Glandular epithelium

Epithelial tissue is present in 2 forms

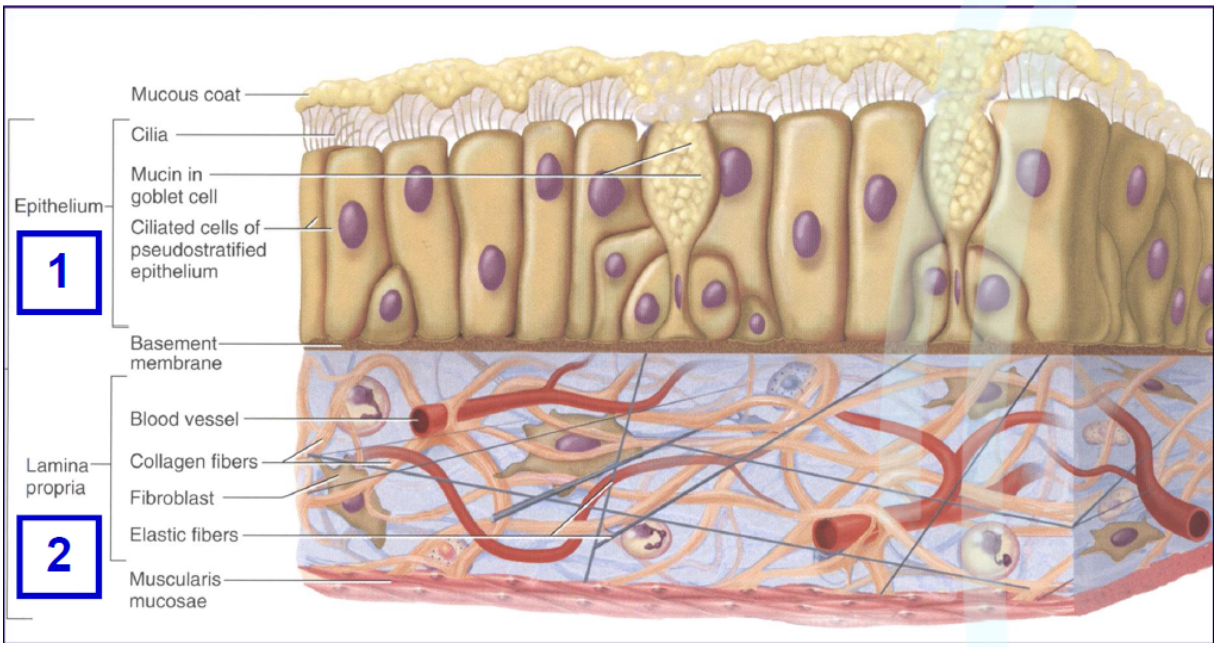
Covering epithelium – as sheets of contiguous cells that cover the body on its external surface and line the body on its internal surface

Glandular epithelium - glands, which originate from invaginated epithelial cells

Glands originate from epithelial cells that leave the surface

Glandular epithelial cells penetrate into the underlying connective tissue, manufacturing a basal lamina around them

The secretory units (+ ducts) are the **parenchyma** of the gland, whereas elements of the connective tissue form the **stroma** of the gland



Glandular epithelia manufacture their product intracellularly by synthesis of macromolecules

Products are packaged and stored in vesicles called **secretory granules**

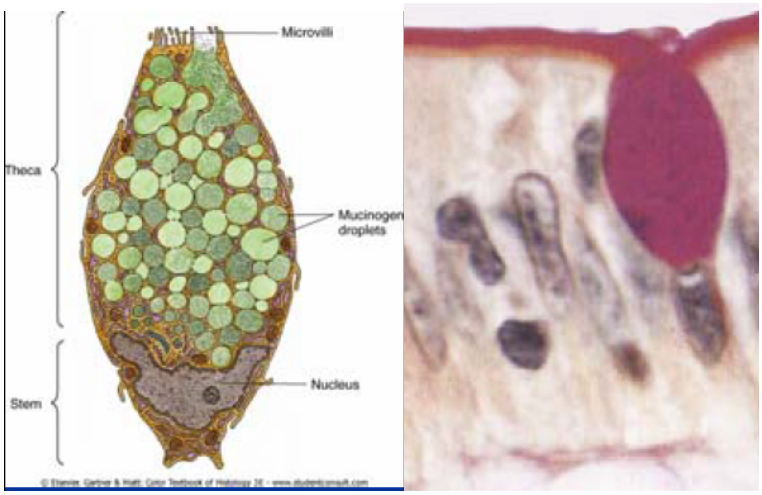
- The secretory product may be
    - a polypeptide hormone (e.g., from the pituitary gland)
    - a waxy substance (e.g., from the ceruminous glands of the ear canal)
    - a mucinogen (e.g., from the goblet cells)
    - milk, a combination of protein, lipid, and carbohydrates (e.g., from the mammary glands)

Gland classification on the basis of the method of product distribution

Exocrine glands secrete their products via ducts onto the external or internal epithelial surface from which they originated.

On the basis of the number of cells (unicellular or multicellular)

- The simplest form of exocrine gland
- Represented by isolated secretory cells in an epithelium – e.g. intestinal or respiratory
- Have basal **stem** and apical theca, filled with membrane bound secretory droplets (mucinogen granules) – their release is stimulated by chemical irritation and parasympathetic innervation

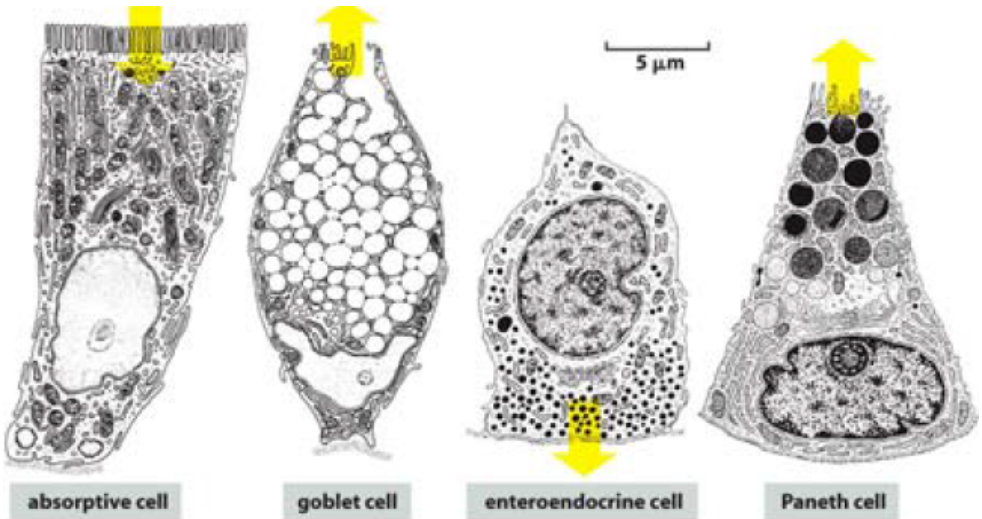


On the basis of their mode of secretion (holocrine, merocrine, apocrine)

On the basis of the nature of their secretion (mucous, serous, or mixed)

Endocrine glands secrete their products into the blood or lymphatic vessels for distribution

The 4 main differentiated cell types found in the epithelial lining of the small intestine



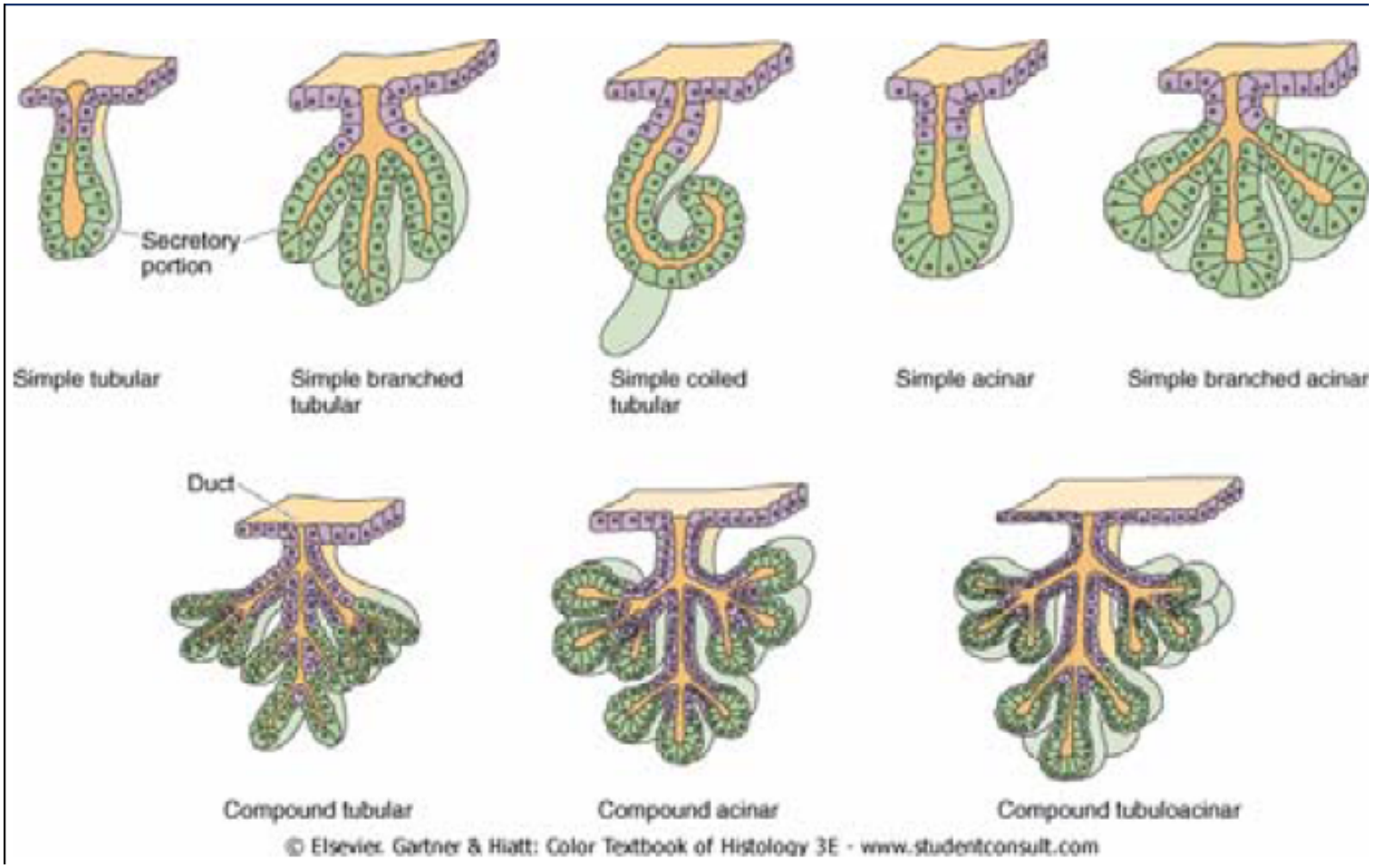
Multicellular exocrine glands

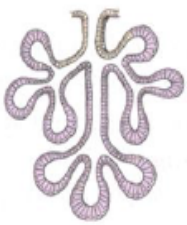
Exist as organized clusters of secretory units, arranged in varying degrees of organization

Do not act alone and independently but instead function as secretory organs

Subclassified according to

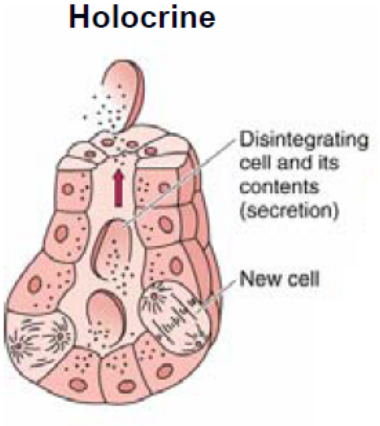
- organization of their secretory and duct components
  - simple - their ducts do not branch
  - compound (branched) - their ducts branch
- shape of their secretory units
  - tubular
  - acinar (alveolar, resembling a grape)
  - tubuloalveolar



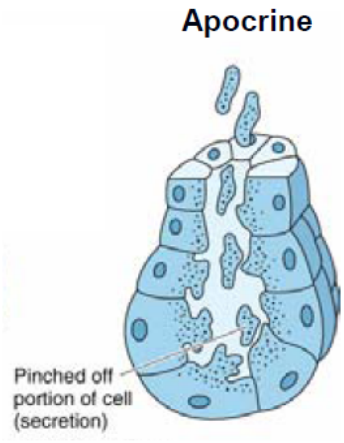
	Classification		Typical Location	Features
Simple Glands	Simple tubular		Large intestine: intestinal glands of the colon	Secretory portion of the gland is a straigh tube formed by the secretory cells (goblet cells)
	Simple coiled tubular		Skin: eccrine sweat gland	Coiled tubular structure is composed of the secretory portion located deep in the dermis
	Simple branched tubular		Stomach: mucus-secreting glands of the pylorus	Branched tubular glands with wide secretory portions are formed by the secretory cells and produce a viscous mucous secretion
	Simple acinar		Urethra: paraurethral and periurethral glands	Simple acinar glands develop as an outpouching of the transitional epithelium and are formed by a single layer of secretory cells
	Branched acinar		Stomach: mucus-secreting glands of cardia	Branched acinar glands with secretory portions are formed by mucus-secreting cells; the short, single-duct portion opens directly into the lumen
Compound Glands	Compound tubular		Duodenum: submucosal glands of Brunner	Compound tubular glands with coiled secretory portions are located deep in the submucosa of the duodenum
	Compound acinar		Pancreas: excretory portion	Compound acinar glands with alveolar-shaped secretory units are formed by pyramid-shaped serous-secreting cells
	Compound tubuloacinar		Submandibular salivary gland, mammary gland, lacrimal gland	Compound tubuloacinar glands can have both mucous branched tubular and serous branched acinar secretory units; they have serous end-caps (demilunes)

Exocrine gland classification on the basis of their mode of secretion

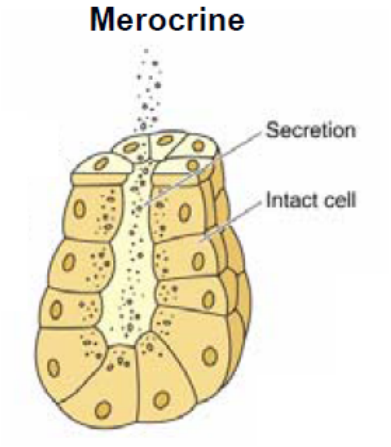
Holocrine glands (e.g., sebaceous gland) – a secretory cell matures, it dies and becomes the secretory product



Apocrine glands (e.g., lactating mammary gland) - a small portion of the apical cytoplasm is released along with the secretory product



Merocrine glands (e.g., parotid gland) – via exocytosis; i.e., neither cell membrane nor cytoplasm becomes a part of the secretion



Larger multicellular glands have additional components

Collagenous connective tissue capsule

Capsule sends septae (strands of connective tissue) into the gland, subdividing it into smaller compartments known as lobes and lobules

Vascular elements, nerves, and ducts utilize the connective tissue septa to enter and exit the gland. In addition, the connective tissue elements provide structural support for the gland.

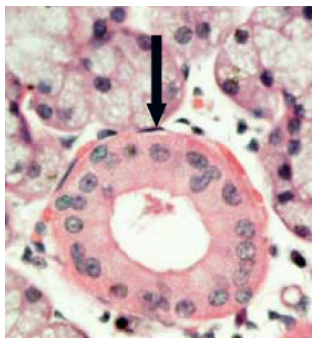
Exocrine glands with merocrine secretion - classification on the basis of the nature of their secretion

Mucous

secrete mucinogens - large glycosylated proteins that, upon hydration, swell to become a thick, viscous, gel-like protective lubricant known as mucin, a major component of mucus

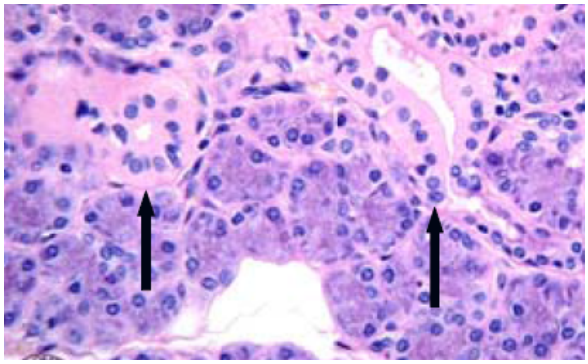
examples: unicellular: goblet cells

multicellular: minor salivary glands of the tongue and palate

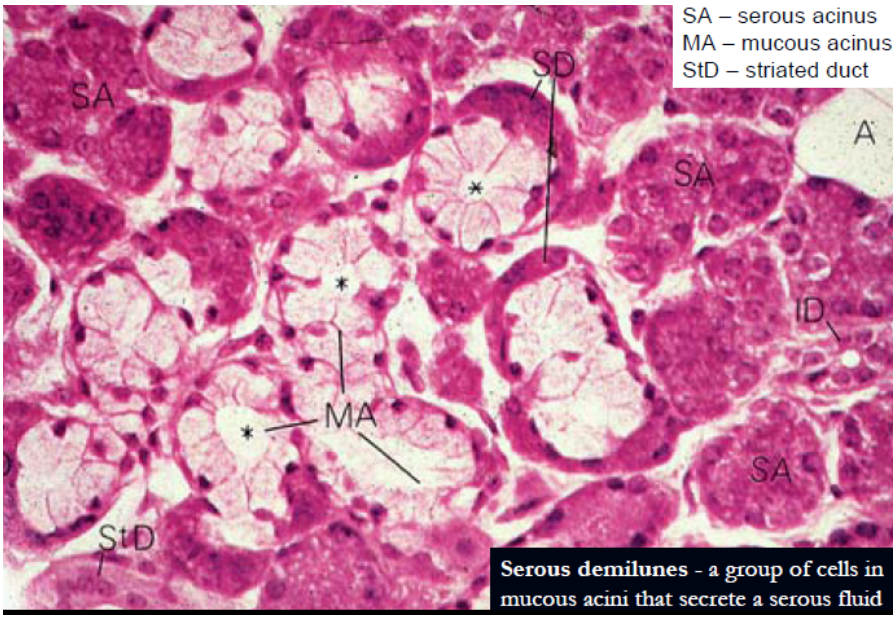


Serous

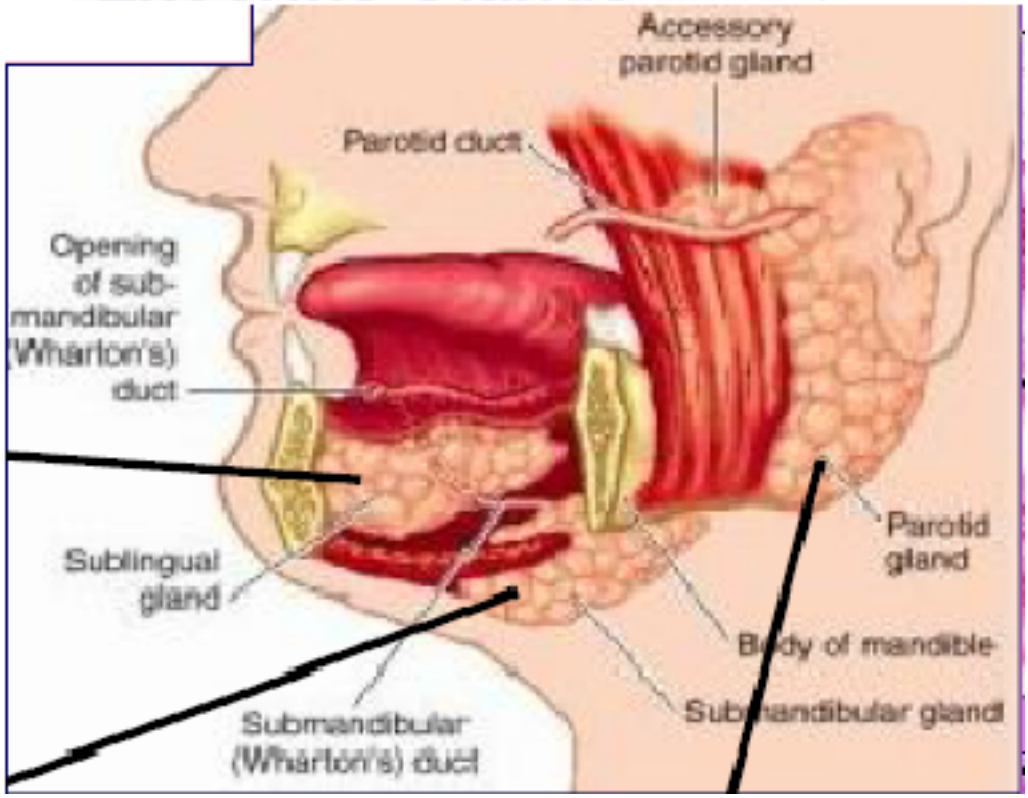
secrete an enzyme-rich watery fluid; examples – pancreas, parotid salivary

