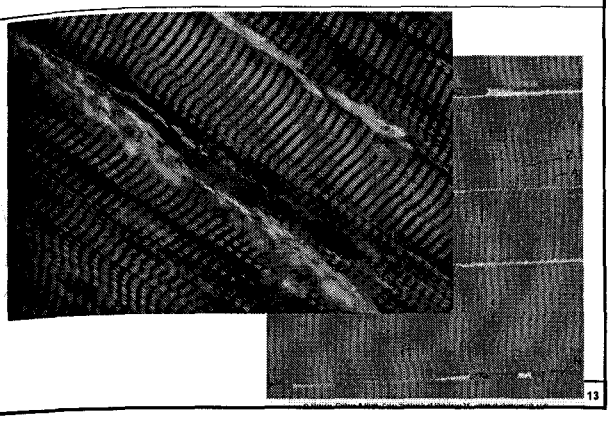
* The entire muscle is surrounded by
  - **Epimysium,** a dense irregular collagenous connective tissue.
  - **Perimysium,** a less dense collagenous connective tissue derive from epimysium, surrounds bundles (**fascicles**) of muscle fibers.
  - **Endomysium,** composed of reticular fibers and an **external lamina** (basal lamina), surrounds each muscle cell
* The connective tissue elements are interconnected, contractile forces exerted by individual muscle cells are transferred to CT, therefore, CT acts in harnessing the contractile forces for motion.



Skeletal Muscle Fibers

* Skeletal muscle fibers are multinucleated cells, with their numerous nuclei peripherally located just beneath the cell membrane, is composed of longitudinal arrays of cylindrical **myofibrils,** each 1 to 2 μm in diameter.
* **Myofibrils** extend the entire length of the cell and are aligned strictly ordered parallel arrangement forming cross-striations of light and dark banding that are characteristic of skeletal muscle viewed in longitudinal section

Cross - striations of skeletal muscle fibers



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Fine Structure of Skeletal Muscle Fibers

* Individual skeletal muscle fibers possess a **sarcolemma** that has **tubular invaginations (T tubules)** that course through the sarcoplasm and are flanked by **2 terminal cisternae** of the **sarcoplasmic reticulum** forming **Triad** of **sarcoplasmic reticulum & transverse tubule system**
* The contractile elements of the skeletal muscle fiber are organized into discrete cylindrical units called **myofibrils**.
* Each myofibril is composed of thousands of **sarcomeres** with their characteristic A, I, and H bands and Z disk.

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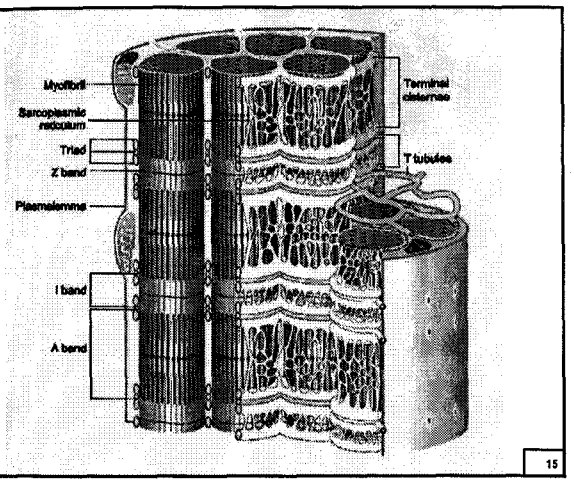

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* The **triad** is always located at the **junction of the A and I bands**, permitting the quick release of calcium ions from the terminal cisternae of the sarcoplasmic reticulum just in the region where the interaction of the thick and thin filaments can produce efficient sarcomere shortening.
* The sarcoplasmic reticulum regulates muscle contraction through controlled sequestering (leading to relaxation) and release (leading to contraction) of **calcium ions (Ca^{2+})** within the sarcoplasm.
* The trigger for the calcium ion release is the wave of depolarization transmitted by T tubules, which causes opening of the calcium release channels of the terminal cisternae, resulting in release of calcium ions into the cytosol in the vicinity of the myofibrils.

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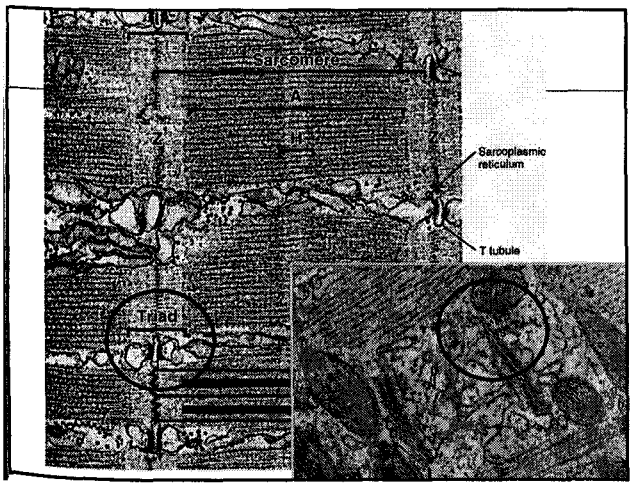
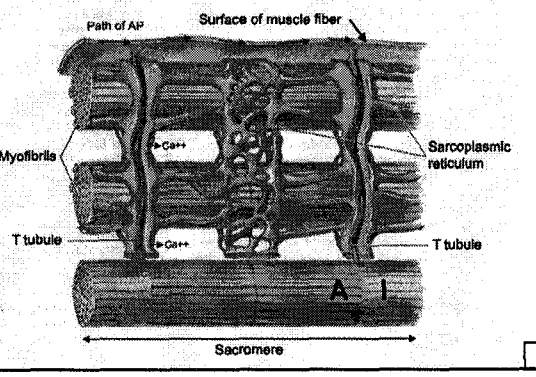


Sarcoplasmic Reticulum & Transvrse Tubule System

Role of Action Potential and Ca++ in Muscle Contraction



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Organization of Myofibrils

* The sarcoplasm is filled with long cylindrical of myofibrils.
* Striated muscle contain 2 types of filaments with 4-main proteins:
  - **Actin**, **Tropomyosin**, **Troponin** of thin filament and
  - **Myosin** of thick filament.
* **thick myofilaments** are rod-like **myosin II** 15 nm in diameter and 1.5 μm long and
* **thin myofilaments** are composed primarily of **actin** and 7 nm in diameter and 1.0 μm long .

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Organization of Myofibrils (cont.)

* Electron microscopy and light microscopy demonstrate the presence of parallel, interdigitating myofilaments and show cross-striation of alternating drak and light bands, known as a **sarcomere** and is the contractile unit of skeletal muscle fibers.
* the thick filaments do not extend the entire length of the sarcomere, and
* the thin filaments projecting from the two Z disks of the sarcomere do not meet in the midline.

Organization of Myofibrils (cont.)

* The dark bands are known as **A bands** (anisotropic), the entire length of the thick filaments
* The light bands as **I bands** (*i*sotropic with polarized light), the thin filament which is bisected by a thin dark line, the **Z disk (Z line)**.
* The center of each A band is occupied by a pale area, the **H band**, the entire length of the thick filaments.
* which is bisected by a thin **M line.**
* The region of the myofibril between two successive Z disks,

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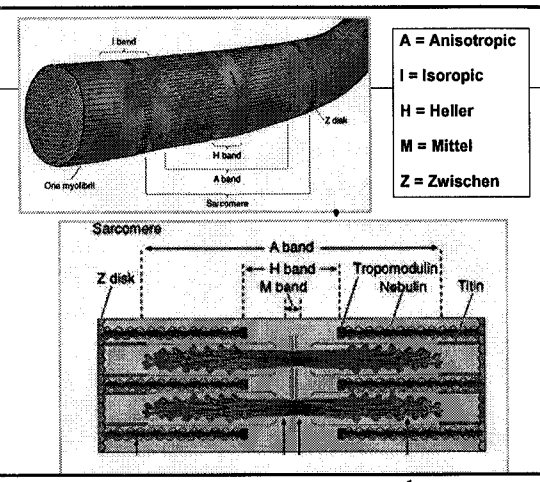
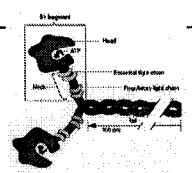


Thick Filament



* Every thick filament is composed of
  - two identical **heavy chains** and
  - two pairs of **light chains.**
* The **heavy chains** can be cleaved by trypsin into:
  - **Light meromyosin,** a rod-like tail composed of most of the two rod-like polypeptide chains wrapped around each other
  - **Heavy meromyosin,** the two globular heads with the attendant short proximal portions of the two rod-like polypeptide chains wrapped around each other