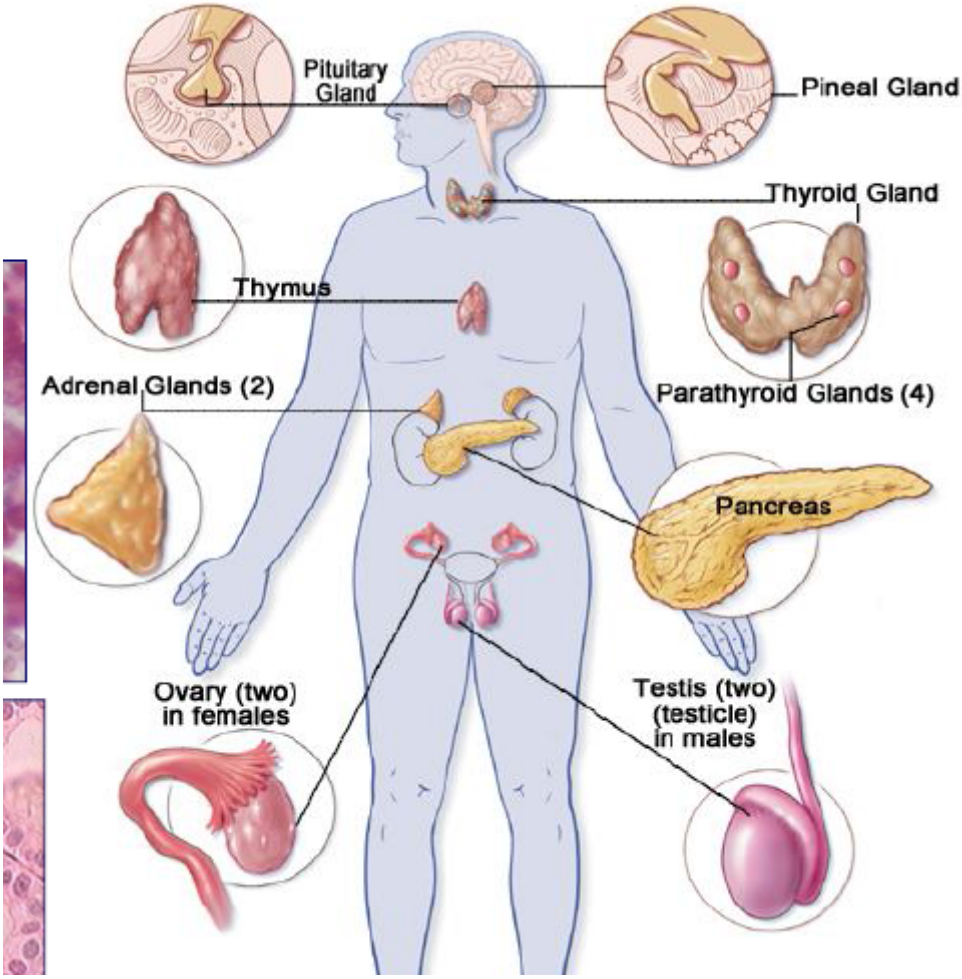


Mixed – have both mucous and serous components



Exocrine Glands





Myoepithelial cells

Stellate or spindle-shaped cells located between the basal lamina and the basal pole of secretory or duct cells in several exocrine glands (eg, sweat, lacrimal, salivary, mammary)

Possess processes which embrace an acinus as an octopus – connected via gap junctions and desmosomes

Specialized for contraction (contain myosin and a large number of actin filaments) - contract around the secretory or conducting portion of the gland and thus help propel secretory products into the duct

Endocrine glands

Ductless, and thus their secretory products are released directly into the bloodstream or the lymphatic system

Their cells can be arranged in cords or in follicles with lumens for storing the secretory product

Overview of the endocrine system

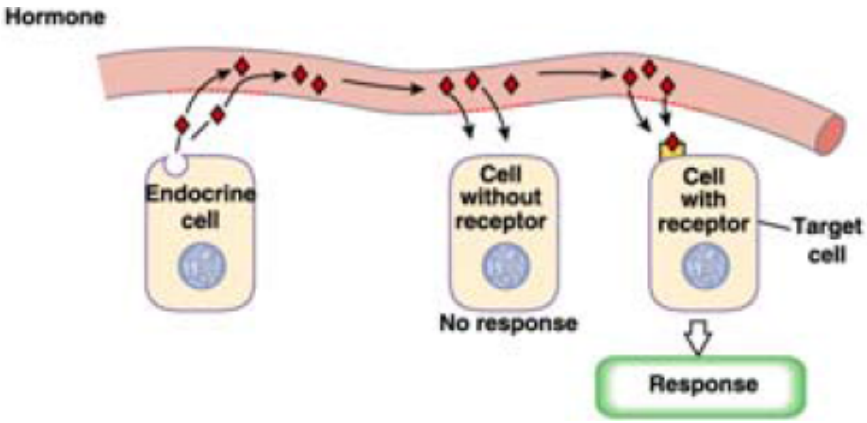
System of ductless glands that secrete hormones

- Hormones are messenger molecules (“first messenger”)
- Circulate in the blood
- Act on distant target cells
- Target cells respond to the hormones for which they have receptors
- The effects are dependent on the programmed response of the target cells
- Hormones are just molecular triggers

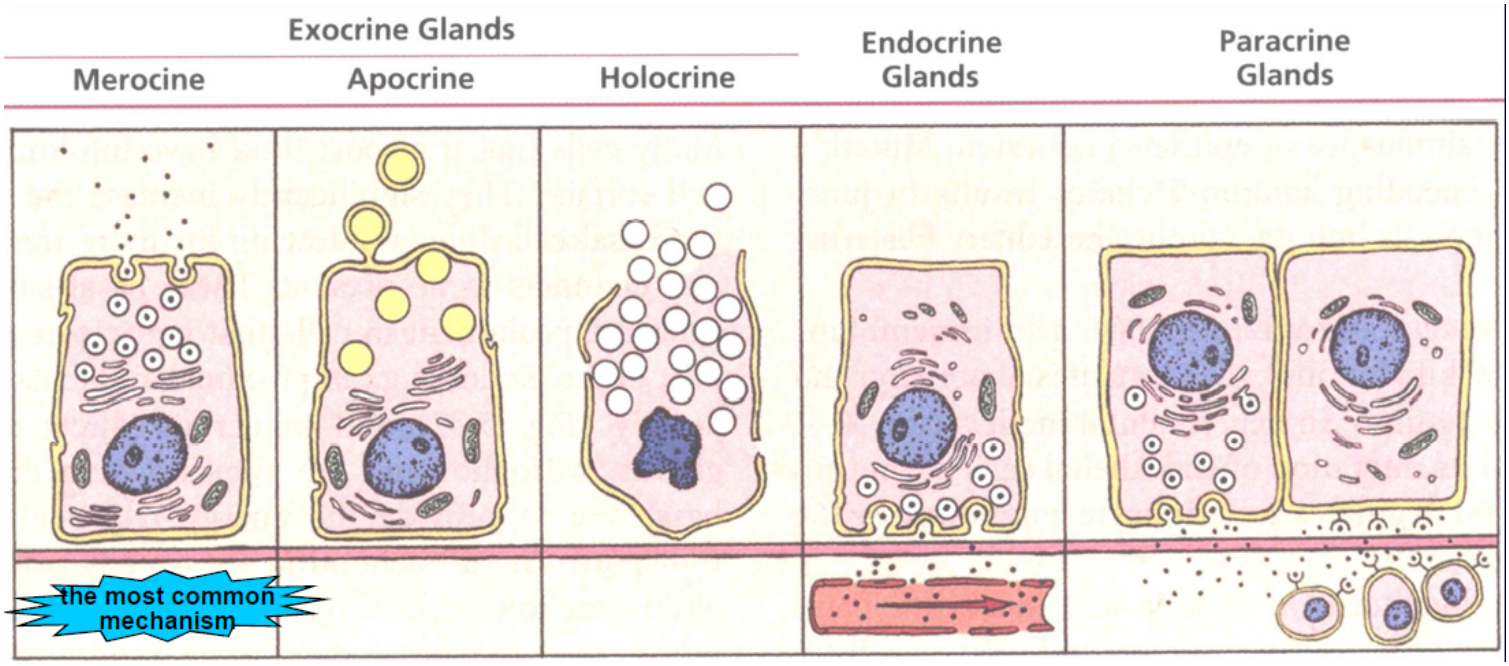
Basic categories of hormones Basic categories of hormones

Hormones are organic chemical messengers produced and secreted by endocrine cells into the bloodstream.

Hormones regulate, integrate and control a wide range of physiologic functions.



Amino acid based: modified amino acids (or *amines*), peptides (short chains of amino acids), and proteins (long chains of amino acids)



Growth

Healing

Water balance & blood pressure

Calcium metabolism

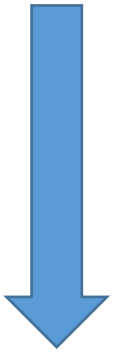
Energy metabolism

Stress

Regulation of other endocrine organs

General histology

Levels of structural organization



Chemical – atoms combined to form molecules

Cellular – cells are made of molecules

Tissue – consists of similar types of cells

Organ – made up of different types of tissues

Organ system– consists of different organs that work closely together

Organismal – made up of the organ systems

Histology

The human body is composed of ~200 different types of cells

The human body is composed of 4 basic kinds of tissues

Epithelial Tissue

Connective Tissue

Muscle Tissue

Nervous Tissue

Tissues: groups of cells which are similar in structure and which perform common or related functions.

Histology: the study of tissues

General – the 4 basic tissues

Systemic – system by system study

Tissue = cells + ECM

The tissues are formed by cells and molecules of the extracellular matrix (ECM) – an intricate meshwork of proteins and polysaccharides that are secreted by the cell and assembled locally

The organs are formed by combination of different tissues in variable proportions

Main characteristics of the four basic types of tissues

Tissue	Cells	ECM	Main Functions
Epithelial	Aggregated polyhedral cells	Small amount	Lining of surface or body cavities, glandular secretion
Connective	Several types of fixed and wandering cells	Abundant amount	Support and protection
Muscle	Elongated contractile cells	Moderate amount	Movement
Nervous	Intertwining elongated processes	None	Transmission of nervous impulses

There are also free cells found in body fluids such as blood and lymph

Organs can be divided into parenchyma, which is composed of the cells responsible for the main functions typical of the organ, and stroma, which is the supporting tissue.

Except in the brain and spinal cord, the stroma is made of connective tissue.

Epithelium (Gr. epi, upon, + thele, nipple)

Composed of closely aggregated polyhedral cells with very little extracellular substance

Epithelial cells have strong adhesion and form cellular sheets that cover the surface of the body and line its cavities

Principal functions

Protection of underlying tissues of the body from abrasion and injury

Secretion of mucus, hormones, enzymes, and so forth, from various glands

Absorption of material from a lumen (e.g., intestinal tract or certain kidney tubules)

Detection of **sensations** via taste buds, retina of the eye, and specialized hair cells in the ear

Contractility (eg, myoepithelial cells)

Epithelial tissue is present in 2 forms

Covering epithelium – as sheets of contiguous cells that cover the body on its external surface and line the body on its internal surface

Glandular epithelium – glands, which originate from invaginated epithelial cells

Origin of epithelium - from all three embryonic germ layers

Ectoderm gives rise to the oral and nasal mucosae, cornea, epidermis of the skin, and glands of the skin and the mammary glands.

Endoderm gives rise to the liver, the pancreas, and the lining of the respiratory and gastrointestinal tract

Mesoderm gives rise to the uriniferous tubules of the kidney, the lining of the male and female reproductive systems, the endothelial lining of the circulatory system, and the mesothelium of the body cavities

Common characteristic features of epithelial cells

- Epithelial cells have **polyhedral form**
- Epithelial cells show **polarity**
- Most epithelia **rest on connective tissue** – it provides support and nutrition to the epithelium (epithelium is avascular!) as well as binds it to underlying structures
- Epithelial cells have **basal lamina** at the interface with connective tissue

Epithelial cells have polyhedral form

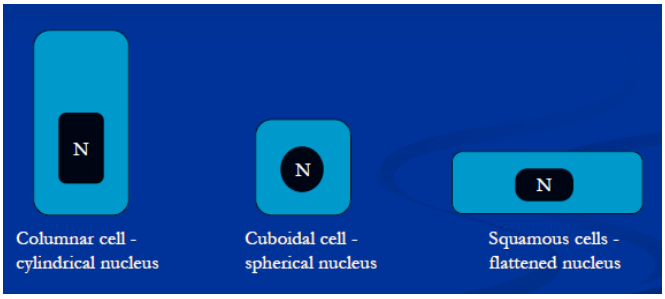
The polyhedral form (ranging from high columnar to cuboidal to low squamous cells) results from their close juxtaposition in cellular layers or masses

The **nuclear form** of epithelial cells often corresponds roughly to the cell shape because the long axis of the nucleus is always parallel to the main axis of the cell

- cuboidal cells have spherical nuclei
- squamous cells have flattened nuclei

The stained cell nucleus is a clue to the shape and number of cells. Nuclear form is also useful to determine whether the cells are arranged in layers, a primary morphologic criterion for classifying epithelia.

Form of epithelial cells and their nucleus



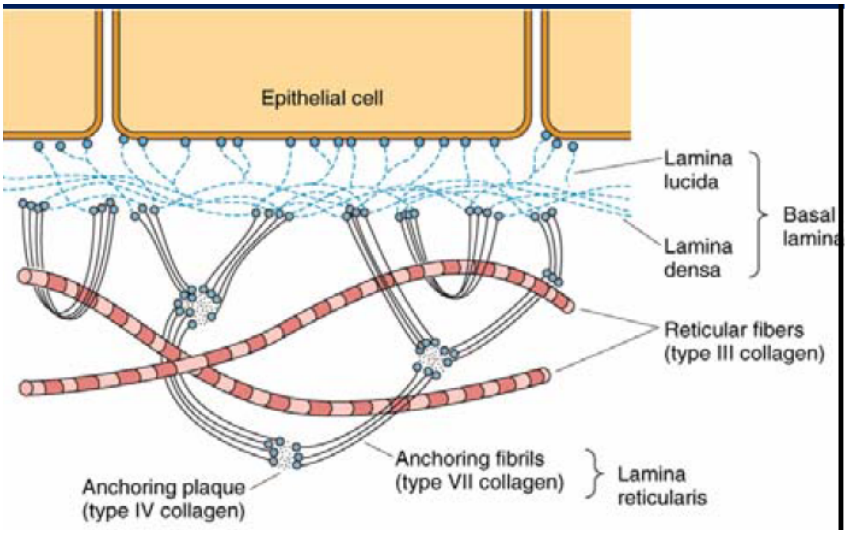
Basement membrane

- Components
  - Basal lamina – produced by epithelial cells
  - Reticular lamina – produced by CT cells
  - Basement membrane is light microscopic term, basal lamina – EM term

Basal lamina

- Lies at the interface of epithelial cells and connective tissue
- Nutrients for epithelial cells must diffuse across the basal lamina
- Blood capillaries never enter an epithelium across a basal lamina
- Nerves enter an epithelium across a basal lamina

Basement membrane – TEM



Lamina lucida - 50-nm-thick electron-lucent region just beneath the epithelium

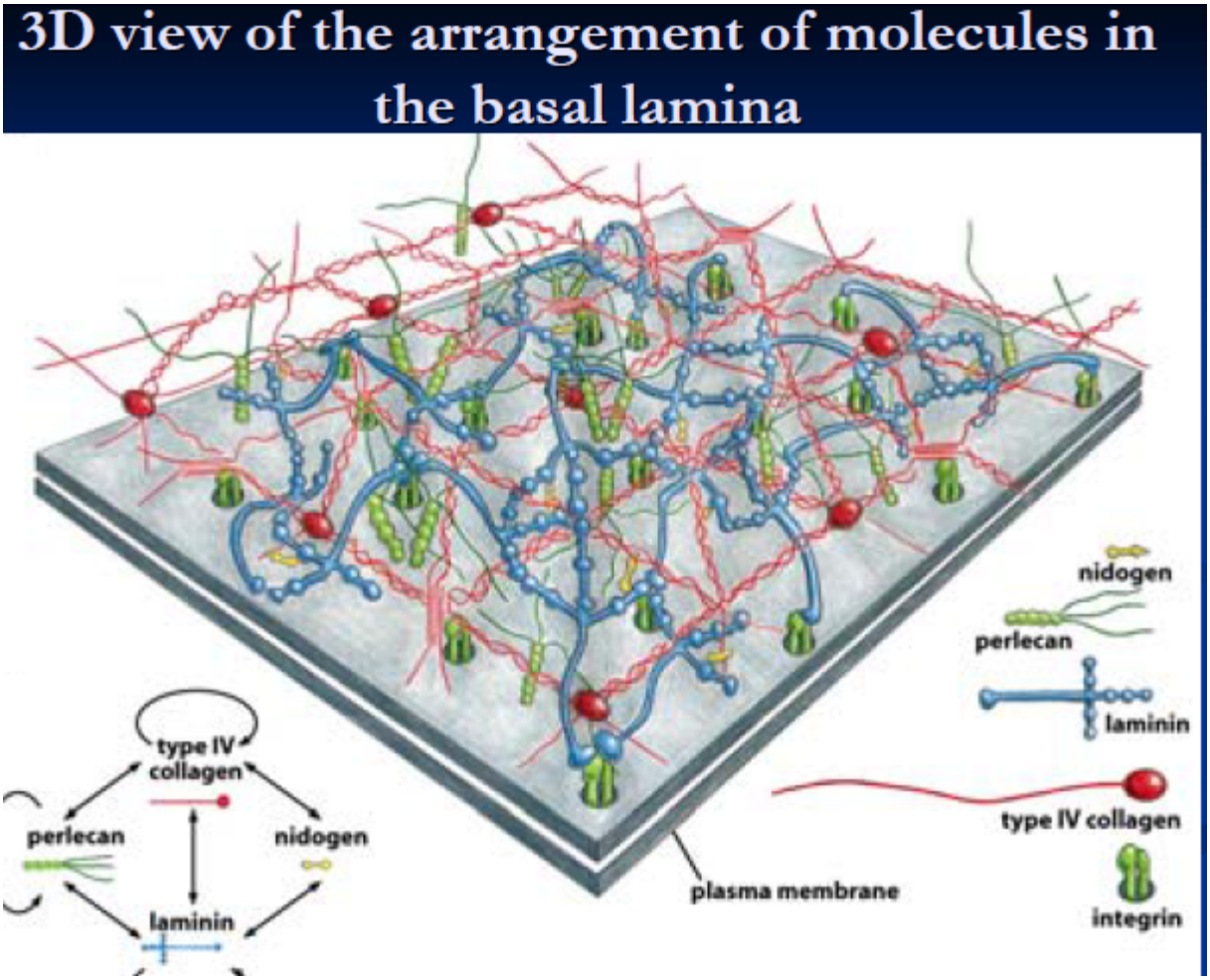
- transmembrane molecules - integrins and dystroglycans
- extracellular glycoproteins laminin and entactin

Lamina densa - 50-nm-thick electron-dense region

meshwork of type IV collagen, coated by the proteoglycan perlecan heparan sulfate GAG

Lamina reticularis

- type I and type III collagen
- fibronectin
- anchoring fibrils (type VII collagen)
- microfibrils (fibrillin)



Basal lamina - functions

- Molecular filter
- Support for the overlying epithelium
- Regulation of mitotic activity, cell differentiation, and migration
- Modulation of cellular metabolism
- Assisting in the establishment of cell polarity

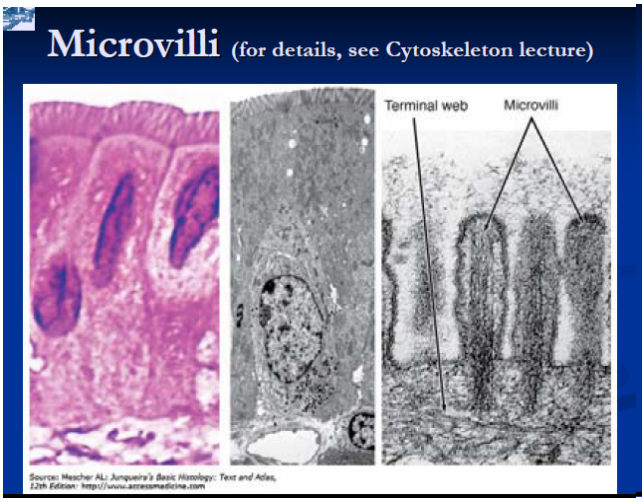
Specializations on the plasmalemma of epithelial cells

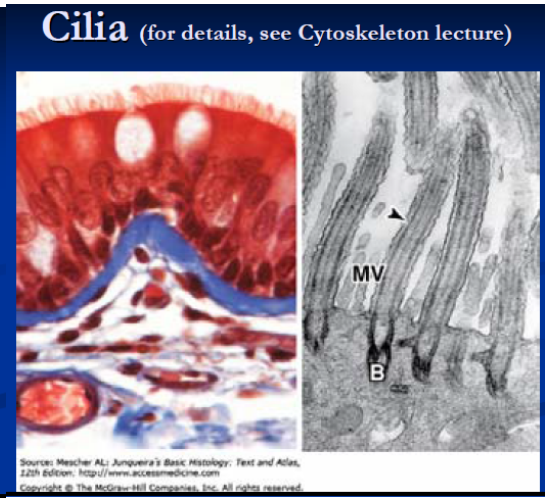
Specializations of the **apical** cell surface

Microvilli & stereocilia - AF

Cilia – MT

Specializations of the **basolateral** cell surface – see Cell Junctions lecture

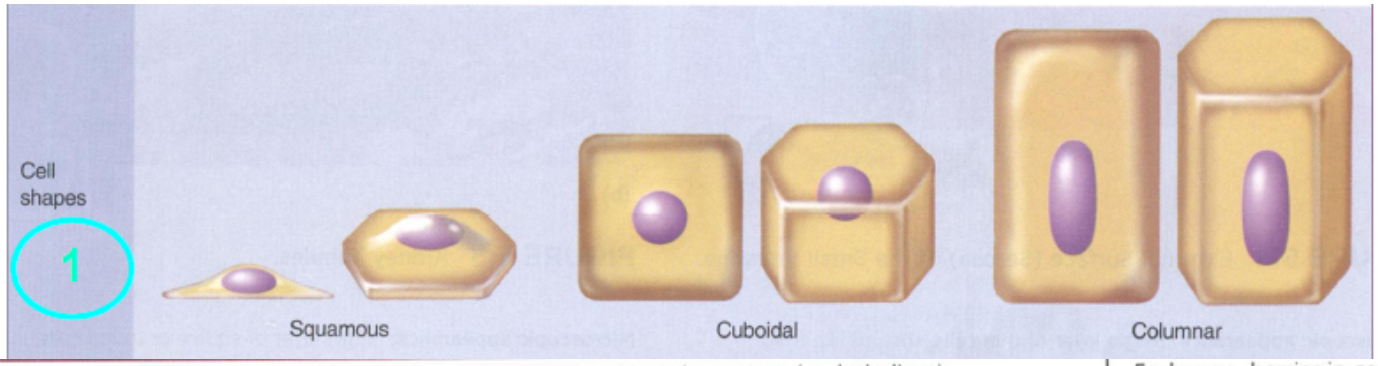




Major types of epithelia

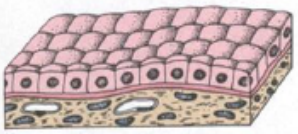
Covering (lining) - the cells are organized in layers that cover the external surface or line the cavities of the body

Glandular (secretory) epithelia - formed by cells specialized to secrete proteins (e.g., in the pancreas), lipids (e.g., adrenal, sebaceous glands), or complexes of carbohydrates and proteins (e.g., salivary glands)



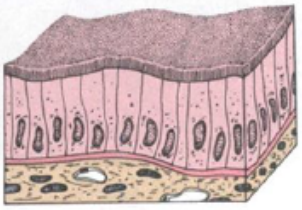
Simple squamous — **1**

- Vascular system (endothelium) — Exchange, barrier in central nervous system
- Body cavities (mesothelium) — Exchange and lubrication
- Bowman's capsule (kidney) — Barrier
- Respiratory spaces in lung — Exchange



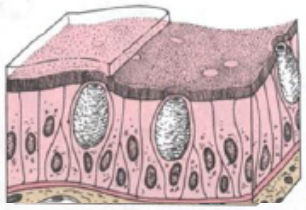
Simple cuboidal — **2**

- Small ducts of exocrine glands — Absorption, conduit
- Surface of ovary (germinal epithelium) — Barrier
- Kidney tubules — Absorption and secretion
- Thyroid follicles



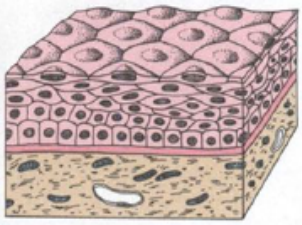
Simple columnar — **3**

- Small intestine and colon — Absorption and secretion
- Stomach lining and gastric glands — Secretion
- Gallbladder — Absorption



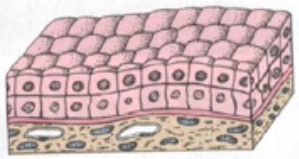
Pseudostratified — **4**

- Trachea and bronchial tree — Secretion, conduit
- Ductus deferens — Absorption, conduit
- Efferent ductules of epididymis



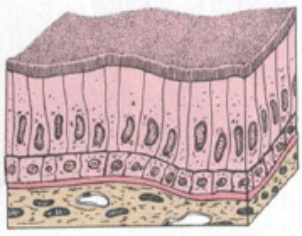
Stratified squamous — **1**

- Epidermis — Barrier, protection
- Oral cavity and esophagus
- Vagina



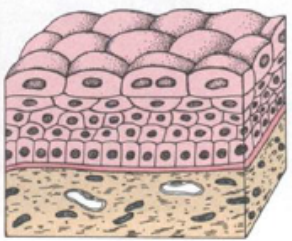
Stratified cuboidal — **2**

- Sweat gland ducts — Barrier, conduit
- Large ducts of exocrine glands
- Anorectal junction



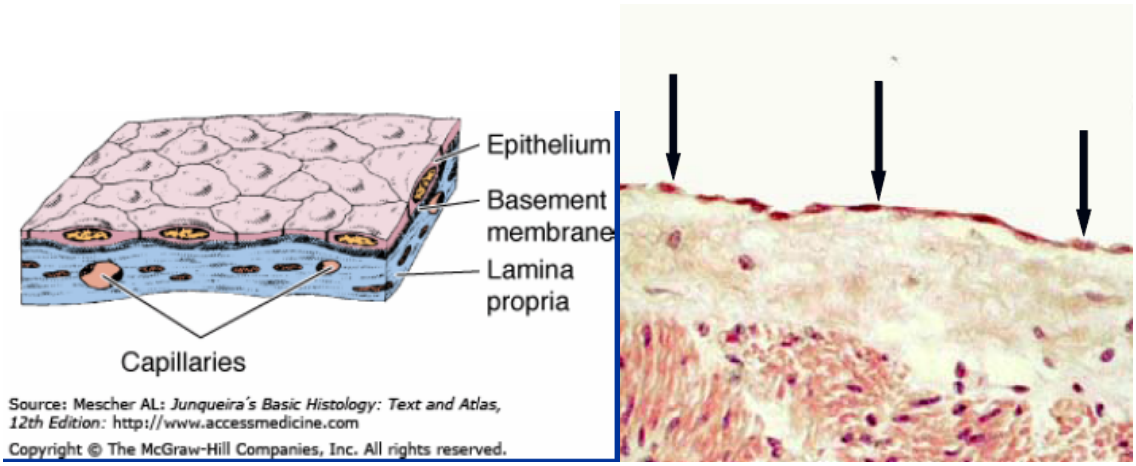
Stratified columnar — **3**

- Largest ducts of exocrine glands — Barrier, conduit
- Anorectal junction



Transitional (urothelium) — **4**

- Renal calyces — Barrier, distensible property
- Ureters
- Bladder
- Urethra

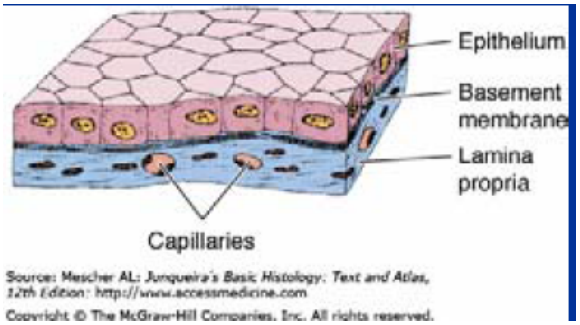


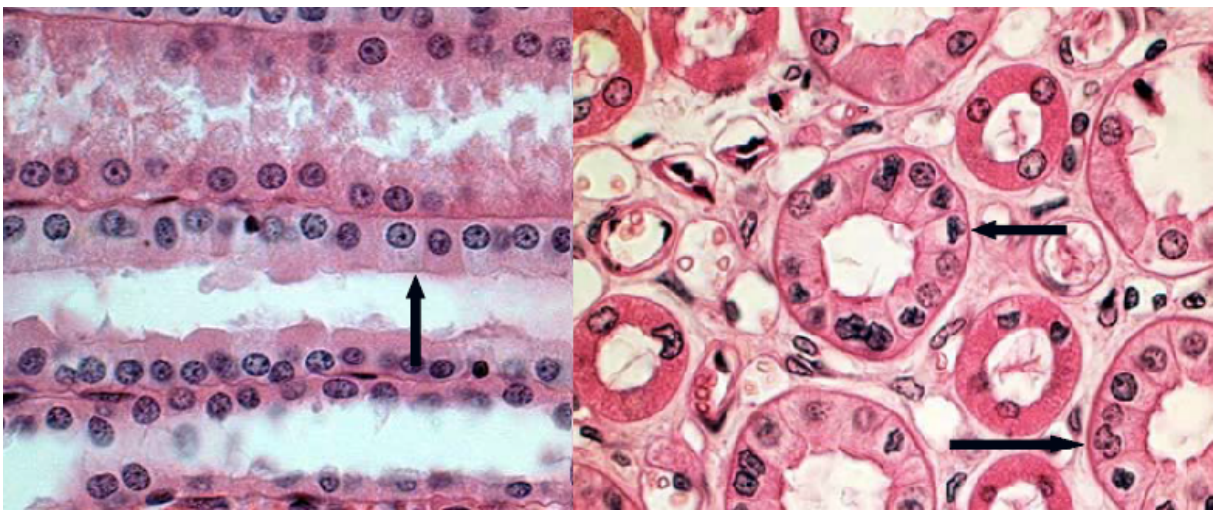
Simple cuboidal epithelium

Simple = 1 layer

Cuboidal = cells roughly as thick as they are wide

Greater thickness often includes cytoplasm rich in mitochondria providing energy for active transport of substances across the epithelium





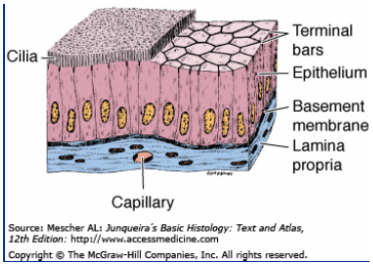
Simple columnar epithelium

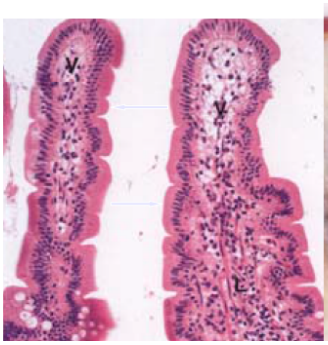
Simple = 1 layer

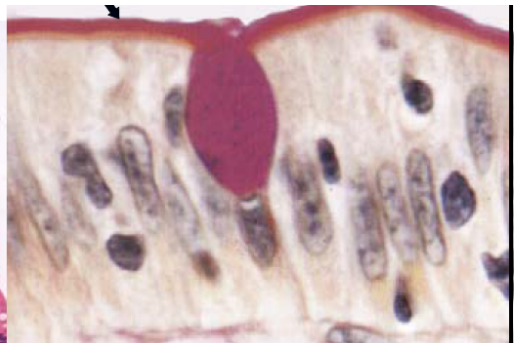
Columnar = cells are taller than they are wide

Specialized for absorption, with microvilli

Tight and adherent junctional complexes at the apical surface





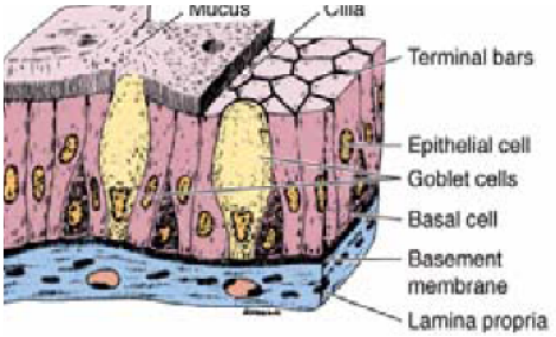


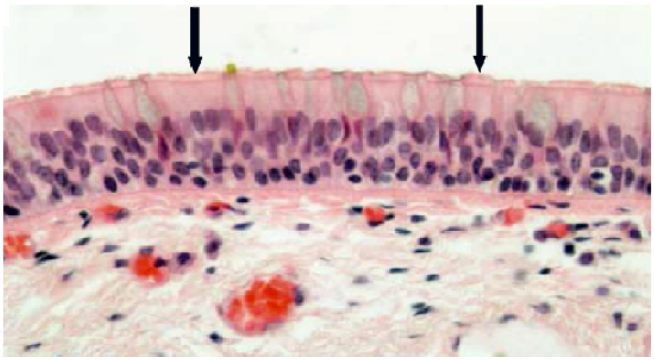
Pseudostratified columnar epithelium

Only appears stratified; all cells are in contact with the basal lamina

Cells are of different heights, their nuclei are located at different levels

Can be ciliated (e.g. upper respiratory tract) or nonciliated (e.g. male urethra)



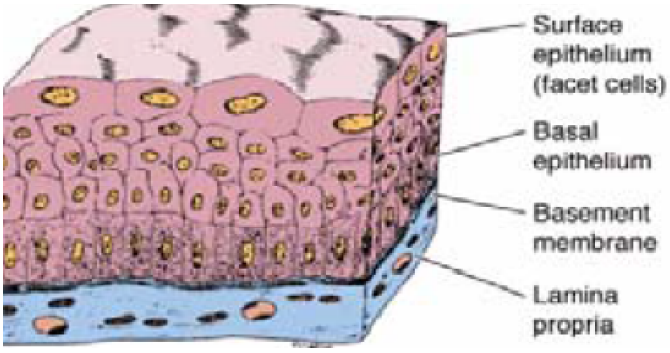


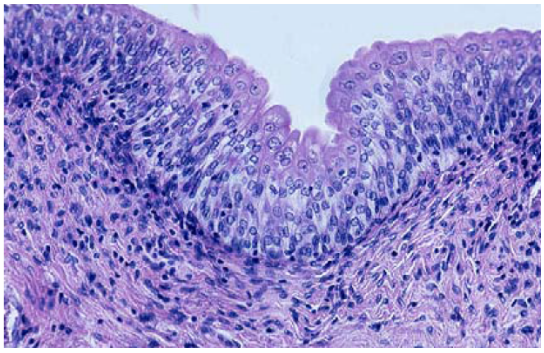
Transitional epithelium (urothelium)

Lines only the urinary bladder, the ureter, and the upper part of the urethra

Composed of many layers of cells

Superficial layer of domelike cells that are neither squamous nor columnar (protective against cytotoxic effects of urine





Stratified squamous epithelium

Nonkeratinized - several layers of cells; the surface most layer possesses nuclei

> Lines wet cavities (e.g. mouth, esophagus, and vagina).
> In such areas where water loss is not a problem, the flattened cells of the epithelial surface layer are living cells containing much less keratin and retaining their nuclei