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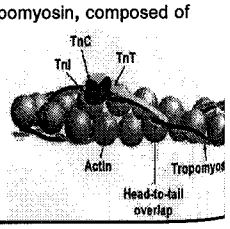
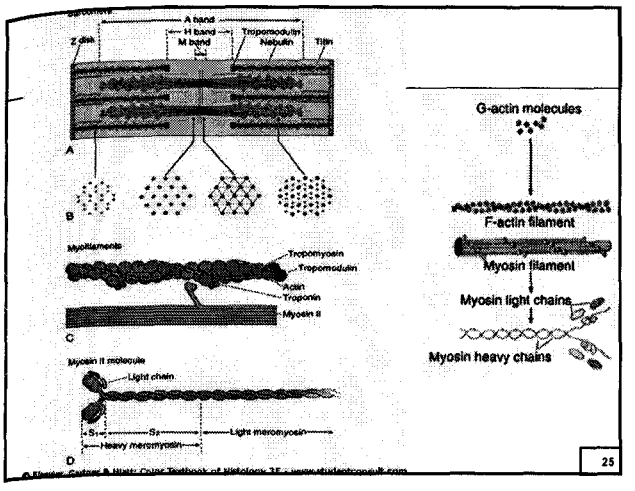
Thin Filament

* **Two chains of F-actin** are wound around each other in a tight helix of F-actin double-stranded helix with two shallow grooves.
* **Tropomyosin molecules,** rod-shaped, occupy the shallow grooves of the double-stranded actin helix.
* **Troponin molecules** are attached to tropomyosin, composed of three globular polypeptides:
  - **TnT** attaches to tropomyosin
  - **TnC** binds to calcium and
  - **TnI** inhibits actin-myosin interaction.





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Muscle Contraction & Relaxation

* The process of contraction, usually triggered by neural impulses, obeys the **all-or-none law,** in that a single muscle fiber either contracts as a result of stimulation or does not respond at all. The strength of contraction of a gross anatomical muscle, such as the biceps, is a function of the number of muscle fibers that undergo contraction.
* The stimulus is transferred at the **neuromuscular junction**.
* During muscle contraction, the thin filaments slide past the thick filaments, as proposed by **Huxley's sliding filament theory.**

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Huxley's sliding filament theory

1. An **impulse**, generated along the **sarcolemma**, is transmitted into the interior of the fiber via the **T tubules**, where it is conveyed to the **terminal cisternae** of the sarcoplasmic reticulum.
2. **Calcium ions** leave the **terminal cisternae** through **voltage-gated calcium release channels,** enter the cytosol, and bind to the **TnC** subunit of troponin, altering its conformation.
3. Conformational change in **troponin** shifts the position of tropomyosin deeper into the groove, unmasking the active site (myosin-binding site) on the **actin molecule**.

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Huxley's sliding filament theory (cont.)

4. **ATP** present on the S1 of myosin is hydrolyzed and the complex binds to the active site on actin
5. **Pi** is released, resulting in a greater bond strength between the actin and myosin II and in a conformational alteration of the S1
6. **ADP** is also released, and the thin filament is dragged toward the center of the sarcomere (**"power stroke"**).
7. **A new ATP molecule** binds to the S1 subfragment, causing the release of the bond between actin and myosin.

* The attachment and release cycles must be repeated numerous times for contraction to be completed.

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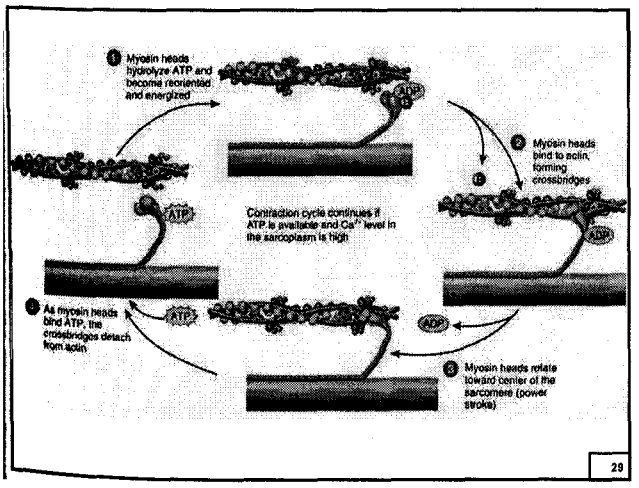

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Energy Sources for Muscle Contraction

* *Energy sources for muscle contraction are*
  - *the phosphogen energy system (ATP & Creatine phosphate),*
  - *glycolysis, and*
  - *the aerobic energy system.*
* **ATP** (3 seconds) and **creatine phosphate** (6 seconds).
* Anaerobic metabolism of glycogen **(glycolysis),** which results in the formation and buildup of **lactic acid**. This is known as the glycogen-lactic acid system. This system provides about 90 to 100 seconds' worth of energy at almost maximal muscle activity.

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Energy Sources for Muscle Contraction (cont.)

* **Aerobic energy system,** uses the normal diet for the manufacture of ATP. The aerobic system does not support maximal muscle activity, but it can sustain normal muscle activity indefinitely if the dietary intake is maintained and the nutrients persist.
* During bursts of muscle contraction, the ADP that is generated is rephosphorylated by two means: (1) **glycolysis,** leading to accumulation of lactic acid, and (2) transfer of high-energy phosphate from creatine phosphate (phosphogen system) catalyzed by **phosphocreatine kinase.**
* During prolonged muscle activity, the **aerobic system** of energy production is employed.

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Neuromuscular Junction

* Each skeletal muscle receives at least two types of nerve fibers: **motor** and **sensory**
* The motor nerve functions in eliciting contraction, whereas the sensory fibers pass to **muscle spindles**
* Each motor neuron and the muscle fibers form a **motor unit.**
* The muscle fibers of a motor unit contract in unison and follow the all-or-none law of muscle contraction
* Some muscles of the eye, a single motor neuron may be responsible for as few as 5 to 10 skeletal muscle fibers, whereas a muscle located in the abdominal wall may have as many as 1000 fibers

Neuromuscular Junction (cont.)

* Motor fibers are **myelinated axons** of **α-motor neurons,** which pass in the connective tissue of the muscle.
* The axon arborizes, eventually losing its myelin sheath (but not its Schwann cells).
* The terminal of each arborized twig becomes dilated and overlies the **motor end plates** of individual muscle fibers.
* Each of these muscle-nerve junctions, known as a **neuromuscular junction,** is composed of an axon terminal, a synaptic cleft, and the muscle cell membrane

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Neuromuscular Junction

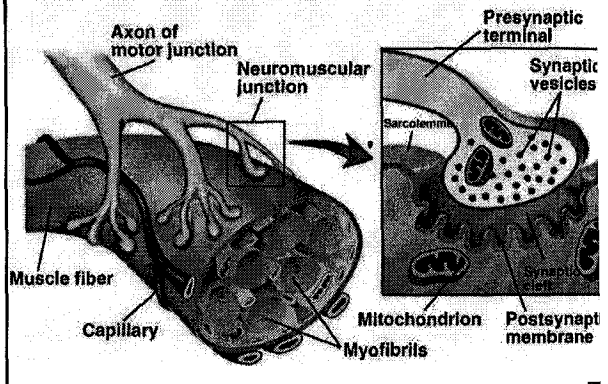
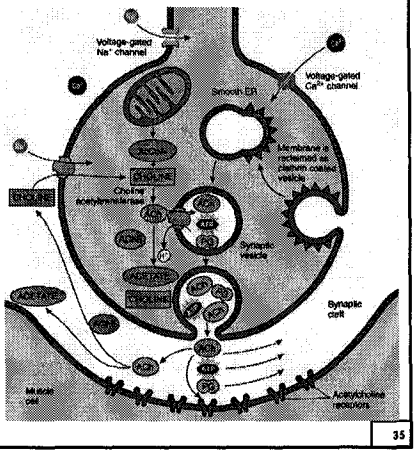


Diagram depicting events occurring at the neuromuscular junction during the release of cetylcholine. AcCoA = acetyl CoA; Ach = acetylcholine; AchE = acetylcholinesterase; ATP, adenosine triphosphate; PG, proteoglycan.



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Muscle Spindles and Golgi Tendon Organs

* The neural control of muscle function requires;
  - ♦ the capability of inducing or inhibiting muscle contraction and
  - ♦ the ability to monitor the status of the muscle and its tendon during muscle activity.
* This monitoring is performed by two types of sensory receptors:
  1. **Muscle spindles,** which provide feedback about the length changes and the rate of length alteration in muscle
  2. **Golgi tendon organs,** which monitor the tension and the rate at which the tension is being produced during movement

Muscle Spindles

* Muscle structure is innervated by both sensory and motor neuron axon axons.
* The muscle spindle's functions are to send **proprioceptive information** about the muscle to the central nervous system, and to respond to muscle stretching or **stretch reflex.**
* This **proprioceptive response** is initiated by the muscle spindle, an **encapsulated sensory receptor** located among, and in parallel with, the muscle cells.

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Muscle Spindles (cont.)