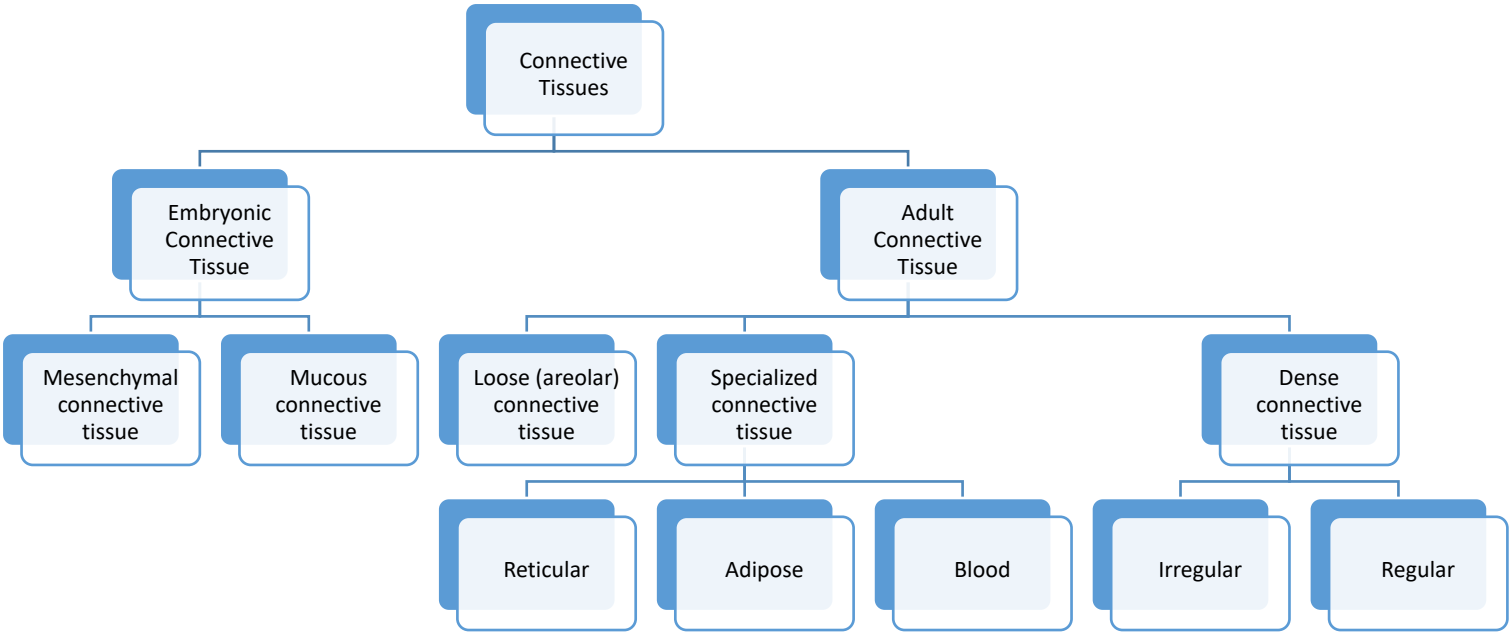
Keratinized - the layers of cells composing the free surface are dead, non-nucleated, and filled with keratin

Composed of *keratinocytes* (synthesize keratin intermediate filament proteins, which give the epidermis its toughness)

Interlocking columns of hexagonal or irregular cells

Connective tissue (CT)

Types of connective tissue



Loose (areolar) connective tissue

- Fills in the spaces of the body just deep to the skin
- lies below the mesothelial lining of the internal body cavity
- is associated with the adventitia of blood vessels, and surrounds the parenchyma of glands
- The loose connective tissue of mucous membranes (as in the alimentary canal) is called the **lamina propria**

Dense connective tissue

Less flexible and far more resistant to stress than is loose connective tissue - adapted to offer resistance and protection

Types

Irregular - the collagen fibers are arranged in bundles without a definite orientation; often found closely associated with loose connective tissue; found in the dermis of skin, the sheaths of nerves, and the capsules of internal organs

Regular - collagen bundles densely packed and oriented into parallel cylinders;

Collagenous - tendons, ligaments, and aponeuroses

Elastic – large arteries, lig. flava, suspensory lig. of the penis

Dense regular CT

- Tight packing of the collagen fibers, so 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

Reticular CT

- **Components:**
    - reticular fibers of type III collagen
    - produced by specialized fibroblasts called reticular cells
- Creates special microenvironments for hematopoietic organs and lymphoid organs (bone marrow, lymph nodes, and spleen)
- Creates a spongelike structure within which cells and fluids are freely mobile

Adipose tissue

- A specialized type of CT in which **adipocytes** (fat cells) predominate
- Adipocytes are combined with loose or irregular connective tissue, often in large aggregates
- Adipose tissue represents ~20% of the body weight of normal person
- Because of a growing worldwide epidemic of obesity and its associated problems, including diabetes and heart disease, *adipocytes are now the most widely studied CT cell*

Adipose tissue functions

The largest **repository of energy** (in the form of triglycerides, the neutral fats) - because triglycerides have a higher caloric value than glycogen, adipose tissue has evolved as a very efficient storage tissue.

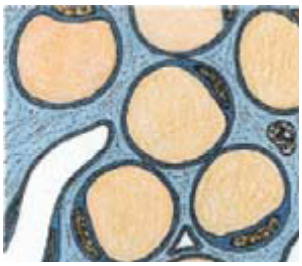
Adipocytes themselves release hormones and a number of important factors, and adipose tissue is now recognized as a major endocrine and signaling organ

Poor heat conductor - contributes to the thermal insulation of the body

Fills up spaces between other tissues and helps to keep some organs in place

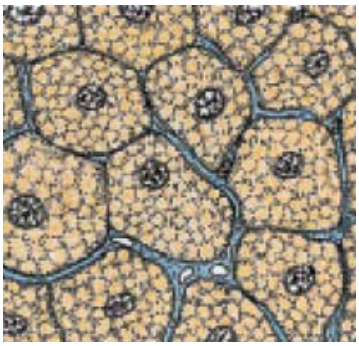
Adipose tissue types

White (unilocular)



- more common type
- triglycerides are stored in a single locus - contain one large central droplet of whitish-yellow fat in their cytoplasm
- peripheral nucleus - **signet ring cell**

Brown (multilocular)



- less common type
- multiple lipid droplets interspersed among abundant mitochondria (heat production) – darker color
- central oval nucleus

Function

- **Heat production**

Amount is maximal at birth – the newborn is exposed to an environment colder than the mother's uterus

In adults it is found only in scattered areas, especially around **the kidneys and adrenal glands, the aorta, and mediastinum**

Excessive formation of adipose tissue is obesity

Adult-onset obesity is generally believed to involve largely increased size or hypertrophy in existing adipocytes

Childhood obesity can involve both hypertrophy and hyperplasia of preadipocytes from mesenchymal cells

Cartilage tissue

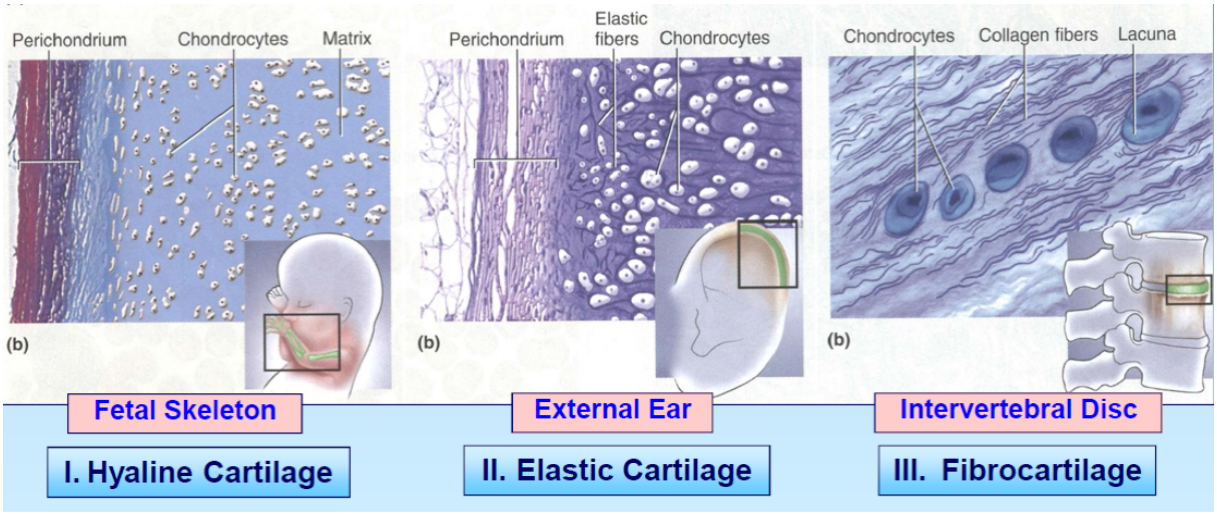
- Has a firm consistency of its ECM allowing to bear mechanical stresses without permanent distortion
- Supports soft tissues
- Facilitates bone movements by being the sliding area for joints, because it is smooth
- Helps the growth of long bones both before and after birth

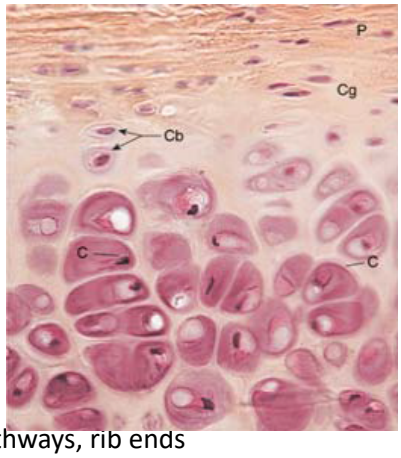
Special features of cartilage

- Constituents:
  - Cells (5%): **chondrocytes** (Gr. *chondros,* cartilage, + *kytos,* cell)
  - ECM (95%): fibers + ground substance (rich in water)
- Avascular – cartilage is nourished by the diffusion of nutrients from capillaries in adjacent connective tissue (perichondrium) or by synovial fluid from joint cavities→low metabolism

- No lymphatic vessels or nerves

- Low regeneration capability





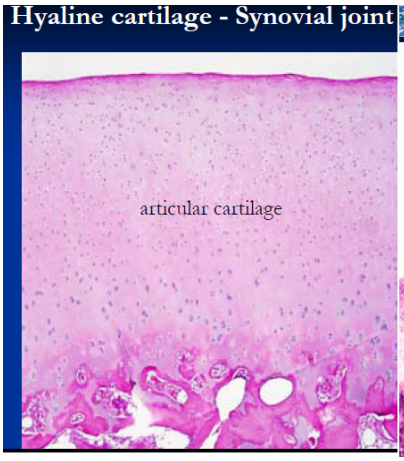
Hyaline cartilage

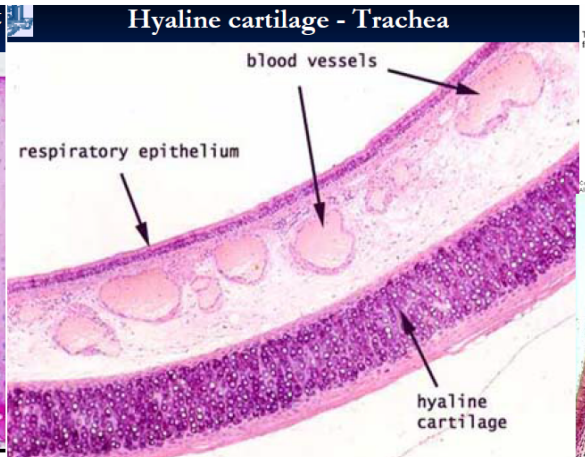
- As perichondrial cells differentiate into chondrocytes, they become round, with an irregular surface

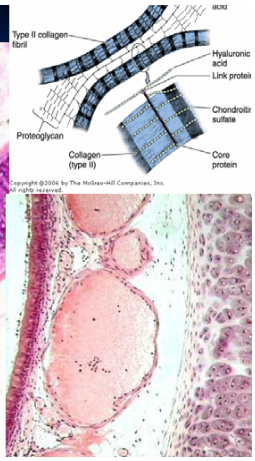
- Hyaline cartilage is the most common type of cartilage
  - embryo →temporary skeleton until it is replaced by bone
  - adult →articular surfaces of movable joints, respiratory pathways, rib ends

- Perichondrium – a layer of dense connective tissue, covering the hyaline & elastic cartilage

- rich in collagen type I fibers and contains numerous fibroblasts
- essential for the growth and maintenance of cartilage







Cellular composition of cartilage

Chondroblasts
From perichondrium
Undifferentiated
Generate chondrocytes

Chondrocytes
10-30 mm in size
Secrete the matrix
round and may appear in groups ofnup to 8 cells originating from mitotic divisions of a single precursor cell →**isogenous groups** (Gr. *isos,* equal, + *genos,* family)
Low matabolic activity
Non-dividing

Fibrocartilage

Intermediate between dense connective tissue and hyaline cartilage →the border areas between these two tissues are not clear-cut

Chondrocytes, either singly or in isogenous groups

Collagen type I →the matrix is acidophilic

No perichondrium

Intervertebral disks, ligament attachment to the cartilaginous surface of bones, symphysis pubis

Irregular bundles of collagen fibers inbetween the groups of chondrocytes
Parallel bundles of collagen fibers along the columns of chondrocytes

Intervertebral disk

- **annulus fibrosus**:
    - dense connective tissue + overlapping laminae of fibrocartilage (collagen
    - type I)
- **nucleus pulposus**:
    - a few rounded cells embedded in a viscous matrix rich in hyaluronic acid and type II collagen fibrils

Bone tissue

Bone is a specialized form of connective tissue
Composed of intercellular calcified material, the **bone matrix,** and three cell types:

- **osteocytes** (Gr. *osteon,* bone, + *kytos,* cell)→found in cavities (**lacunae**) within the matrix
- **osteoblasts** (*osteon* + Gr. *blastos,* germ)→synthesize the organic components of the matrix
- **osteoclasts** (*osteon* + Gr. *klastos,* broken), multinucleated giant cells involved in the resorption and remodeling of bone tissue

Special features of bone
The main constituent of the adult skeleton, supportsfleshy structures, protects vital organs
Serves as a reservoir of calcium, phosphate, and other ions (99% of body calcium is in the skeleton)
Harbors the bone marrow, where blood cells are formed
Highly vascularized
Metabolically very active
Good regeneration capability

Types of bone tissue
Primary (=woven) bone tissue – temporary →replaced by secondary bone tissue osteoid = bone matrix with lessminerals (i.e. organic)

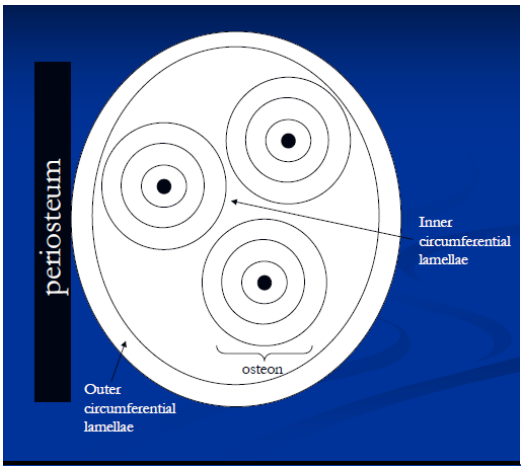
Secondary (lamellar) bone tissue – composed of **osteons** (complexes of concentric lamellae of bone surrounding a canal containing blood vessels, nerves, and loose connective tissue)

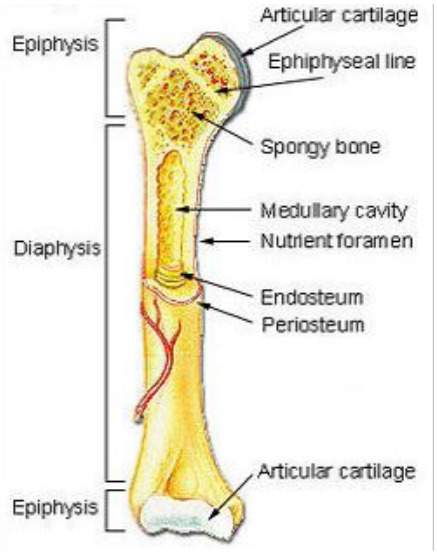
Individual osteocytes are connected by gap junctions

The Haversian system: **Osteons**

- Size: 100 to 400 µm in diameter
- On average 30 lamellae, each 3 µm thick
- About 21 million osteons in the adult skeleton
- Haversian canal mean diameter - 50 µm
- No osteocyte is more than 200 µm from a blood vessel →distance is a limiting factor in cellular survival

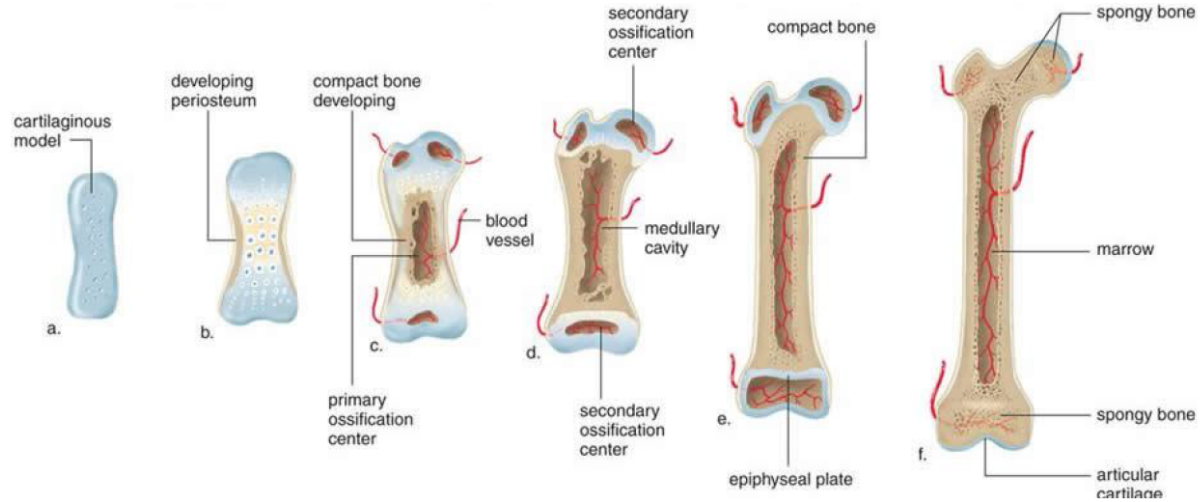
- Periosteum
    - Outer fibrous layer (Sharpey's fibers)
    - Inner cellular layer (osteoprogenitors)
- Endosteum (osteoprogenitors)

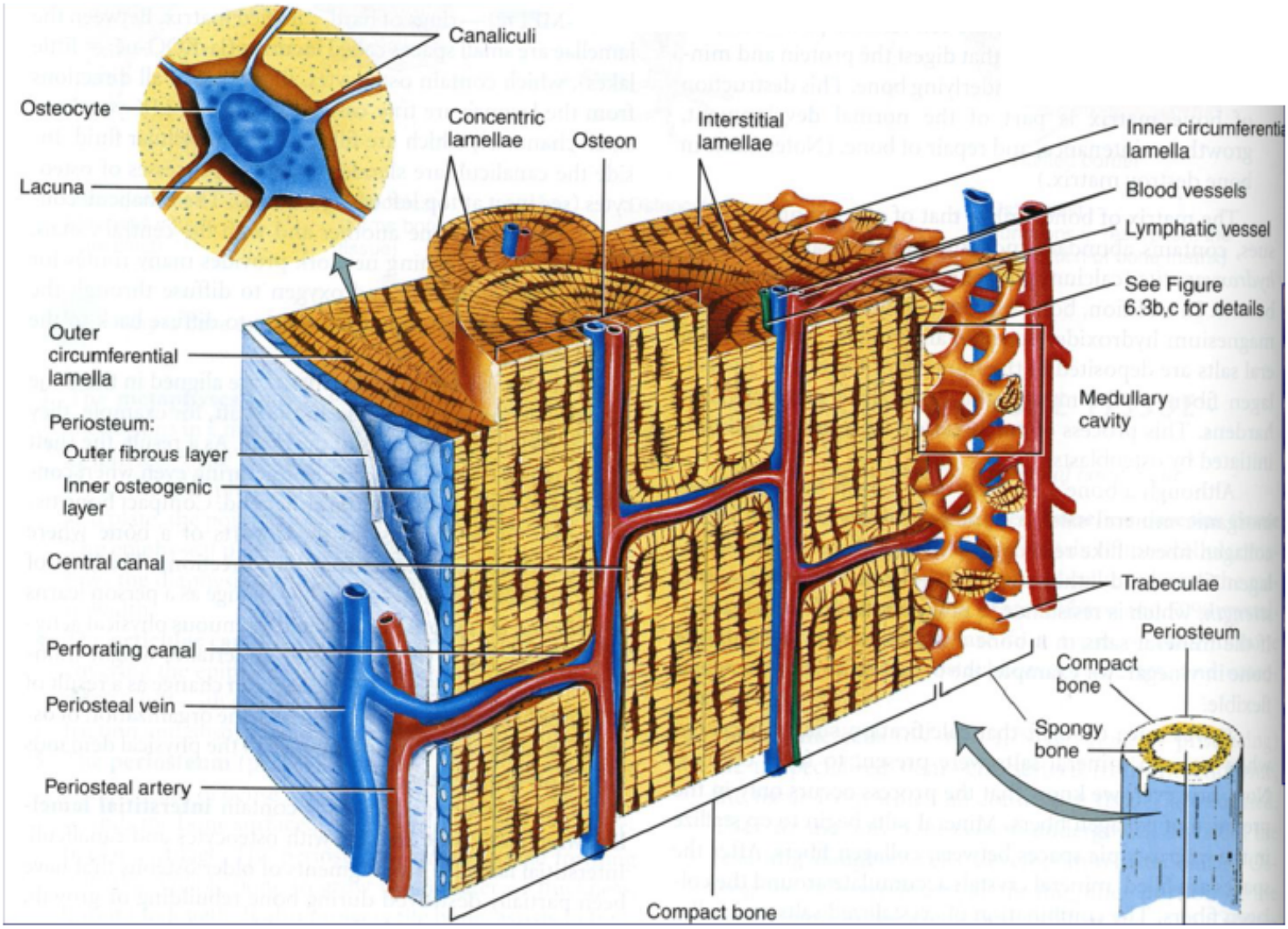




Osteocytes are derived from osteoblasts which are derived from osteoprogenitors (osteogenic cells)

Osteoclasts are derived from bone marrow stem cells which are fused →osteoclasts have many nucle




Canaliculi
Osteocyte
Lacuna
Concentric lamellae
Osteon
Interstitial lamellae
Inner circumferential lamella
Blood vessels
Lymphatic vessel
See Figure 6.3b,c for details
Outer circumferential lamella
Periosteum:
Outer fibrous layer
Inner osteogenic layer
Central canal
Perforating canal
Periosteal vein
Periosteal artery
Medullary cavity
Trabeculae
Periosteum
Compact bone
Spongy bone
Compact bone

Connective tissue (CT)

Cells & Extracellular matrix

Tissue = cells + ECM

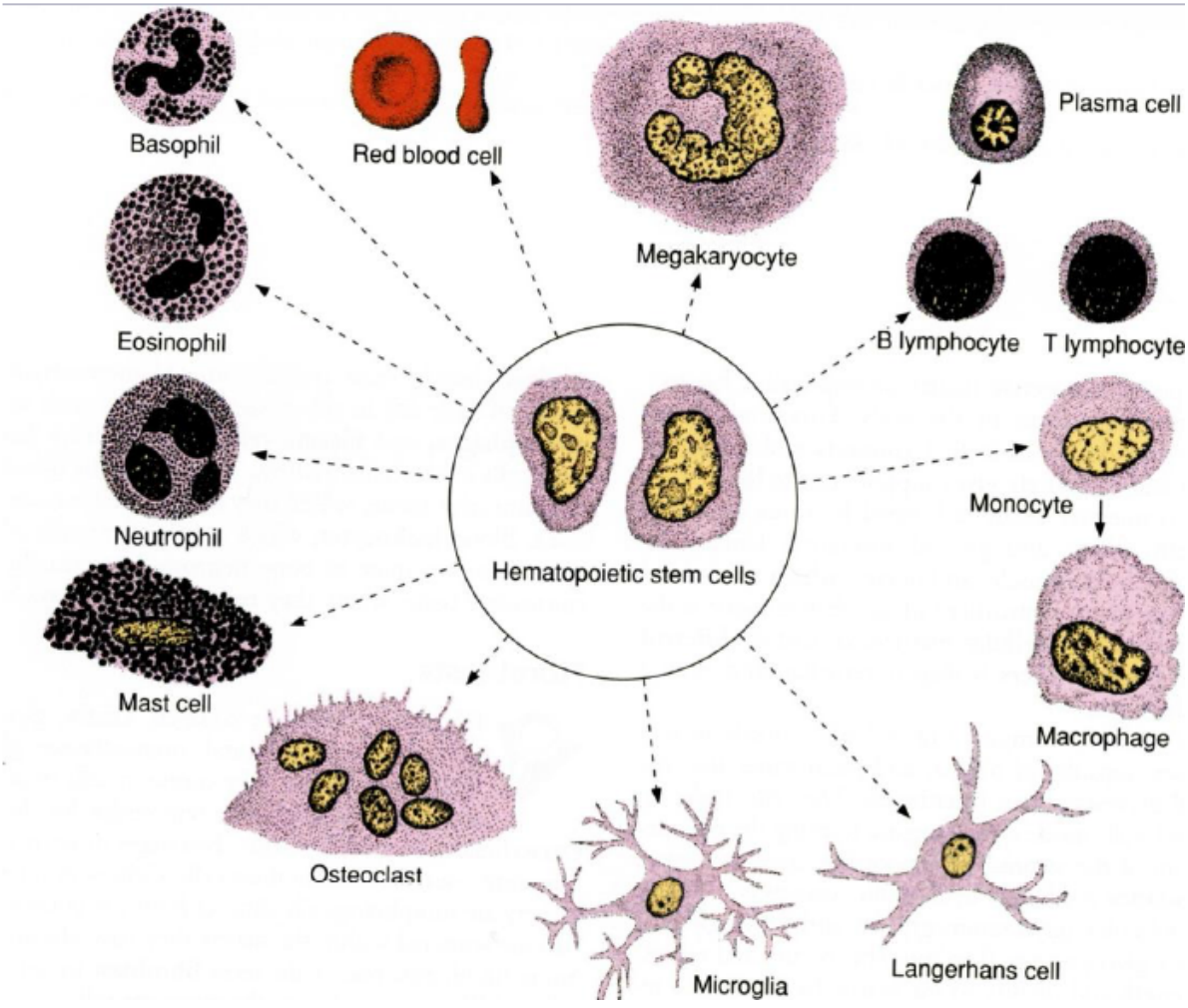
The tissues are formed by cells and molecules of the **extracellular matrix** (ECM) – an intricate network of proteins and polysaccharides that are secreted by the cell and assembled locally

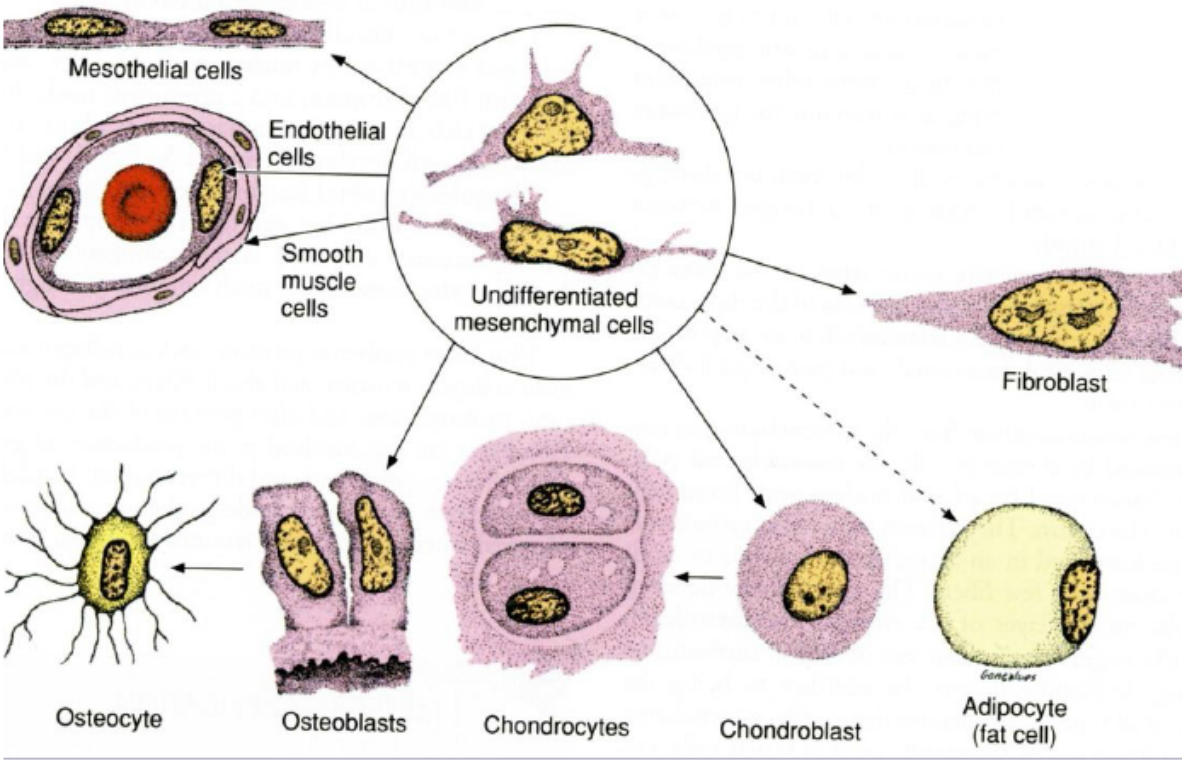
The organs are formed by combination of different tissues in variable proportions

Connective tissue forms a continuum with epithelial tissue, muscle, and nervous tissue as well as with other components of connective tissues to maintain a functionally integrated body

Origin

- CT develops from **mesenchyme** (multipotential cells of the embryo)
- Mesenchyme develops mostly from mesoderm
- In certain areas of the head and neck, mesenchyme also develops from *neural crest* cells of the developing embryo

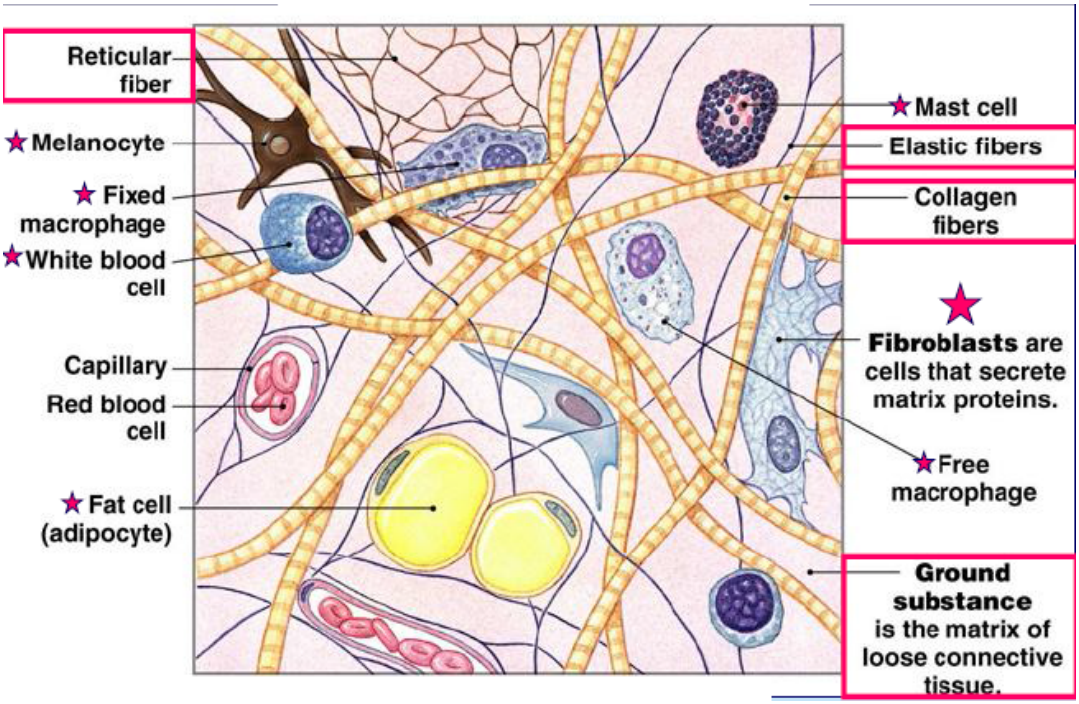




Functions of CT

- **Support and protection**
- **Forms a reservoir of factors controlling cell growth and differentiation**
- **Provides the medium through which nutrients and metabolic wastes are exchanged between cells and their blood supply**
- **Adipose tissue is the largest endocrine organ in the body**

Structural elements of CT



Cells of the CT

- **Permanent residents (fibroblasts, macrophages, mast cells, adipocytes, mesenchymal cells)**
- **Transient (wandering) cells – primarily migrating from blood (Neut, Eo, Ly, plasma cells)**
- **ECM - unlike the other tissue types (epithelium, muscle, and nerve), which consist mainly of cells, ECM is the major constituent of connective tissue**

Protein fibers - collagen, reticular, and elastic

Ground substance - anionic macromolecules and multiadhesive glycoproteins that stabilizes the ECM by binding to cells and to other ECM components

Fibroblasts

Features of fibroblasts

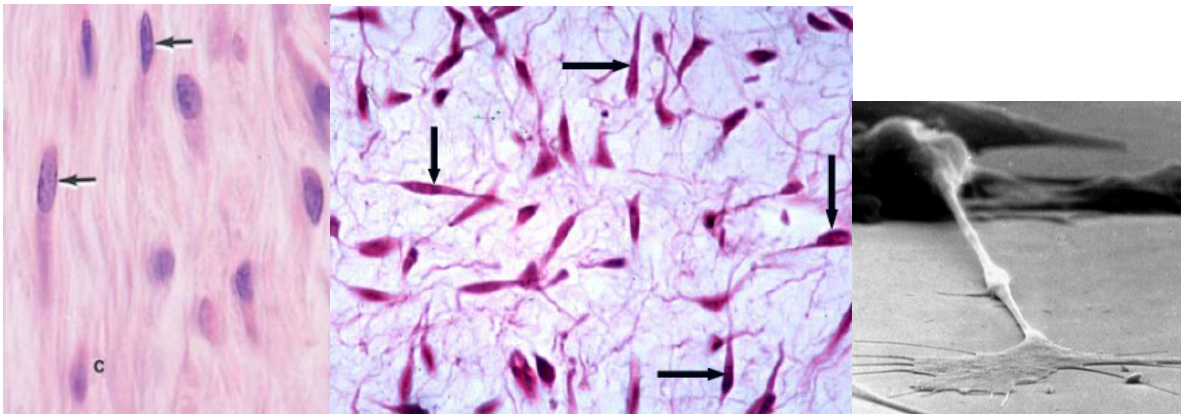
- **The most common CT cells**
- **Synthesize ECM components - collagen, elastin, glycosaminoglycans, proteoglycans and multiadhesive glycoproteins**
- **Cells with intense synthetic activity are called fibroblasts, distinct from the quiescent cells that are scattered and have already synthesized called fibrocytes**

LM features of fibroblasts

Large active nuclei and eosinophilic cytoplasm

Spindle-shaped nucleus

The nuclei (arrows) are clearly seen, but the cytoplasmic processes resemble the collagen bundles (C) that fill the extracellular matrix and are difficult to distinguish in H&E-stained sections

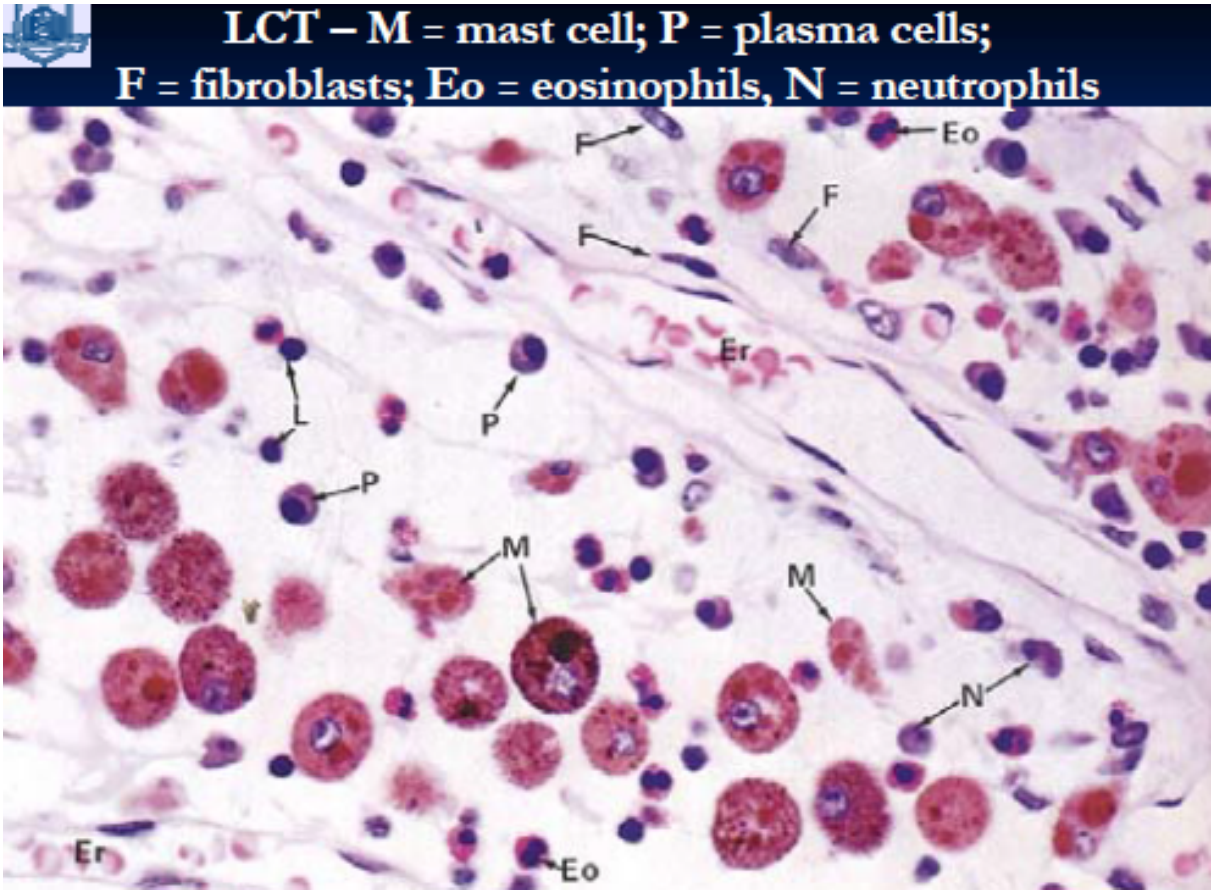


Myofibroblasts are modified fibroblasts that demonstrate characteristics similar to those of both fibroblasts and smooth muscle cells

Defense cells of the CT

Neutrophils, Plasma cells, Mast cells, and Macrophage

Cell Type	Location	Main Function
Monocyte	Blood	Precursor of macrophages
Macrophage	Connective tissue, lymphoid organs, lungs, bone marrow	Production of molecules that participate in inflammation
Kupffer cell	Liver	Same as macrophages
Microglia cell	Nerve tissue of the central nervous system	Same as macrophages
Langerhans cell	Skin	Antigen processing and presentation
Dendritic cell	Lymph nodes	Antigen processing and presentation
Osteoclast	Bone (fusion of several macrophages)	Digestion of bone
Multinuclear giant cell	Connective tissue (fusion of several macrophages)	Segregation and digestion of foreign bodies