* Each muscle spindle is composed of 8 to 10 elongated, narrow, very small, modified muscle cells called **intrafusal fibers,** surrounded by the fluid-containing **periaxial space,** which in turn is enclosed by the **capsule.**
* The connective tissue elements of the capsule are continuous with the collagen fibers of the perimysium and endomysium.
* The skeletal muscle fibers surrounding the muscle spindle are unremarkable and are called **extrafusal fibers,** receive their normal nerve fibers, which are the large, rapidly conducting axons of **α-efferent (motor) neurons.**

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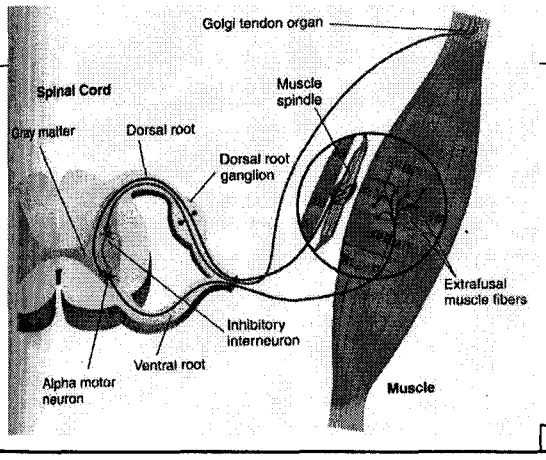

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Muscle Spindles (cont.)

* Intrafusal fibers are of two types:
  - **nuclear bag fibers**
    - nuclear bag 1 fibers for **dynamic,** innervated by (1) **primary sensory ending (dynamic & Ia sensory endings)** and (2) **dynamic γ motor neuron.**
    - nuclear bag 2 fibers for **static,** innervated by (1) **secondary sensory nerve endings (static & II sensory nerve endings)** and (2) **static γ motor neuron.**
  - **nuclear chain fibers** innervated by **secondary sensory nerve endings**
* The central regions of the intrafusal fibers do not contract.

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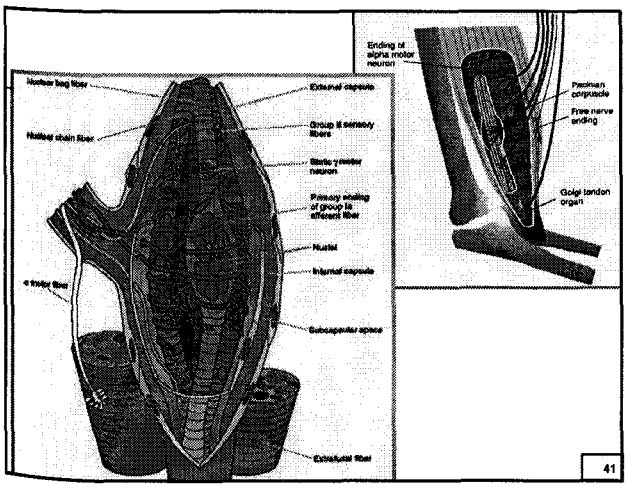

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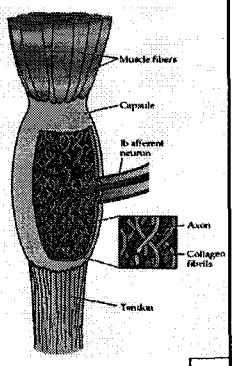
Golgi Tendon Organs (Neurotendinous Spindles)

* Proprioceptive sensory receptor organ that is located at the insertion of skeletal muscle fibers into the tendons of skeletal muscle, response for **stretching** as the muscle shortens
* Golgi tendon organs are composed of **wavy collagen fibers** and the nonmyelinated continuation of a single **type Ib axon** that ramifies as free nerve endings in the interstices between the **collagen fibers.**



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Cardiac Muscle

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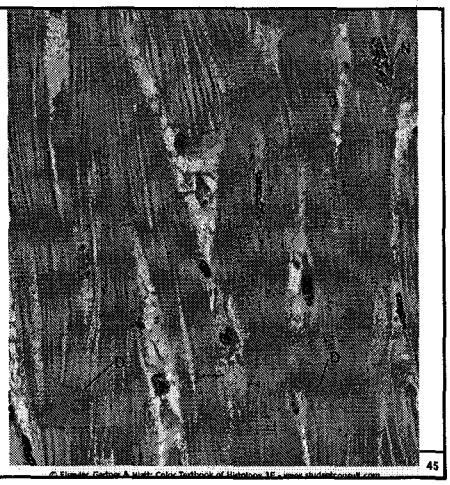
Cardiac Muscle

* Cardiac muscle (heart muscle), another form of striated muscle, is found only in the heart and in pulmonary veins where they join the heart.
* Cardiac muscle differs from skeletal and smooth muscles in that it possesses an
  - ♦ **inherent rhythmicity**
  - ♦ **contract spontaneously**
* Cardiac muscle cells form highly specialized end-to-end junctions, referred to as **intercalated disks**.

Cardiac Muscle with Cross-striation



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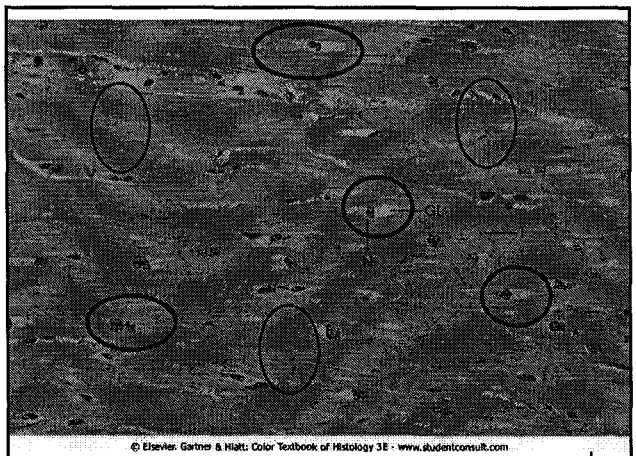
Energy Supply to Cardiac Muscle

* Almost half the volume of the cardiac muscle cell is occupied by mitochondria.
* **Glycogen**, to a certain extent, but mostly **triglycerides** (~60% during basal rate) form the energy supply of the heart.
* Because the oxygen requirement of cardiac muscle cells is high, they contain an abundant supply of myoglobin.



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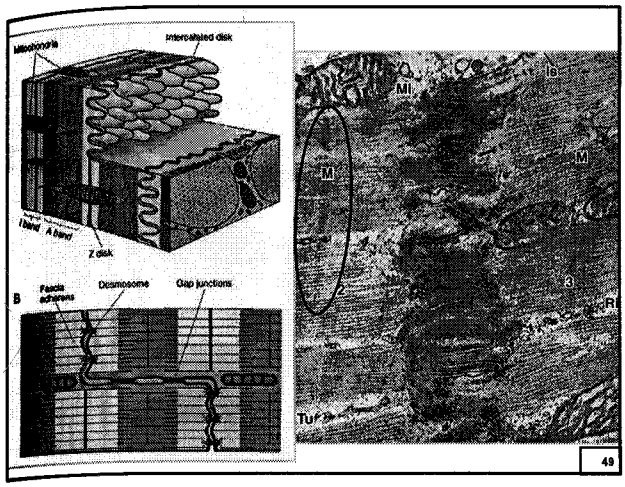
Intercalated Disks

* The **cell membrane junctions** approximate each other, so that in most areas they are separated by a space of less than 15 to 20nm.
* Intercalated disks have
  - ♦ **transverse portions,** where fasciae
    - ✧ **Adherentes,** analogous to **Z disks** and
    - ✧ **desmosomes**, as well as
  - ♦ **lateral portions** rich in
    - ✧ **gap junctions,** permitting rapid flow of information from one cell to the next



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* The organelles and bandings of cardiac muscle fibers are identical with those of skeletal muscle.
* The mode and mechanism of contraction are virtually identical in the two striated muscles.
* Several major differences from skeletal muscle should be noted;
  - the arrangement of one lateral expansion of the sarcoplasmic reticulum and of T tubules forming a **dyad close to Z line**,
  - the Ca^{2+} supply of cardiac muscle enter the cardiac muscle cells is through the large calcium-sodium channels of the plasmalemma, and
  - the duration of the action potential and restore resting potenial are faster.

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Smooth Muscle

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Smooth Muscle

* The cells of smooth muscle exhibit **no striations**, **no system of T tubules**, and is **involuntary muscle.**
* Smooth muscle is found in
* the walls of hollow viscera (e.g., the gastrointestinal tract, some of the reproductive tract, and the urinary tract), walls of blood vessels, larger ducts of compound glands, respiratory passages, and small bundles within the dermis of skin.
* Smooth muscle is not under voluntary control; it is regulated by the **autonomic nervous system**, **hormones** (such as bradykinins), and **local physiological conditions**.