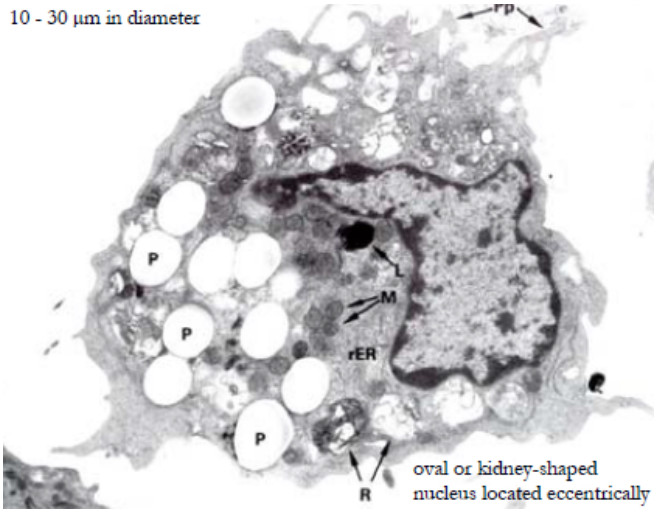
Macrophages

Derive from bone marrow precursor cells that divide, producing monocytes which circulate in the blood

Monocytes cross the wall of venules and capillaries to penetrate the connective tissue, where they mature and acquire the morphologic features of macrophages (increase in cell size, protein synthesis, number of Golgi complexes and lysosomes)

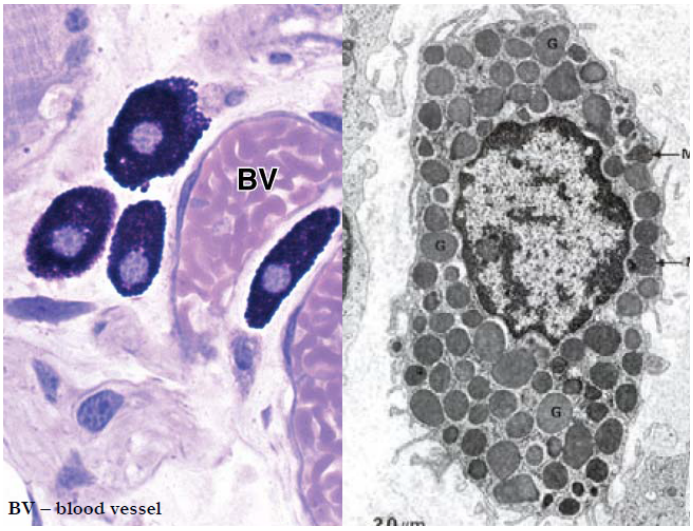
Along with other monocyte-derived cells, they comprise a family of cells called the mononuclearphagocyte system

Long-living cells - may survive for months in the tissues



Mast cells

- **Large, oval or round connective tissue cells, 20-30 mm in diameter**
- **Their cytoplasm is filled with basophilic secretory granules**
- **Heparin, a sulfated glycosaminoglycan that acts locally as an anticoagulant**
- **Histamine, which promotes increased vascular permeability and smooth muscle contraction**
- **Serine proteases, which activate various mediators of inflammation**
- **Eosinophil and neutrophil chemotactic factors which attract those leukocytes**
- **Leukotrienes C4, D4, and E4 (or the slow-reacting substance of anaphylaxis, SRS-A) which also trigger smooth muscle contraction**
- **Display metachromasia - can change the color of some basic dyes (e.g., toluidine blue) from blue to purple or red**



- **Originate from stem cells in the bone marrow (have a separate progenitor from other blood cells)**
- **Mast cells promote allergic reactions known as immediate hypersensitivity reactions - occur within a few minutes after penetration by an antigen of an individual previously sensitized to the same antigen**

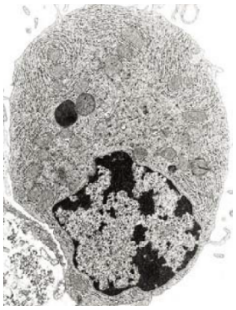
Pericytes

- **Surround endothelial cells of capillaries and small venules**
- **Have their own basal lamina – technically are outside the CT compartment**
- **Derived from mesenchymal cells**

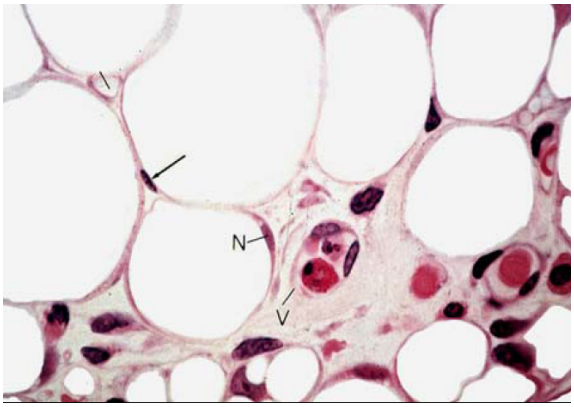
- **Possess characteristics of endothelial cells and smooth muscle cells – may function in contraction**

Plasma cells

- **Antibody-producing cells derived from B cells**
- **Large, ovoid cells that have a basophilic cytoplasm due to their richness in rough ER**
- **Nucleus - spherical but eccentrically placed**



Adipocytes

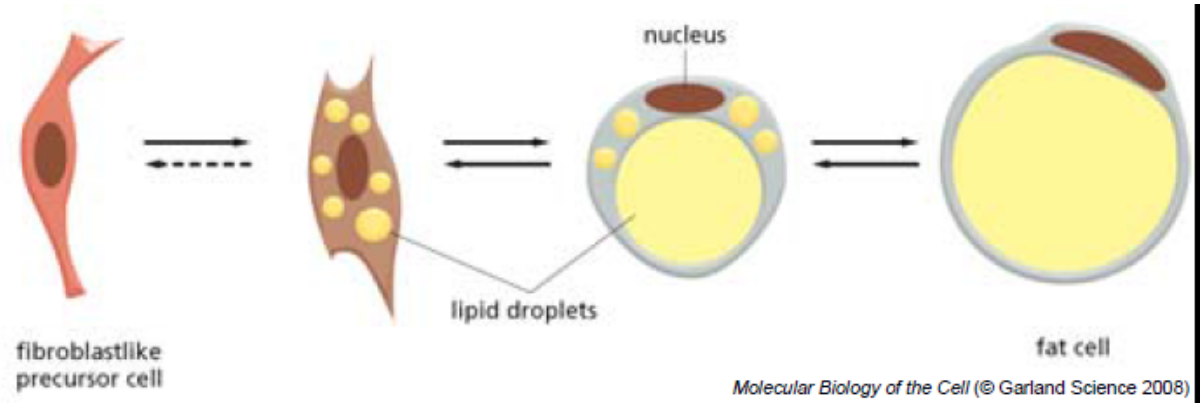


The development of a fat cell

A fibroblastlike precursor cell is converted into a mature fat cell by the accumulation and coalescence of lipid droplets

The process is at least partly reversible

The cells in the early and intermediate stages can divide, but the mature fat cell cannot



Mesenchymal cells

Undifferentiated cells, spindle-shaped

Extend processes which contact other cells – gap junctions

Extracellular matrix of CT

Protein fibers - proteins that polymerize into elongated structures

Collagen fibers

- **Made up of a family of proteins – collagens**
- **Collagen is the most abundant protein in the human body, representing 30% of its dry weight**
- **The collagens are produced by fibroblasts and several other cell types**
- **More than 20 types of collagen have been identified and designated with Roman numerals**

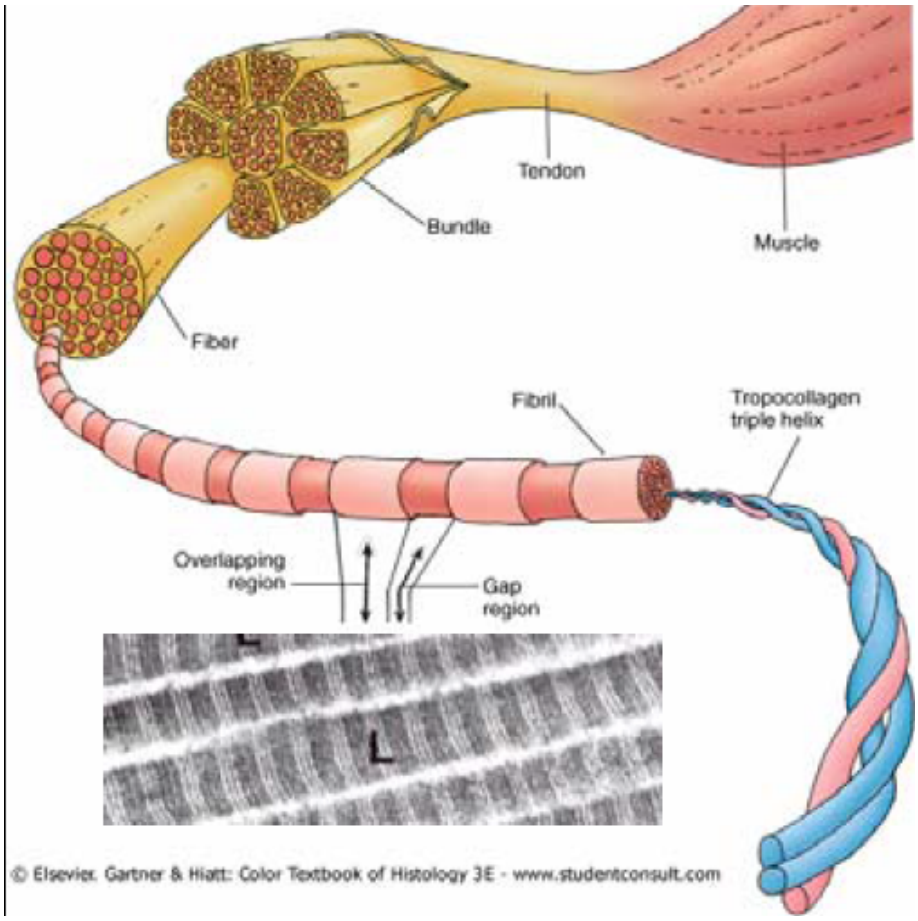
Collagen molecule structure

Fibrillary collagen molecule is triple-helix structure composed of three polypeptide chains (alpha-chains).

An alpha-chain consists of repeated triplet sequences (Gly-X-Y; X-commonly proline, Y-hydroxyproline) – totally ~1000 amino acids. A total 42 different collagen alpha-chains (42 different collagen genes are identified). However, less than 40 types of collagen molecules are known.

Collagen type I is the most abundant and widespread

Collagen type	Main location	Specific features
Type I	Bones, tendons, organ capsules, dentin	Most abundant, Typical collagen fibers (64 nm banding)
Type II	Hyaline cartilage Elastic cartilage	Very thin fibrils
Type III	Reticular fibers	Often associated with type I
Type IV	Basal lamina associated with epithelial and endothelial cells	Amorphous (non-fibrous)



Fibril-associated collagens

Mediate the interactions of collagen fibrils with one another and with other matrix macromolecules

Type IX molecules bind to type-ll-collagencontaining fibrils in cartilage & cornea

Type XII molecules bind to type-I-collagencontaining fibrils in tendons and various other tissues.

Network-forming collagens

Fibrillar structure is absent in type IV and type VII collagen because the propeptides are not removed from the procollagen molecule.

Its procollagen molecules assemble into dimers, which then form a meshwork

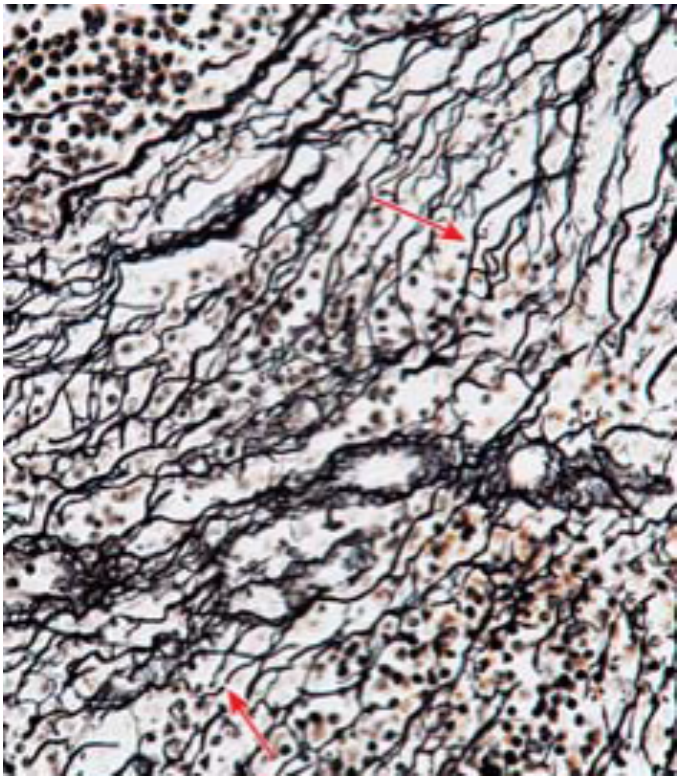
Reticular fibers

Consist mainly of collagen type III (in the past thought to be distinct from collagen)

Form networks of very thin and heavily glycosylated fibers in certain organs

Not visible in H&E preparations but can be stained black by impregnation with silver salts

Particularly abundant in hematopoietic organs (eg, spleen, lymph nodes, red bone marrow)



Elastic fibers

Thinner than collagen fibers

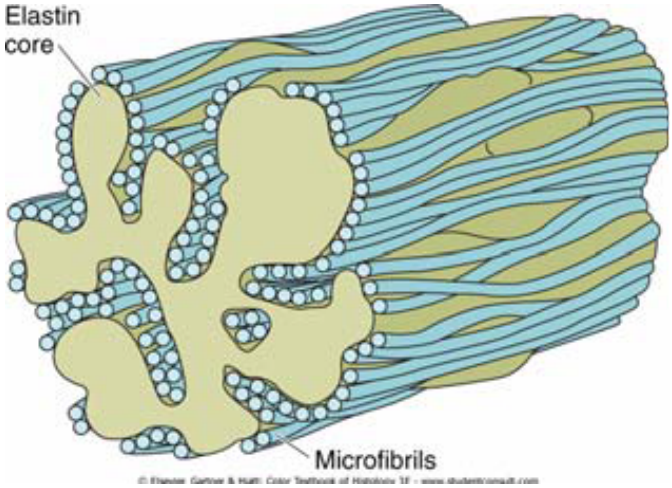
Form networks interspersed with collagen bundles in many organs subject to much bending or stretching (e.g. large arteries; 50% of the dry weight of the aorta)

Major components

Elastin – synthesized as proelastin (tropoelastin) molecules which assemble to form fibrils →fibers; elastin molecules are globular (molecular mass 70 kDa) and are secreted by fibroblasts in connective tissue and by smooth muscle cells in the walls of blood vessels

Microfibrils composed of fibrillin (350 kDa) and other glycoproteins

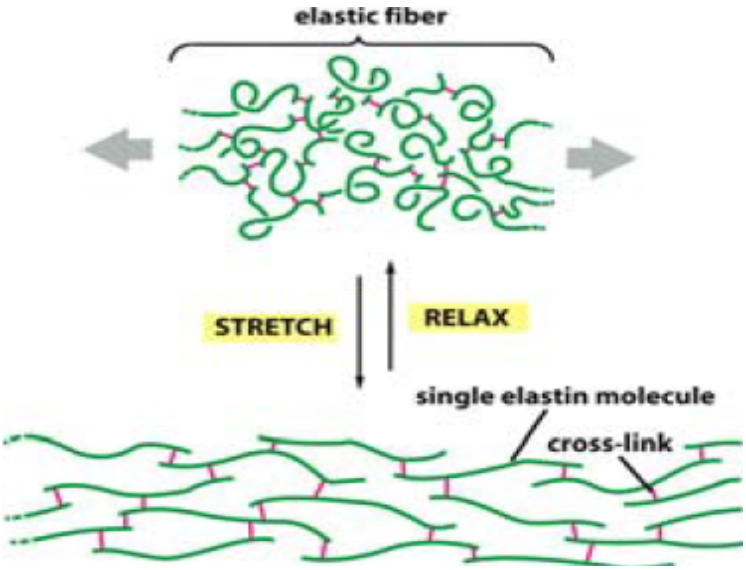
Elastic fibers – structure



The core of elastic fibers is composed of elastin and is surrounded by a sheath of microfibrils

During the formation of elastic fibers, the microfibrils are elaborated first, and the elastin is then deposited in the space surrounded by the microfibrils

Stretching a network of elastin molecules



Elastin chains are held together in such a fashion that four lysine molecules, each belonging to a different elastin chain, form covalent bonds with each other to form desmosine cross-links.

They are highly deformable and they impart a high degree of elasticity to elastic fibers - may be stretched to about 150% of their resting lengths before breaking

Ground substance

highly hydrophilic complex of anionic macromolecules

glycosaminoglycans

Proteoglycans – functions

- **Providing hydrated space in the matrix (swelling pressure)**
- **Act as co-receptors of growth factors (FGFs, TGF-beta)**
- **Inhibition of activity of growth factors (TGF-beta)**
- **Bind/regulate activity of matrix enzymes**
- **Involvement in collagen fiber formation (decorin)**

multiadhesive glycoproteins (laminin, fibronectin, and others) - stabilize the ECM by binding to receptor proteins (integrins) on the surface of cells

Muscle tissue

Skeletal muscle

The Musculoskeletal System Consists of Bones, Joints and Muscles

1) **Osteology** (Gr. osteon – bone)
   - The skeletal system is composed of bones, cartilages, and ligaments joined tightly to form a strong, flexible framework for the body.
   - Cartilage, the forerunner of most bones in embryonic and childhood development, covers many joint surfaces in the mature skeleton.
   - Ligaments hold bones together at the joints.

2) **Arthrology** (Gr. arthron – joint)
   - Arthrology is the science concerned with the anatomy, function, dysfunction, and treatment of joints.
   - In order for the skeleton to serve the purposes of protection and movement, the bones must be joined together.
   - A joint, or articulation, is any point at which two bones meet, regardless of whether they are movable at that point

3) **Myology** (Gr. myos – muscle)
   - The muscular system consists of about 600 skeletal muscles - striated muscles that are usually attached to bones.
   - The term does not include smooth or cardiac muscle. Myology, the study of muscles, it relates muscle attachments to the bone structures and muscle function to the joint movements.

Osteology

Functions of the Skeletal System

Support:
- Bones of the legs, pelvis, and vertebral column hold up the body; nearly all bones provide support for musclesor many other soft organs.

Protection:
- Bones enclose and protect the brain, spinal cord, lungs, heart, pelvic viscera, and bone marrow.

Movement:
- Skeletal muscles would serve little purpose if not for the rigid attachment and leverage provided by bones. Leg and arm movements are the most obvious examples of skeletomuscular movement.

Blood formation:
- Red bone marrow is the major producer of blood cells, including most cells of the immune system.

Electrolyte/Metabolic balance:
- The skeleton is the body's main mineral reservoir. It stores calcium and phosphate releasing them according to the body's physiological needs.

Acid-base balance:

- Bone buffers the blood against excessive pH changes by absorbing or releasing alkaline salts.