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Smooth Muscle

* There are two types of smooth muscle:
  - Cells of **multiunit smooth muscle** can **contract independently** of one another, because each muscle cell has its own nerve supply.
  - Cell membranes of **unitary (single-unit, vascular, visceral) smooth muscle** form gap junctions with those of contiguous smooth muscle cells, and nerve fibers form synapses with only a few of the muscle fibers. Thus, cells of unitary smooth muscle **cannot contract independently** of one another.
* some smooth muscle is capable of exogenous **protein synthesis.**

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Smooth Muscular Fibers

* Smooth muscle fibers are **fusiform,** elongated cells, oval nucleus housing two or more nucleoli,
* Cytoplasm is unremarkable, but with special stain **dense bodies** and **myofilaments** are present.
* During muscle shortening, the nucleus assumes a characteristic **"corkscrew appearance,"** as a result of the method of smooth muscle contraction.
* Each smooth muscle cell is surrounded by an **external lamina** and **reticular fibers**, function in harnessing the force of contraction.

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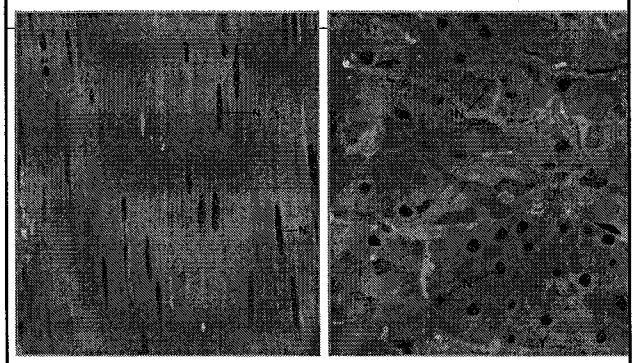
Smooth Muscle



Longitudinal section | Cross section

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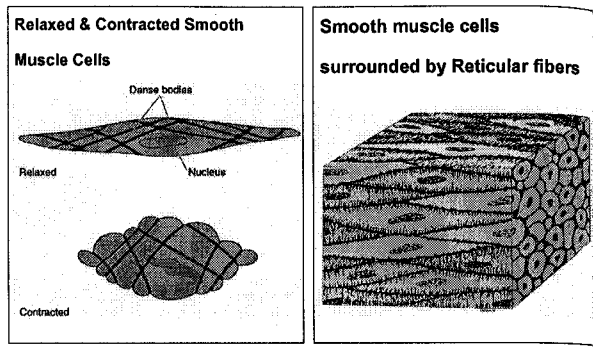
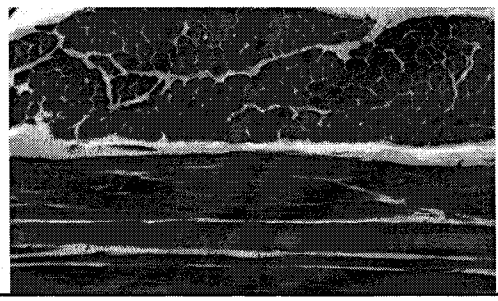


* Smooth muscle cells usually form sheets of various thicknesses, although they may also occur as individual cells.
* Sheets of smooth muscle cells are frequently arranged in **two layers perpendicular to each other**, as in the digestive and urinary systems. This arrangement permits **waves of peristalsis**.



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Fine Structure of Smooth Muscle

* Two poles of the nucleus, contains numerous mitochondria, Golgi apparatus, rough endoplasmic reticulum (RER), smooth endoplasmic reticulum (SER), and inclusions such as glycogen.
* Extensive array of interweaving **thin filaments** (7 nm) and **thick filaments** (15 nm) is present.
* The thin filaments are composed of actin (with its associated **caldesmon,** a protein that blocks the active site of F-actin, and **tropomyosin,** with the notable absence of **troponin**).
* The thick filaments are composed of the same **myosin II** that is present in skeletal muscle.

Fine Structure of Smooth Muscle (cont.)

* Myofilaments of smooth muscle are lined up so that the **heavy meromyosin heads** (S1) project from the thick filaments throughout the length of the filament, with the two ends lacking heavy meromyosin.
* The middle of the filament possesses heavy meromyosin, resulting in the availability of a larger surface area for the interaction of actin with myosin II and permitting **contractions of long duration.**
* There is a system of intermediate filaments;
* In unitary smooth muscle consist of **vimentin** and **desmin** and
* In multiunit smooth muscle consists of only **desmin.**
* These intermediate filaments and thin filaments insert into **dense bodies,** formed of **α-actinin** and other Z disk-associated proteins.

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Smooth Muscle Contraction

* The all-or-none law for striated muscle contraction does not apply to smooth muscle.
* The entire cell, or only a portion of the cell, may contract at a given instant even though the method of contraction probably follows the sliding filament theory of contraction.
* The force of contraction is relayed, through the association of myofilaments with dense bodies, to the **intermediate filaments**, which act to **twist** and **shorten** the cell along its longitudinal axis.

Smooth Muscle Contraction (cont.)

* Associated with the cell membrane domains are structures known as **caveolae** that act **as T tubules** (as of skeletal and cardiac muscle) in regulating the **cytosolic free calcium ion** concentration.
* Calcium ions, released from the sarcoplasmic reticulum as well as entering the cell at plasma membrane caveolae, bind to **calmodulin**
* **Ca^{2+}-calmodulin complex** binds to **caldesmon**, causing its release from the active site of F-actin, and then activates **myosin light chain kinase.**

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Smooth Muscle Contraction (cont.)

* Myosin light chain kinase phosphorylates one of the myosin light chains permitting the **unfolding** of the light meromyosin moiety to form the typical, **"golf club"-shaped myosin II molecule**
* The phosphorylated light chain permits the interaction between actin and the S1 subfragment of myosin II that results in contraction.
* Both phosphorylation and the attachment-detachment of the myosin cross-bridges occur slowly, contraction takes longer time.
* Thus, smooth muscle contraction is **prolonged and requires less energy.**

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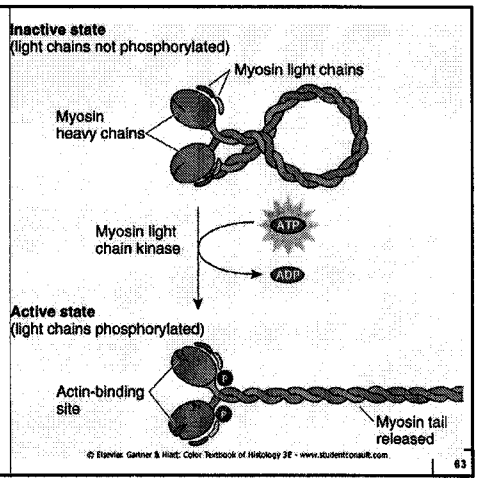
Smooth Muscle Contraction



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Myoepithlial Cells and Myofibroblasts

* Myoepithelial cells are modified to assist in the delivery of the secretory products into the ducts of the gland.
* Myoepithelial cells are flattened and possess long processes that wrap around the glandular units.
* Myoepithelial cells contain both actin and myosin.
* Mechanisms and control of contraction in myoepithelial cells resemble those in smooth muscle.

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Comparison of the three types of muscle

Feature	Skeletal Muscle	Cardiac Muscle	Smooth Muscle
Sarcomeres and myofibrils	Yes	Yes	No
Nuclei	Multinucleated; peripherally located	One (or two); centrally located	One; centrally located
Sarcoplasmic reticulum	Well-developed with terminal cisterns	Poorly defined; some small terminals	Some smooth endoplasmic reticulum
T tubules	Yes; small, involved in triad formation	Yes; large, involved in dyad formation	No
Cell junctions	No	Intercalated disks	Nexus (gap junctions)
Contraction	Voluntary; "all or none"	Involuntary; rhythmic and spontaneous	Involuntary; slow and forceful; not "all or none"
Calcium control	Calsequestrin in terminal cisternae	Calcium from extracellular sources and the sarcoplasmic reticulum	Calcium from extracellular sources (via caveolae) and thesarcoplasmic/ endoplasmic reticulum
Calcium binding	Troponin C	Troponin C	Calmodulin
Regeneration	Yes, via satellite cells	No	Yes
Mitosis	No	No	Yes
Nerve fibers	Somatic motor	Autonomic	Autonomic
Connective tissue	Epimysium,perimysium, and endomysium	Connective tissue sheaths and endomysium	Connective tissue sheaths and endomysium
Distinctive features	Long; cylinder-shaped; many peripheral nuclei	Branched cells; intercalated disks; one or two nuclei	Fusiform cells, with no striations; single nucleus

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End of Muscular Tissue

66

Nervous Tissue

1

Nervous Tissue

- The **most complex system** in the human body, composed of as many as a 100 million neurons with at least 1000 interconnections of each neuron, forms the complex system of neuronal communication.
- Certain neurons have **receptors,** on their terminals, that are specialized for receiving different types of stimuli and **transducing** them into nerve impulses that be conducted to nerve centers.
- These impulses are then transferred to other neurons for processing and **transmission** to higher centers for **perceiving sensations** or for initiating **motor responses**.

2

Cells of the Nervous System

- The cells of the nervous system are divided into **two categories:**
- **neurons**, the cells responsible for the reception and transmission of nerve impulses to and from the CNS are the neurons; and
- **neuroglial cells**, which support and protect neurons.

3

Structure and Function of Neurons

- Neurons are composed of three distinct parts:

1. a **cell body**, known as the **perikaryon** or **soma**
   - neurons in the CNS are polygonal with many cell processes
   - neurons in the dorsal root ganglion (a sensory ganglion of the PNS) are round with only one process exits
   - A group of cell body in CNS is called **Nucleus**, in PNS is called **Ganglion**
2. multiple **dendrites**, and
3. a single **axon (nerve fiber)**.

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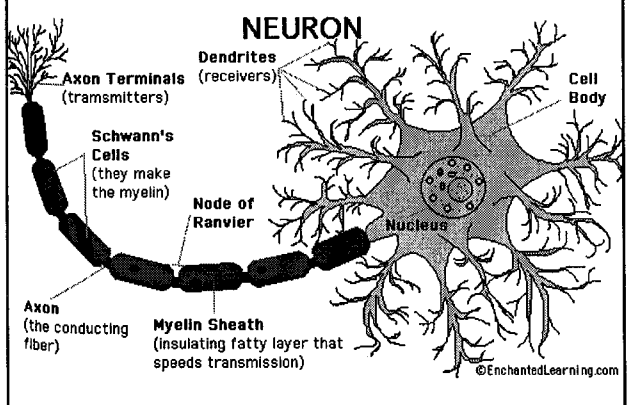

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1. Neuronal Cell Body (Soma, Perikaryon)

- The cell body is the most conspicuous region of the neuron, but the largest volume of the neuron's cytoplasm is located in the processes originating from the cell body.
- The **nucleus** is large, usually spherical to ovoid, and centrally located.
- A well-defined **nucleolus** is also common.

6

Neuronal Cell Body (cont.)

- RER and polyribosomes stack forming basophilic material called **Nissl bodies.**
- RER is absent at the **axon hillock,** the region on the cell body where the axon arises.
- A prominent **Golgi complex** with characteristic of protein-secreting cells, be responsible for the packaging of neurotransmitter substances or enzymes.
- Numerous **mitochondria** are scattered throughout the cytoplasm of the soma, dendrites, and axon.

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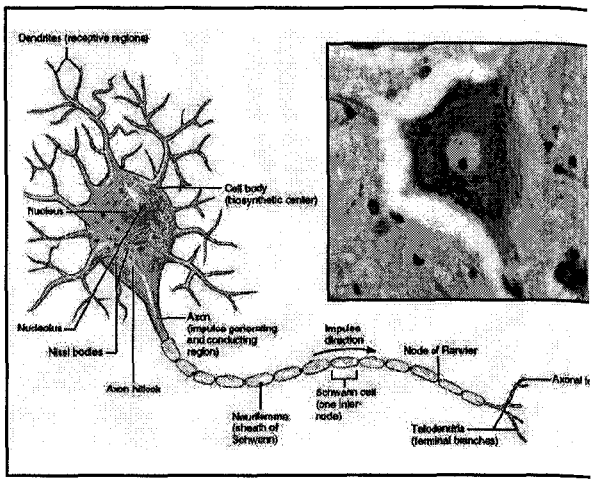

Neuronal Cell Body (cont.)

- There are two types of inclusion;
- **melanin granules:** dark brown granules, derived from dihydroxyphenylalanine (DOPA), or methyldopa
- **Lipofuscin**: yellowish brown pigment granule, an irregularly shaped, the remnant of lysosomal enzymatic activity, increase in number with advancing age
- **Lipid droplets:** faulty metabolism or from energy reserves
- **Secretory granules:** are observed in neurosecretory cells; many of them contain signaling molecules

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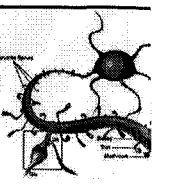
2. Dendrites



- Dendrites are the receptive plasma membrane arises from the cell body contain sparse or are absent Golgi complexes.
- The branching of dendrites, which results in numerous **synaptic terminals**, permits a neuron to receive and integrate multiple of impulses.
- **Spines** located on the surfaces of some dendrites permit them to form synapses with other neurons.
- These **spines diminish** with age and poor nutrition, and they may exhibit structural changes in persons with trisomy 13 and trisomy 21 (**Down syndrome**).

3. Axon (Nerve Fiber)

- The axon arises from the cell body at the **axon hillock** as a single, process extending longer distances from the cell body.
- In some instances, axons of motor neurons may be 1 meter or more in length.
- Axon thickness is directly related to conduction velocity, so that velocity increases as axon diameter increases.
- Some axons possess **collateral branches,** which arise at right angles from the axonal trunk.
- As the axon terminates, it may ramify, forming many small branches or **terminal arbor.**

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Axon (cont.)

- The **axon hillock,** a pyramid-shaped region of the soma, is devoid of ribosomes and is usually located on the opposite side of the soma from the dendrites.
- The beginning point of myelin sheath is called the **initial segment,** where excitatory and inhibitory impulses are summed to determine whether propagation of an action potential is to occur.
- The **axolemma** (plasmalemma) of the initial segment is a thin that resembles the layer located at the **nodes of Ranvier.**
- The axoplasm contains SER, RER and polyribosomes, mitochondria, microtubules, and microfilaments.

Axon (cont.)

- Axons have **myelin sheath** is referred to as **myelinated axons.**
- Axons lacking myelin sheaths are called **unmyelinated axons.**
- In addition to impulse conduction, an important function of the axon is **axonal transport** of materials between the soma and the axon terminals.
  - **anterograde transport,** the direction is from the cell body to the axon terminal, transport organelles and vesicles
  - **retrograde transport,** the direction is from the axon terminal to the cell body, transport building blocks of cytoskeleton and enzymes.
- Axonal transport is crucial to **trophic relationships** within the axon because it is located between neurons and muscles or glands.
- If these relationships are interrupted, the target cells **atrophy.**

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Classification of Neurons

- Neurons are classified into three major types according to **morphology**:
  - 1. Bipolar neuron
  - 2. Unipolar (Pseudounipolar) neuron
  - 3. Multipolar neuron
- Neurons are classified into three major types according to **function**
  - 4. Sensory (Afferent) neuron
  - 5. Motor (Efferent) neuron
  - 6. Interneuron

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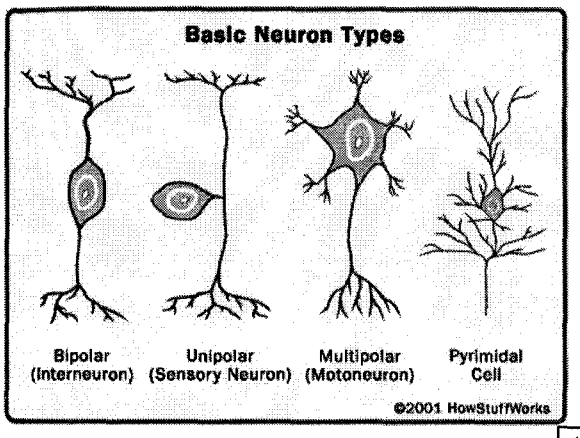

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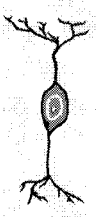
Bipolar Neurons

- **Bipolar neurons** possess two processes emanating from the soma, a single dendrite and a single axon.
- Bipolar neurons are located in the vestibular and cochlear ganglia and in the olfactory epithelium of the nasal cavity.



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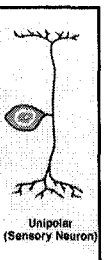
Unipolar neurons

- **Unipolar neurons (pseudounipolar neurons)** processes migrate around the cell body during development, fuse into a single process, branches into a peripheral branch and a central branch, both can propagate nerve impulses
- The central branch enters the CNS, and the peripheral branch proceeds to its destination in the body.
- Impulse passes from the dendritic (receiving) end of the peripheral process to the central process without involving the cell body.
- Unipolar neurons are present in the **dorsal root ganglia** and in some of the **cranial nerve ganglia.**



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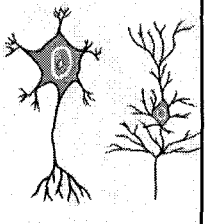
Multipolar neurons

- **Multipolar neurons,** the most common type, possess multiple dendrites and a single axon.
- They are present throughout the nervous system, and most of them are **motor neurons.**
- Some multipolar neurons are named according to their morphology (e.g., pyramidal cells) or after the scientist who first described them (e.g., Purkinje cells).