Detoxification:

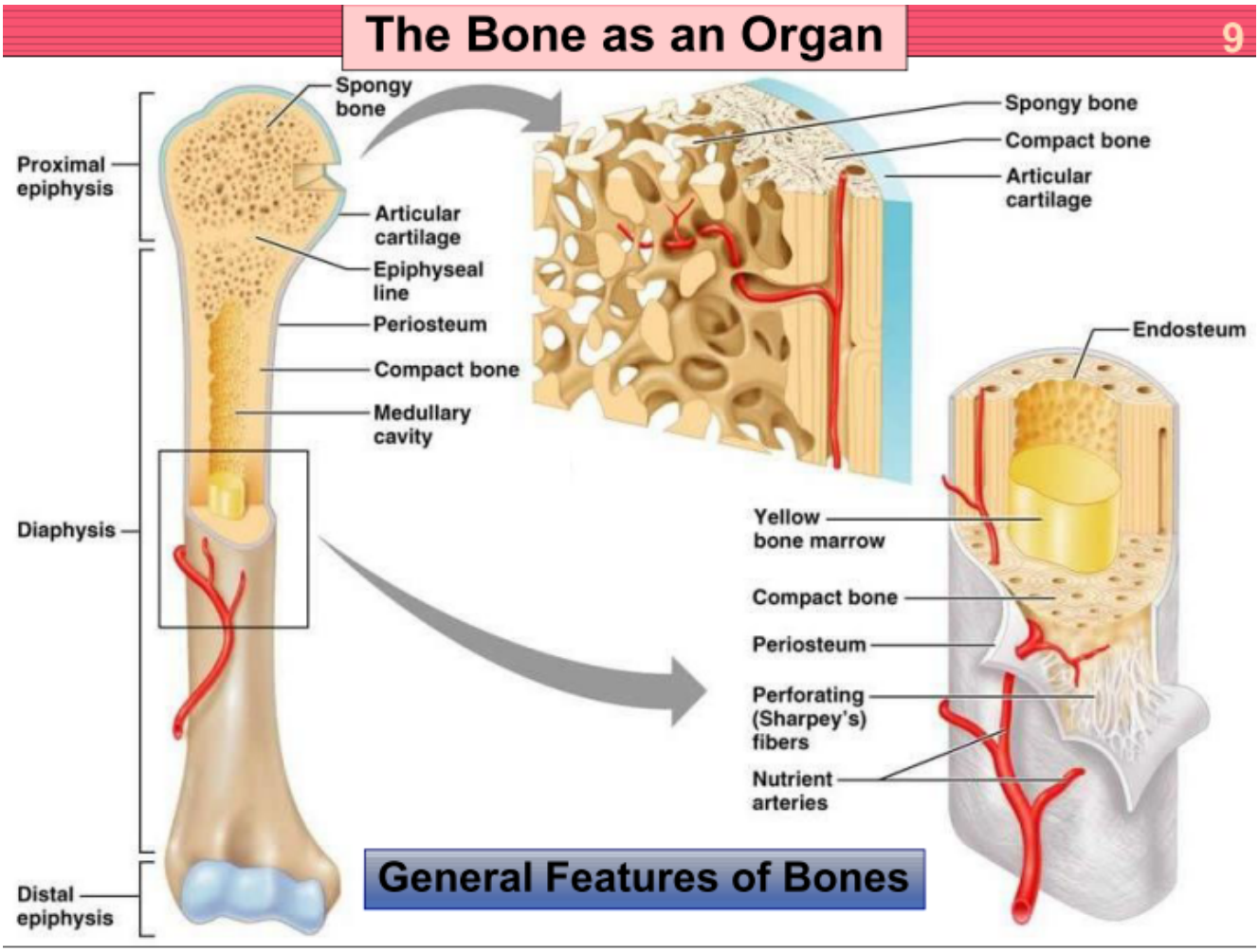
- Bone tissue removes heavy metals and other foreign elements from the blood and thus reduces their effects on nervous and other tissues.

Transferring:

- … of acoustic energyin the middle ear

Bones and Osseous Tissue

- The word bone can denote an organ or it can denote just the osseous tissue.
- Osseous tissue is only one of the tissues that make up a bone. Also present are blood, bone marrow, cartilage, adipose tissue, nervous tissue, and fibrous connective tissue.
- Bone, or osseous tissue, is a connective tissue in which the matrix is hardened by the deposition of calcium phosphateand otherminerals.
- The hardening process is called mineralization or calcification. Bone is not the hardest substance in the body; that distinction goes to tooth enamel.
- Blood vessels penetrate into the bone through minute holes called nutrient foramina.

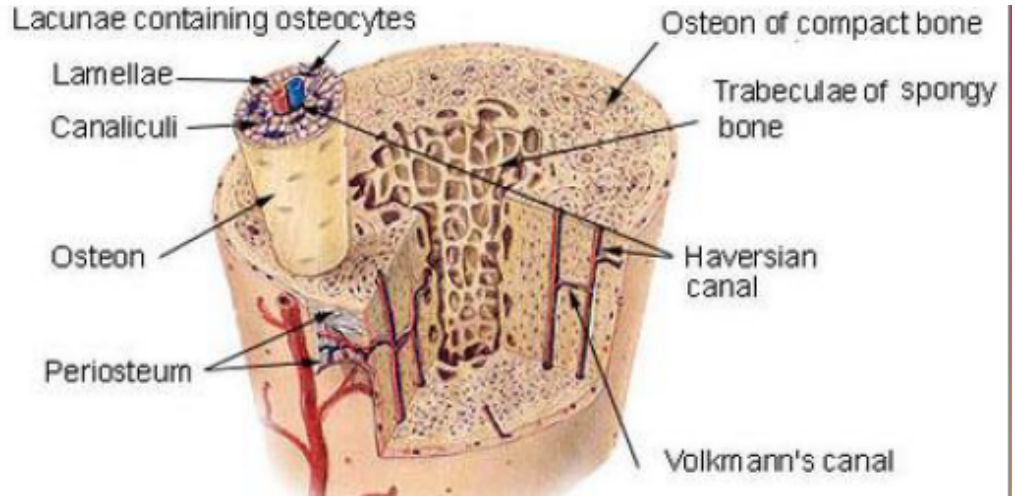


Bone substance

- Substantia compacta – compact bone
- Substantia spongiosa – spongy bone

Bone Structure

- The skeleton is composed of ¾ compact bone and ¼ spongy bone by weight.
- In this frontal section of the femur (thighbone), the trabeculae of spongy bone can be seen oriented along lines of mechanical stress applied by the weight of the body.
- Spongy bone is well designed to impart strength to a bone while adding a minimum of weight.
- Its trabeculae are not randomly arranged as they might seem at a glance, but develop along the bone's lines of stress.
-



Trabecular or Cancellous Bone

- This kind of bone represents only 20% of the skeletal mass
- But: 80% of the bone surface.
- Trabecular bone is less dense, more elastic and has a higher turnover rate than cortical bone.
- Trabecular bone is found in the epipheseal and metaphysal regions of long bones and throughout the interior of short bones.
- Trabecular bone constitutes most of the bone tissue of the axial skeleton: bones of the skull, ribs and spine.
- Trabecular bone is rigid but appears spongy.
- The center of the bone contains red, yellow marrow, bone cells and other tissues.

Compact bone

- Cortical bone represents nearly 80% of the skeletal mass.
- It is also called compact bone, because it forms a protective outer shell around every bone in the body.
- Cortical bone has a slow turnover rate and a high resistance to bending and torsion.
- It provides strength where bending would be undesirable as in the middle of long bones.
- Compact bone shows onionlike concentric lamellae - layers of matrix concentrically arranged around a central (haversian) canal and connected with each other by canaliculi. A central canal and its lamellae constitute an osteon (haversian system) -the basic structural unit of compact bone.
- Not all of the matrix is organized into osteons. The inner and outer boundaries of dense bone are arranged in circumferential lamellae that run parallel to the bone surface. Between osteons, there are irregular regions called interstitial lamellae.
- Blood vessels, along with nerves, enter the bone tissue through nutrient foramina on the surface. These open into narrow perforating (Volkmann) canals that cross the matrix and feed into the central canals.
- The innermost osteocytes around each central canal receive nutrients from these blood vessels and pass them along through their gap junctions to neighboring osteocytes. Thus, the cytoplasmic processes of the osteocytes maintain a two-way flow of nutrients and wastes between the central canal and the outermost cells of the osteon.

The Bone as an Organ

- ➔ A long bone is composed of a cylinder of dense white osseous tissue; this is called compact (dense) bone.
- ➔ The cylinder encloses a space called the medullary cavity, which contains bone marrow.
- ➔ At the ends of the bone, the central space is occupied by a more loosely organized form of osseous tissue called spongy (cancellous) bone.
- ➔ The joint surface where one bone meets another is covered with a layer of hyaline cartilage called the articular cartilage.
- ➔ Externally, a bone is covered with a sheath called periosteum that provides strong attachment and continuity from muscle tendon to bone.
- ➔ This has a tough, outer fibrous layer of collagen and an inner osteogenic layer of bone-forming cells. Some collagen fibers of the outer layer are continuous with the tendons that bind muscle to bone, and some penetrate into the bone matrix as perforating (Sharpey) fibers.
- ➔ The osteogenic layer is important to the growth of bone and healing of fractures.
- ➔ There is no periosteum over the articular cartilage.
- ➔ The internal surface of a bone is lined with endosteum, a thin layer of reticular connective tissue and osteogenic cells that give rise to other types of bone cells.

Bones: classified into four groups according to their shapes and corresponding functions:

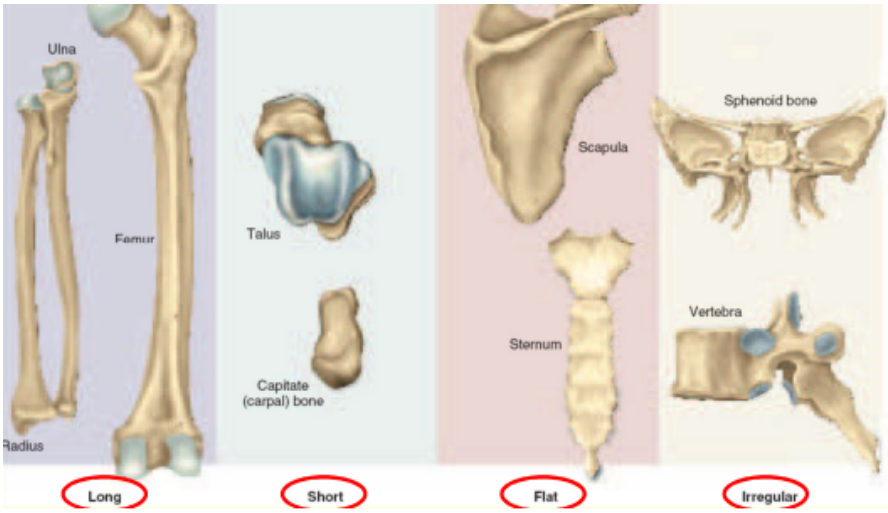
1) **Long bones**

- are conspicuously longer than wide.
- Long bones include the humerus of the arm, the radius and ulna of the forearm, the metacarpals and phalanges of the hand, the femur of the thigh, the tibia and fibula of the leg, and the metatarsals and phalanges of the feet.

2) **Short bones**
   - are more nearly equal in length and width. They include the carpal (wrist) and tarsal (ankle) bones. They have limited motion and merely glide across one another, enabling the ankles and wrists to bend in multiple directions.

3) **Flat bones**
   - enclose and protect soft organs and provide broad surfaces for muscle attachment. They include most cranial bones and the ribs, sternum (breastbone), scapula (shoulder blade), and os coxae (hipbone).

4) **Irregular bones**
   - have elaborate shapes that do not fit into any of the preceding categories. They include the vertebrae and some of the skull bones, such as the sphenoid and ethmoid.



Internal Structure of Bone

1) **Long bones:**

- The principal features of a long bone are ist shaft, called the diaphysis, and an expanded head at each end called the epiphysis.
- The diaphysis provides leverage, while the epiphysis is enlarged to strengthen the joint and provide added surface area for the attachment of tendons and ligaments.

2) Short bones:
- Short bones are more nearly equal in length and width.
- They include the carpal (wrist) and tarsal (ankle) bones.

3) Flat bones:
- In flat bones of the skull, two layers of compact bone enclose a middle layer of spongy bone like a sandwich.
- The spongy layer is called the diploe.
- Flat bones contain varying amounts of bone marrow.

4) Irregular bones
- Irregular bones have elaborate shapes that do not fit into any of the preceding categories.
- They include the vertebrae and some of the skull bones, such as the sphenoid and ethmoid.

Bones of the Skeletal System

- The skeleton is divided into two regions: the axial skeleton, which forms the central supporting axis, and the appendicular skeleton, which includes the limbs (appendages or extremities) and the bones that attach them to the axial skeleton.
- The axial skeleton includes the skull, auditory ossicles, hyoid bone, vertebral column, and thoracic cage - ribs and sternum.
- The appendicular skeleton includes the bones of the upper limb andpectoral girdle and the bones of the lower limb and pelvic girdle.
- It is often stated that there are 206 bones in the skeleton, but this is only a typical adult count.
- At birth there are about 270, and even more bones form during childhood.
- With age, however, the number decreases as separate bones fuse.
  →For example, each half of the adult pelvis is a single bone called the os coxae, which results from the fusion of three childhood bones - the ilium, ischium, and pubis. This number varies even among adults.
- One reason is the development of sesamoid bones - bones that form within some tendons in response to stress.
- The patella (kneecap) is the largest of these; most of the others are small, rounded bones in such locations as the knuckles.
- Another reason for adult variation is that some people have extra bones in the skull called sutural, or wormian, bones.

Muscle

Special type of cells, which are specialized for contraction, that permits animals to move. Organisms harness the contraction of muscle cells and the arrangement of the extracellular components of muscle to permit locomotion, constriction, pumping, and other propulsive movements.

General functions of muscle tissue

Movement (obvious – whole body walking, or grabbing; less obvious - heart, stomach, intestines, urinary bladder)

Maintenance of posture

Joint stabilization

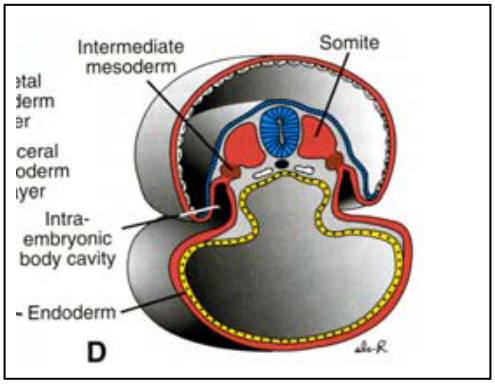
Heat generation (85% of all body heat is generated by muscles)

Special functional characteristics of muscle

Excitability	Chemical signal →electrical changes
Conductivity	Stimulation of a muscle fiber triggers a wave of excitation that travels rapidly along the muscle fiber
Contractility	Only one action: to shorten
	Shortening generates pulling force
Elasticity	Recoils passively after being stretched
Extensibility	Stretch with contraction of an opposing muscle