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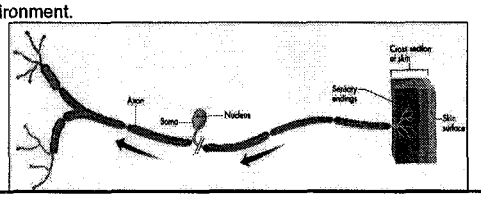
Sensory (afferent) neurons

- **Sensory (afferent) neurons** carry information from the sense organs (such as the eyes and ears) to the brain.
- **Sensory neurons** receive sensory input at their dendritic terminals and conduct impulses to the CNS for processing.
- Those located in the periphery of the body monitor changes in the environment, and those within the body monitor the internal environment.



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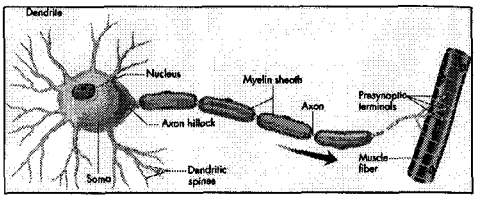
Motor (efferent) neurons

- **Motor (efferent) neurons** have long axons and carry information from the central nervous system to the muscles and glands of the body.
- **Motor neurons** originate in the CNS and conduct their impulses to muscles, glands, and other neurons.



Interneurons

- **Interneurons** have short axons and communicate only within their immediate region.
- **Interneurons,** located completely in the CNS, function as interconnectors or integrators that establish networks of neuronal circuits between sensory and motor neurons and other interneurons.
- Interneurons are responsible for the complex functioning of the body.

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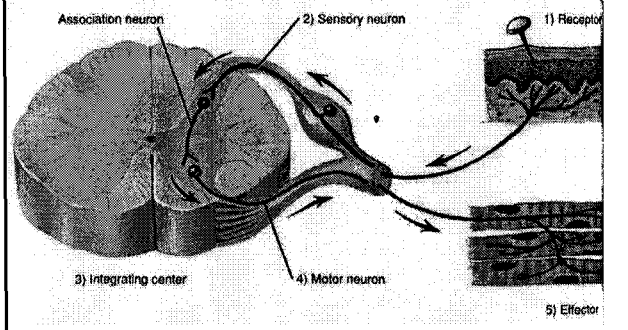
Sensory-motor-interneurons in Reflex Arc



Neuroglial Cells

- Cells whose function is the **metabolic** and **mechanical support** and **protection** of neurons
- Neuroglial cells undergo mitosis, do not react to or propagate nerve impulses, form gap junctions with other neuroglial cells.
- Neuroglial cells that reside exclusively in the CNS include
  - ***astrocytes**,
  - ***oligodendrocytes**,
  - ***microglia** (microglial cells), and
  - ***ependymal cells**.
- Neuroglial cells locate in the PNS are **Schwann cells**.

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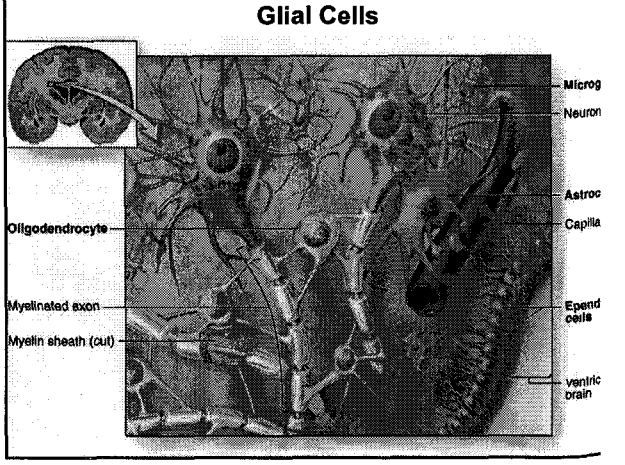
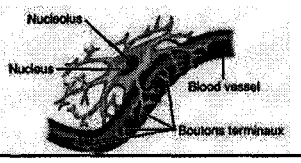
Glial Cells



Astrocytes

- Astrocytes are the largest of the neuroglial cells and exist as two distinct types:
- (1) **protoplasmic astrocytes** in the gray matter of the CNS and
- (2) **fibrous astrocytes** present mainly in the white matter of the CNS.
- Cell processes end as **pedicels** (vascular feet) that come into contact with blood vessels, contact the pia mater forming the **pia-glial membrane**, located adjacent to neuronal cell bodies are a form of **satellite cells.**



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Astrocytes function

- Astrocytes function in **scavenging ions**, neurotransmitters, and remnants of neuronal metabolism, such as potassium ions (K^+), glutamate, and γ-aminobutyric acid (GABA), accumulated in the microenvironment of the neurons, especially at the nodes of Ranvier.
- These cells also contribute to **energy metabolism** within the cerebral cortex by releasing glucose from their stored glycogen.
- Astrocytes located at the periphery of the CNS form a continuous layer over the blood vessels and assist in maintaining the **blood-brain barrier.**
- Astrocytes are also recruited to damaged areas of the CNS, where they form **cellular scar tissue**.

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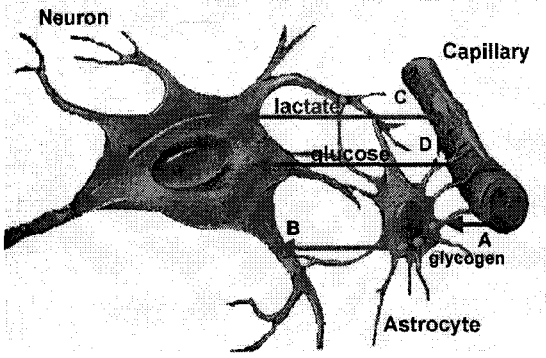
Astrocyte function



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Oligodendrocytes

- Oligodendrocytes resemble astrocytes but are smaller and contain fewer processes with sparse branching.
- Oligodendrocytes function similarly to the Schwann cells of the PNS, except that a **single oligodendrocyte** may wrap **several axons** with segments of myelin, whereas a single Schwann cell wraps only one axon with myelin.

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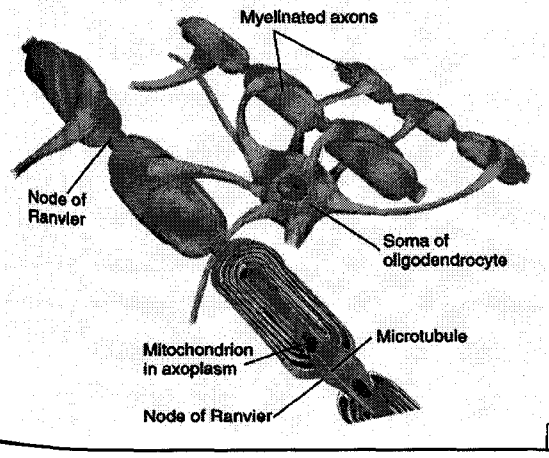

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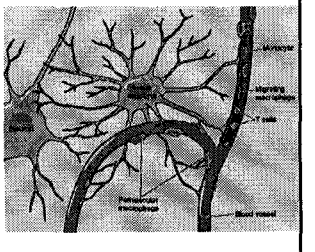
Microglial Cells

- Microglial cells are small, dark-staining cells that faintly resemble oligodendrocytes, **function as phagocytes** in clearing debris and damaged structures in the CNS, protecting the nervous system from viruses, microorganisms, and tumor formation
- Microglial cells act as antigen-presenting cells and secrete cytokines.



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Ependymal Cells

- Ependymal cells (ependymocytes) are low columnar to cuboidal epithelial cells **lining** the ventricles of the brain and central canal of the spinal cord.
- Ependymal cells form an **internal limiting membrane** lining the ventricle and an **external limiting membrane** beneath the pia, both formed by thin fused pedicels.
- Modifications of some of the ependymal cells in the ventricles of the brain participate in the formation of the **choroid plexus,** which is responsible for secreting and maintaining the chemical composition of the **cerebrospinal fluid (CSF).**

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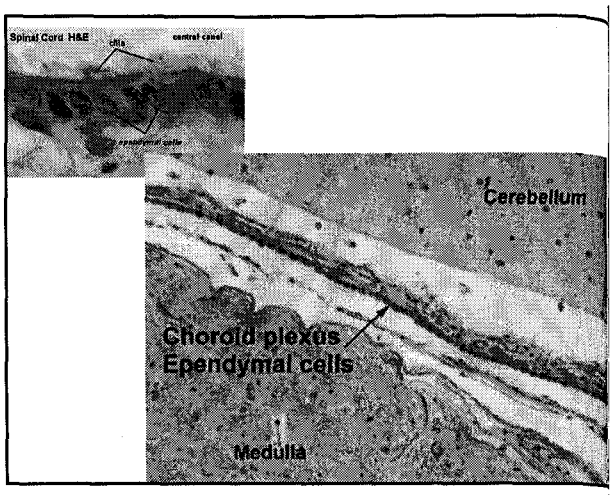

Schwann Cells

- **Schwann cells** are located in the **PNS**, flattened cells, flattened nucleus, a small Golgi apparatus, and a few mitochondria.
- They can form either **myelinated** or **unmyelinated** coverings over axons;
- the plasmalemma of the Schwann cell organized into a sheath that is wrapped several times around the axon producing the myelin are called **internodal segments.**
- Interruptions in the myelin sheath at regular intervals along the length of the axon, are called **nodes of Ranvier.**

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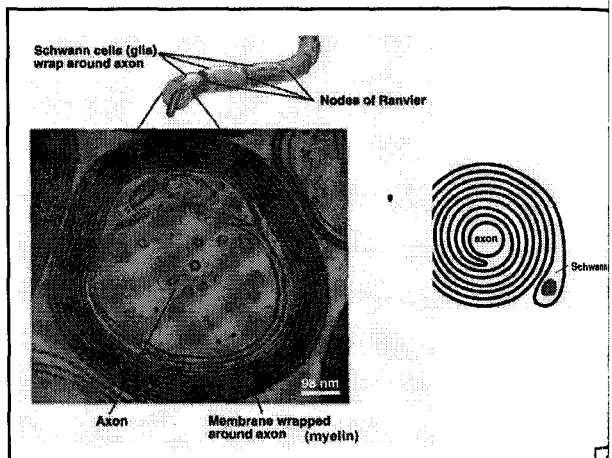

Synapsis and the Transmission of the Nerve Impulse

- Synapses are the sites where nerve impulses are transmitted from a **presynaptic cell** (a neuron) to a **postsynaptic cell** (another neuron, muscle cell, or cell of a gland).
- Synapses thus permit neurons to communicate with each other and with effector cells (muscles and glands).
- Impulse transmission at synapses can occur as
  - Electrical synapsis or
  - Chemical synapsis.

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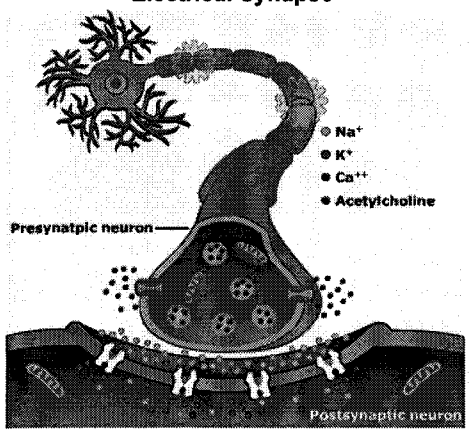
Electrical synapses

- **Electrical synapses** are uncommon in mammals, they are present in the brain stem, retina, and cerebral cortex.
- Electrical synapses are usually represented by **gap junctions** that permit **free movement of ions** from one cell to another.
- When this ion movement occurs between neurons, there is a **flow of current.**
- Impulse transmission is much **faster** across electrical synapses than across chemical synapses.

Electrical Synapse



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Chemical synapses

- **Chemical synapses** are the most common mode of communication between two nerve cells by **neurotransmitters (NT)**.
- The neurotransmitter (NT) releases **presynaptic membrane,** diffuses across the synaptic cleft to **gated ion-channel receptors** on the **postsynaptic membrane.**
- Binding of **NT-receptors** initiates the opening of ion channels, change the permeability of the postsynaptic membrane, transport ions and reversing its membrane potential or initating action potential.

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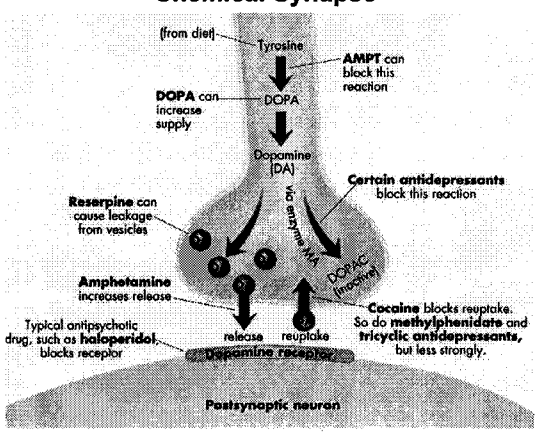
Chemical Synapse



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Chemical synapses (cont.)

- Neurotransmitters do not accomplish the reaction events at the postsynaptic membrane; they only **activate the response**.
- When the stimulus at a synapse results in depolarization of the postsynaptic membrane to a threshold value that initiates an action potential, it is called an **excitatory postsynaptic potential.**
- A stimulus at the synapse that results in maintaining a membrane potential or increasing its hyperpolarization is called an **inhibitory postsynaptic potential.**

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Types of Synapsis

- Various types of synaptic contacts between neurons have been observed. The following synapses are the most common:
  - **Axodendritic synapse** -between an axon and a dendrite
  - **Axosomatic synapse** -between an axon and a soma
  - **Axoaxonic synapse** -between two axons
  - **Dendrodendritic synapse** -between two dendrites

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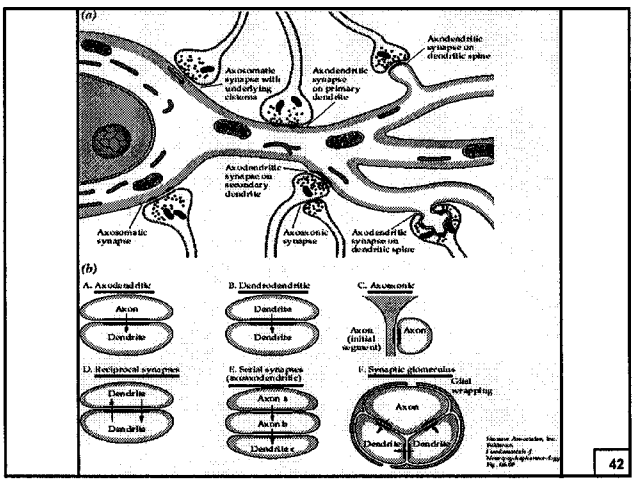

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Synaptic Morphology (cont.)

- Axon of presynaptic cells forms a bulbous expansion at its terminal end called **bouton terminal.**
- The cytoplasm contains mitochondria, a few elements of SER, and an abundance of synaptic vesicles.
- **Synaptic vesicles** are spherical structures (40 to 60 nm in diameter) filled with neurotransmitter substance, transported to the axon terminal via **anterograde transport**.
- Enzymes located in the axoplasm protect neurotransmitters from degradation.

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Synaptic Morphology (cont.)

- The **presynaptic membrane** releases one or more **neurotransmitters** into the **synaptic cleft,** a small gap (20 to 30 nm), located between the presynaptic membrane of the first cell and the **postsynaptic membrane** of the second cell.
- When an action potential reaches the presynaptic membrane, it initiates opening of the **voltage-gated calcium ion (Ca^{2+}) channels,** permitting Ca^{2+} influx and causes synaptic vesicles emptying neurotransmitter into the synaptic cleft via **exocytosis.**

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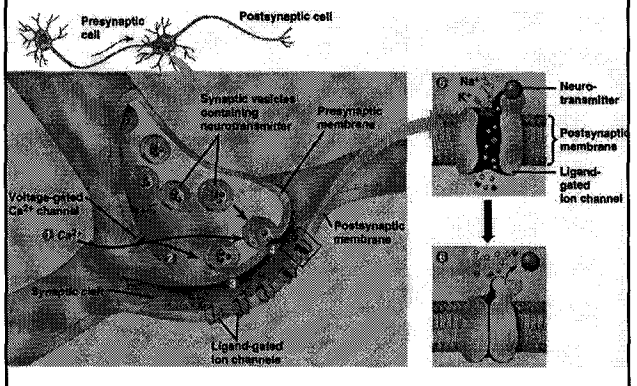
Synnapse



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Synaptic Morphology (cont.)

- The **postsynaptic membrane** is a thickened portion of the plasma membrane of the postsynaptic cell, contains **neurotransmitter receptors.**
- Coupling of the neurotransmitter with the receptors in the plasmalemma initiates response of the postsynaptic membrane.
  - **depolarization** (an excitatory response) or
  - **hyperpolarization** (an inhibitory response)
- Glial cells have been shown to increase synaptogenesis, synaptic efficacy, and action-potential firing.

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Synaptic Morphology (cont.)

- The relative **thickness** and **density** of the presynaptic and postsynaptic membranes, coupled with the width of the synaptic cleft, generally correlate with the nature of the response.
- A thick postganglionic density and a 30-nm-wide synaptic cleft constitutes an **asymmetric synapse,** which is usually the site of **excitatory responses.**
- A thin postsynaptic density and a 20-nm-wide synaptic cleft constitutes a **symmetric synapse**, which is usually the site of **inhibitory responses.**

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Neurotransmitters / Neuromodulators

- Neurotransmitters are signaling molecules, act on two types of receptors:
  - 1. those directly associated with **ion channels** and
  - 2. those associated with **G proteins or receptor.**
- Signaling molecules that act as "first messenger systems" (i.e., act on receptors directly associated with ion channels) retain the name **neurotransmitters,** which acts directly, fast, and lasting less than 1 msec.
- Signaling molecules that invoke the "second messenger system" now are referred to as **neuromodulators** or **neurohormones,** which are much slower and may last as long as a few minutes.

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Neurotransmitters / Neuromodulators (cont.)

- There are perhaps 100 known neurotransmitters (and neuromodulators), represented by the following three groups:
  - 1. Small-molecule transmitters
  - 2. Neuropeptides
  - 3. Gases

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Small-molecule transmitters

- Small-molecule transmitters are of three major types:
  - 1. **Acetylcholine** (the only one in this group that is not an amino acid derivative)
  - 2. **Amino acids**: glutamate, aspartate, glycine, and γ-aminobutyric acid (GABA)
  - 3. **Biogenic amines**: (monoamines) serotonin and the three catecholamines: dopamine, norepinephrine (noradrenaline), and epinephrine (adrenaline).

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Neuropeptides

- **Neuropeptides,** many of which are neuromodulators, form a large group. They include:
  - 1. **Opioid peptides**: enkephalins and endorphins
  - 2. **Gastrointestinal peptides**: substance P, neurotensin, and vasoactive intestinal peptide
  - 3. **Hypothalamic-releasing hormones**: thyrotropin-releasing hormone and somatostatin
  - 4. **Hormones**: antidiuretic hormone and oxytocin.

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Gases

- **Gases** may act as neuromodulators.
- The ones that do are
  - nitric oxide (NO) and
  - carbon monoxide (CO).

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Neurotransmitter	Compound Group	Function
Acetylcholine	Small molecule transmitter; not derived from amino acid	Myoneural junctions, all parasympathetic synapses, and preganglionic sympathetic synapses
Norepinephrine	Small molecule transmitter; biogenic amine; atecholamine	Postganglionic sympathetic synapses (except for eccrine sweat glands)
Glutamate	Small molecule transmitter; amino acid	Presynaptic sensory and cortex: most common excitatory neurotransmitter of CNS
γ-Aminobutyric acid (GABA)	Small molecule transmitter; amino acid	Most common inhibitory neurotransmitter of CNS
Dopamine	Small molecule transmitter; biogenic amine; atecholamine	Basal ganglia of CNS; inhibitory or excitatory, depending on receptor
Serotonin	Small molecule transmitter; biogenic amine	Inhibits pain; mood control; sleep
Glycine	Small molecule transmitter; amino acid	Brain stem and spinal cord; inhibitory
Endorphins	Neuropeptide; opioid peptide	Analgesic; inhibit pain transmission?
Enkephalins	Neuropeptide; opioid peptide	Analgesic; inhibit pain transmission?

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Nerves

- **Nerves** are bundles of nerve fibers (axons), located outside the central nervous system and surrounded by three connective tissue sheaths.
- **Epineurium** is composed of dense, irregular, collagenous connective tissue containing thick elastic fibers that completely ensheathe the nerve.
- **Perineurium** is composed of dense connective tissue but is thinner than epineurium.
- **Endoneurium** is a loose connective tissue composed of a thin layer of reticular fibersan, important factor in regulation of the microenvironment of the nerve fiber.

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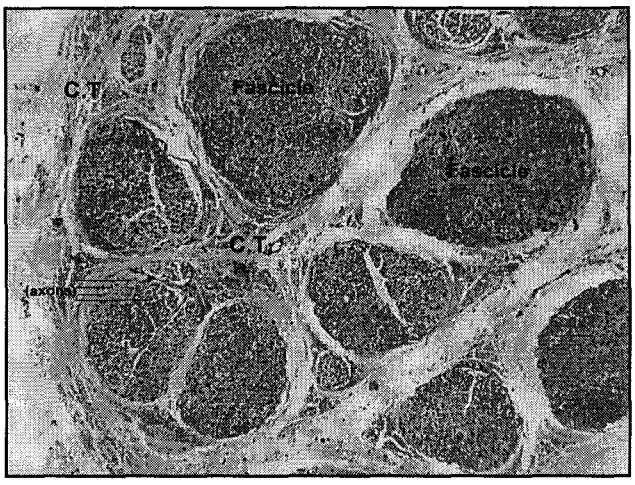
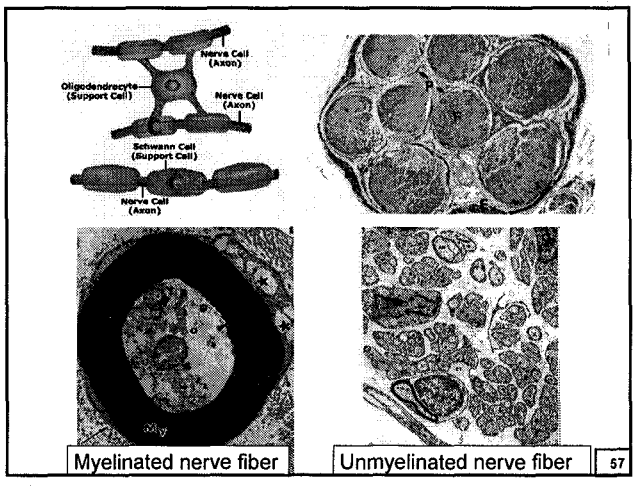
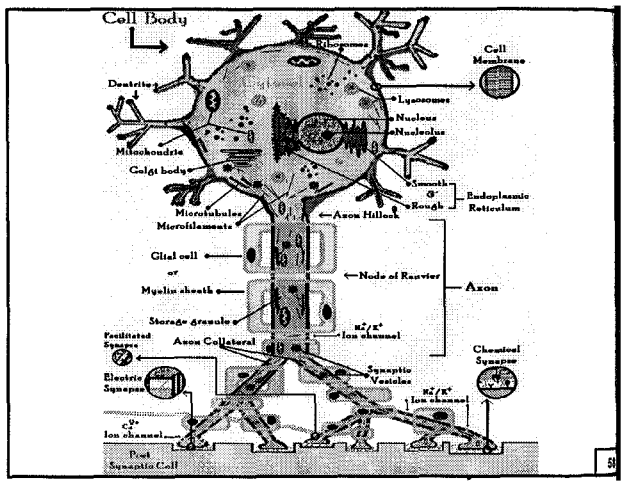


Classification of Nerves

- **Myelinated** Nerve fibers, the conduction velocity ranges from about 0.5 to 2 m/sec
- **Unmyelinated** nerve fibers, the action potential "jumps" from node to node, a process called **saltatory conduction** the conduction velocity ranges from 15 to 120 m/sec.
- **Sensory (afferent)** nerve fibers carry sensory input from the cutaneous areas of the body and from the viscera back to the CNS for processing.
- **Motor (efferent)** nerve fibers originate in the CNS and carry motor impulses to the effector organs.
- The sensory roots and motor roots of the spinal cord unite to form **mixed peripheral nerves,** the **spinal nerves,** which carry both sensory and motor fibers.



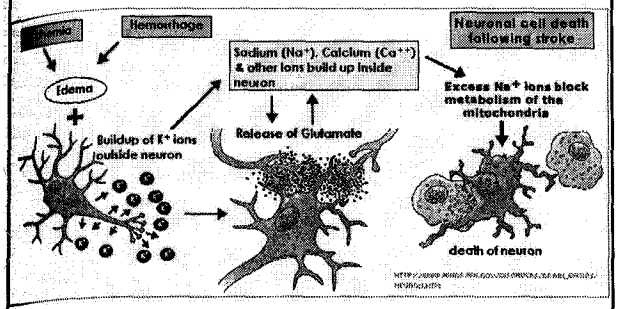


Death of Neaurons

- Although neurons are the longest living cells in the body, large numbers of them die during migration and differentiation.
- The lives of some neurons can take abnormal turns. Some diseases of the brain are the result of the unnatural deaths of neurons.
- In **Parkinson's disease**, neurons that produce the neurotransmitter dopamine die off in the basal ganglia, an area of the brain that controls body movements. The brain can no longer control the body and people shake and jerk in spasms.
- In **Huntington's disease**, a genetic mutation causes over-production of a neurotransmitter called glutamate, which kills neurons in the basal ganglia. As a result, people twist and writhe uncontrollably.

- In **Alzheimer's disease**, unusual proteins build up in and around neurons in the neocortex and hippocampus, parts of the brain that control memory. When these neurons die, people lose their capacity to remember and their ability to do everyday tasks. Physical damage to the brain and other parts of the central nervous system can also kill or disable neurons.
- **Blows to the brain**, or the damage caused by a stroke, can kill neurons outright or slowly starve them of the oxygen and nutrients they need to survive.
- **Spinal cord injury** can disrupt communication between the brain and muscles when neurons lose their connection to axons located below the site of injury. These neurons may still live, but they lose their ability to communicate.

Neuron death results from the release of excess glutamate.



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End of Nervous Tissue

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