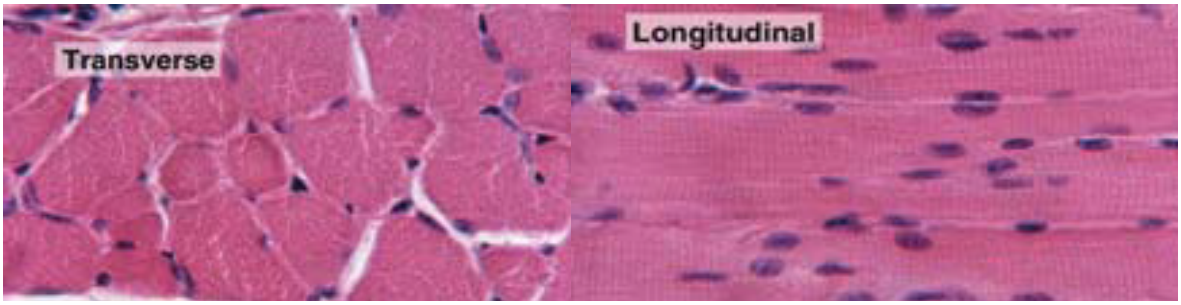
Muscle tissue types

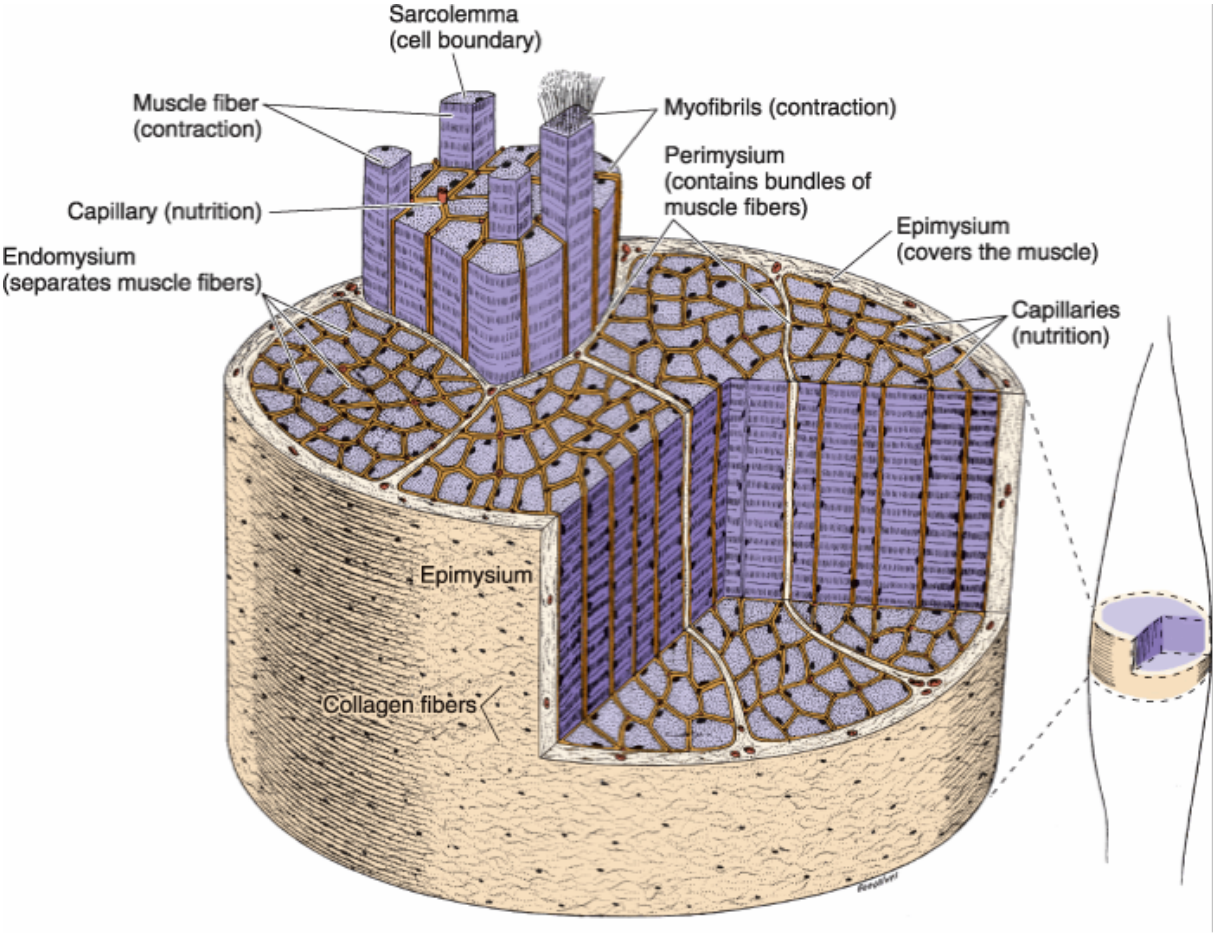
Skeletal muscle

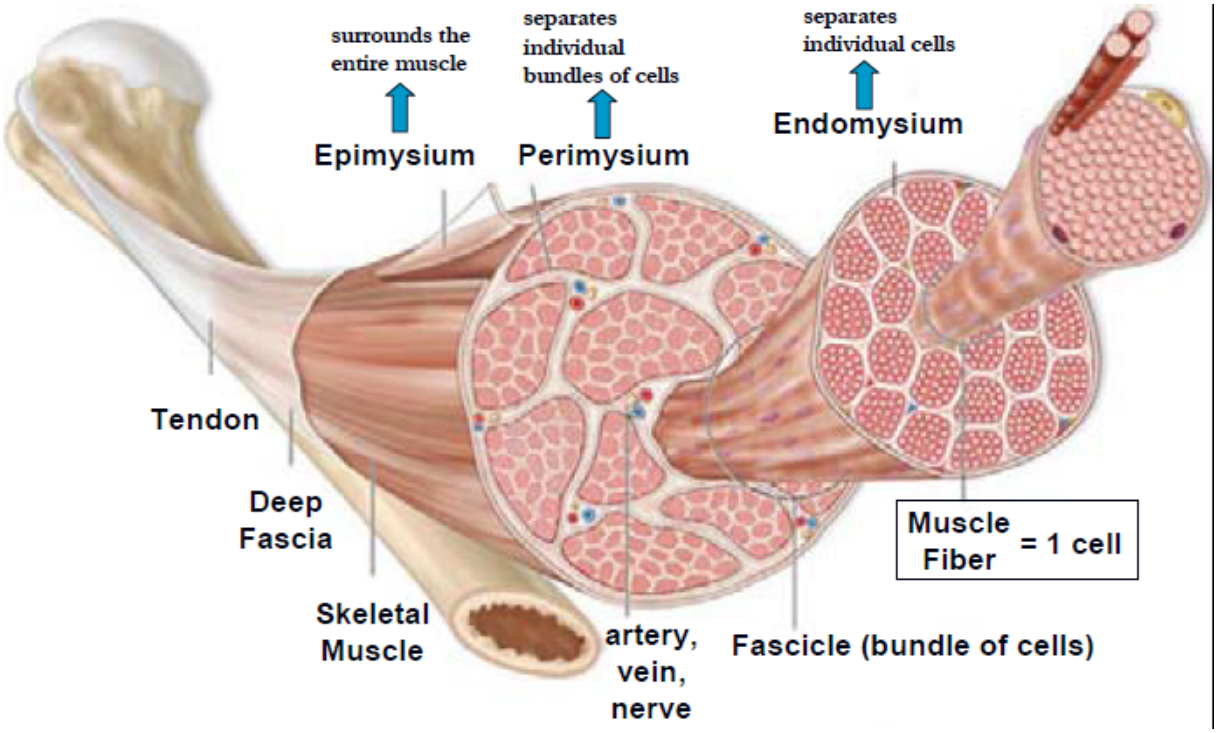


Attach to and move skeleton
40% of body weight
Cells with obvious striations
Contractions are voluntary
Many nuclei
Peripheral nucleus
Skeletal muscle develops embryologically from somatic mesodermal tissue

Somites (segmental paired blocks of mesoderm) are completely formed by day 30
Mesodermal somites separate into the dermatomes and segmental myotomes
At the end of the 8th week, the primordia of individual muscles can be appreciated




Sarcolemma
(cell boundary)
Muscle fiber
(contraction)
Myofibrils (contraction)
Perimysium
(contains bundles of
muscle fibers)
Capillary (nutrition)
Epimysium
(covers the muscle)
Endomysium
(separates muscle fibers)
Capillaries
(nutrition)
Epimysium
Collagen fibers


surrounds the
entire muscle
separates
individual
bundles of cells
separates
individual cells
Epimysium
Perimysium
Endomysium
Tendon
Deep
Fascia
Skeletal
Muscle
artery,
vein,
nerve
Fascicle (bundle of cells)
Muscle
Fiber
= 1 cell

The cellular units of skeletal muscle are the muscle fibers/fibres

Consistent in size within a given muscle, but different in different muscles
Diameter - 10 to 100 µm
Length – up to 30 cm

Fibers →multinucleate cells (embryonic cells fuse)

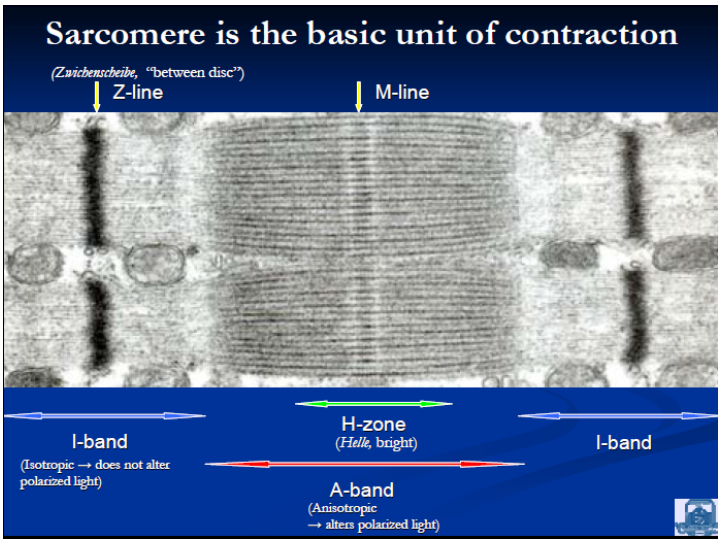
The contractile proteins are organized into cylindrical myofibrils

Transverse striations →alignment across the fibre of repeating elements - the sarcomeres

Fibers (each is one cell) have striations
Myofibrils are made up of **myofilaments**

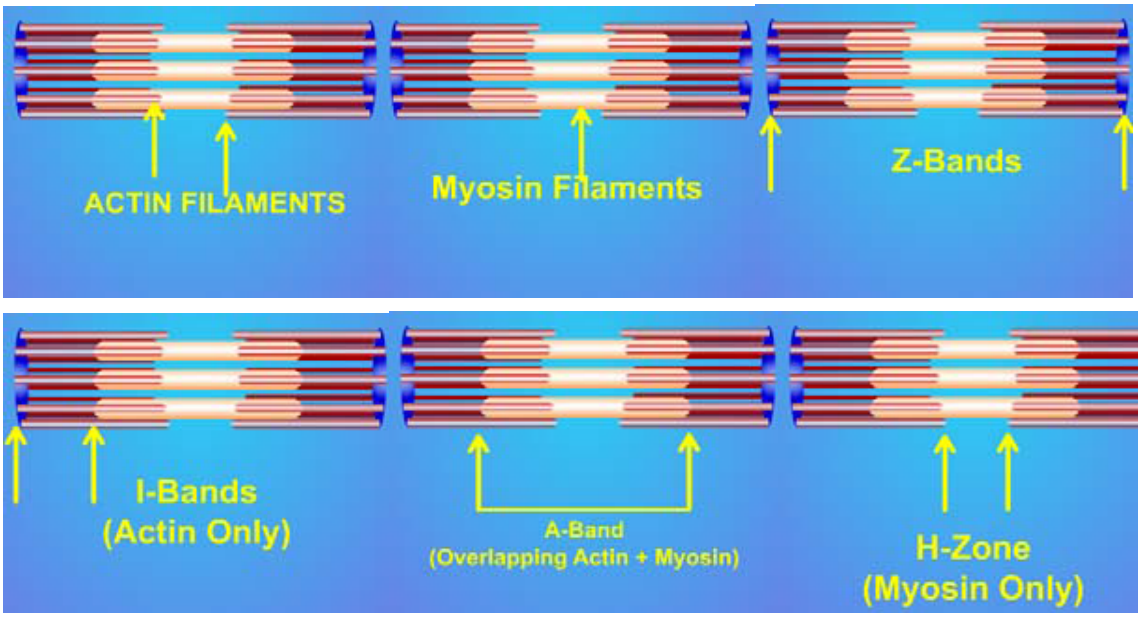
Sarcomere

Basic unit of contraction
Myofibrils are long rows of repeating sarcomeres
Boundaries: **Z discs** (or lines)

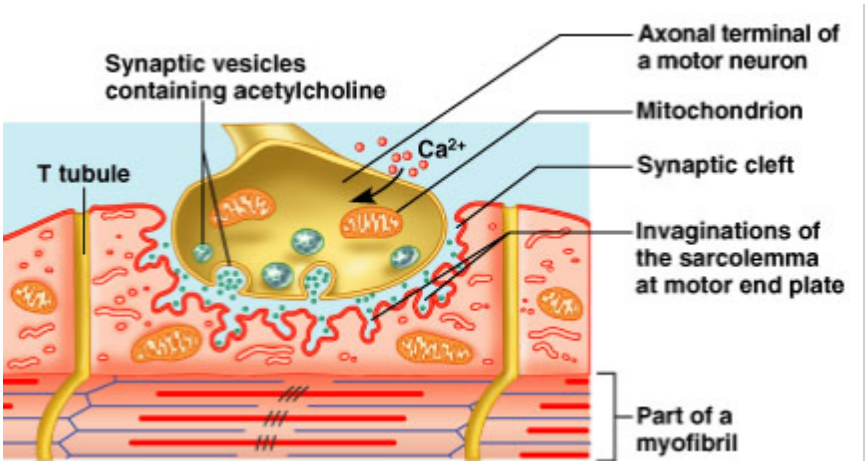


Myofilaments

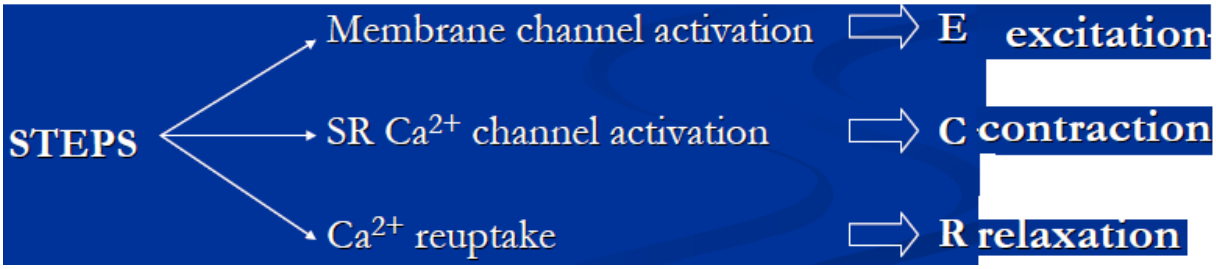
- **Made of three types of filaments (ormyofilaments):**
  - Thick (myosin) - 1.6 mm long and 15 nm wide
  - Thin (actin) - 1 mm long and 8 nm wide
  - Elastic (titin) →1 nm wide; resists overstretching; emerges from the core of a thick filament and links it to a Z disc



Acetylcholine initiates skeletal muscle contraction



Lateral propagation of the action potential down the T-tubule



Dystrophin
The cloning of the *dystrophin* gene and the characterization of its protein product, dystrophin (1987), significantly contributed to both clinical and basic research into the muscular dystrophies (MD), such as Duchenne (DMD) and Becker (BMD).

The dystrophin–glycoprotein complex (DGC) is a multisubunit complex that connects the cytoskeleton of a muscle fiber to its surrounding extracellular matrix.

Other similarities between muscle tissues

- Their cells are called *fibers* because they are elongated
- Contraction depends on *myofilaments*
- Actin
- Myosin
- Other proteins
- Plasma membrane is called *sarcolemma*

- Some muscle cell organelles have specific names

- Sarcoplasm(Gr. *sarkos,* flesh, + plasma, thing formed)→cytoplasm (excluding the myofibrils)

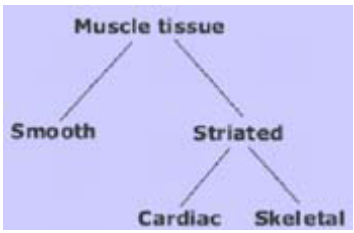
- Sarcoplasmic reticulum →smooth endoplasmic reticulum

- Sarcolemma (*sarkos* + Gr. *lemma,* husk) →cell membrane, plasmalemma

Muscle tissue

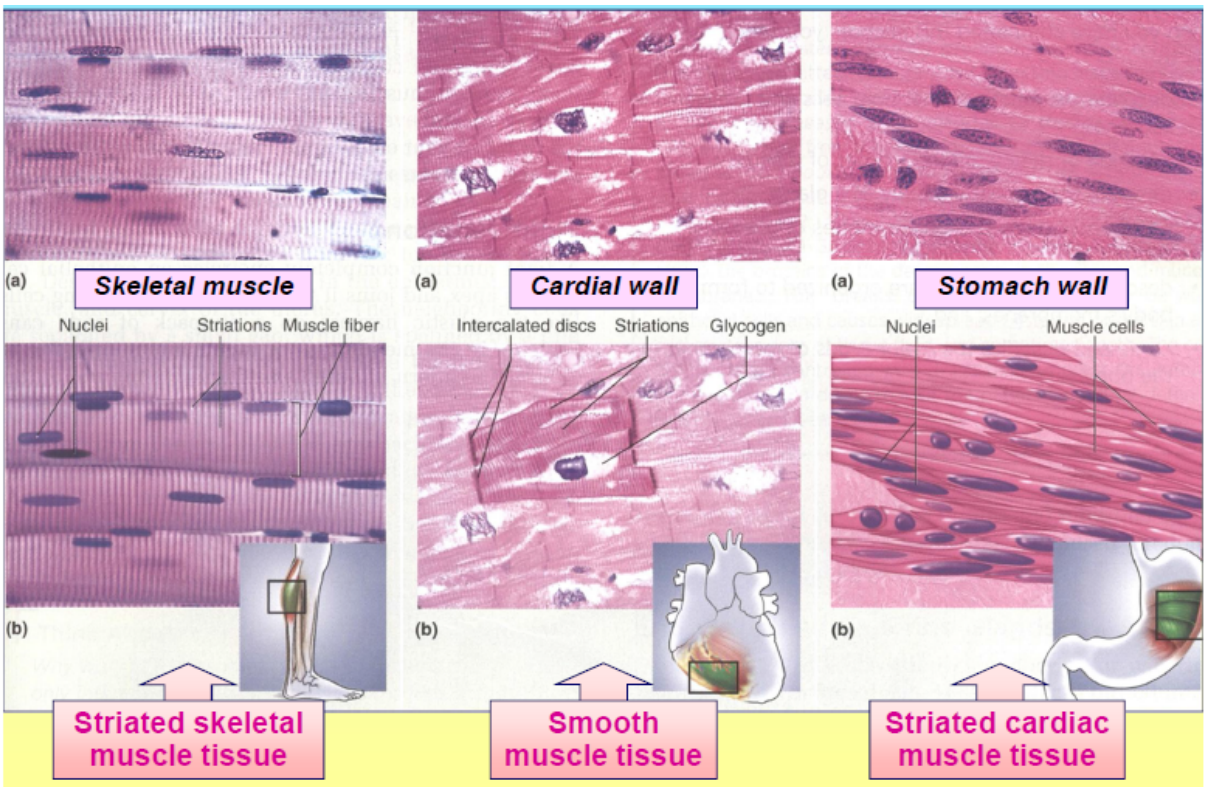
Smooth muscle

Smooth muscle is composed of myocytes (fibers) with a fusiform shape, which lack visible striations (i.e. smooth)



Major locations of smooth muscle

- Walls of vessels
- Respiratory tubes
- Digestive tubes
- Urinary organs
- Reproductive organs
- Larger ducts of compound glands
- Inside the eye
- Dermis of skin (small bundles)

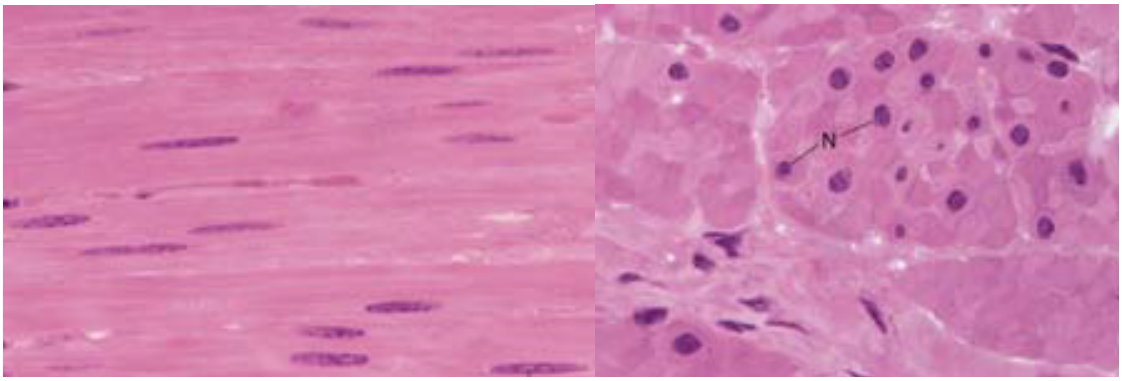


Smooth muscle cells – leiomyocytes

- **Size**: less than 10 µm in diameter, 100-200 µm in length (uterine smooth muscle cells undergo a marked increase in size and number during pregnancy)
- Possess only **1 centrally located nucleus**
- Surrounded by a delicate sheath of **endomysium**
- **Do not possess a system of T tubules** → have numerous plasma membrane invaginations resembling caveolae
- Grouped into sheets: often running perpendicular to each other
- **Contractions are slow, sustained and resistant to fatigue**
- Does not always require a nervous signal: can be stimulated by stretching or hormones

Smooth muscle – basic histological features

Longitudinal-Section Cross-Section



1 nucleus

Centrally positioned nucleus

No sarcomere → no striations → smooth (unstriated) appearance

Eosinophilic cytoplasm & minimal endomysium

Sarcoplasmic reticulum – not well developed

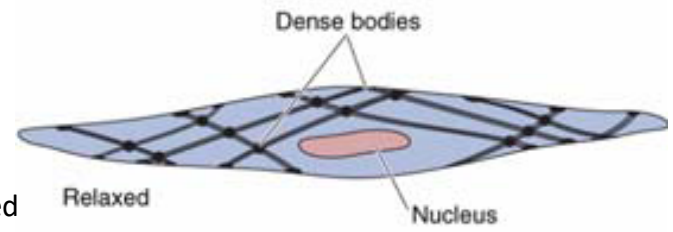
No intercalated disks, but many gap junctions

Instead of Z-disks SM cells have dense bodies

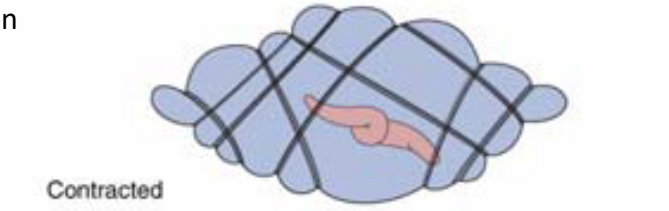
Thin filaments →**actin**, caldesmon (blocks the active site of F-actin), and tropomyosin, but no troponin

Thick filaments →**myosin II** (same as in skeletal muscle)

Intermediate filaments (vimentin and desmin)



Dense bodies are small, dark-staining areas → associated with the thin and intermediate filaments →serve as anchors for thin filaments and to transmit the force of contraction to adjacent cells

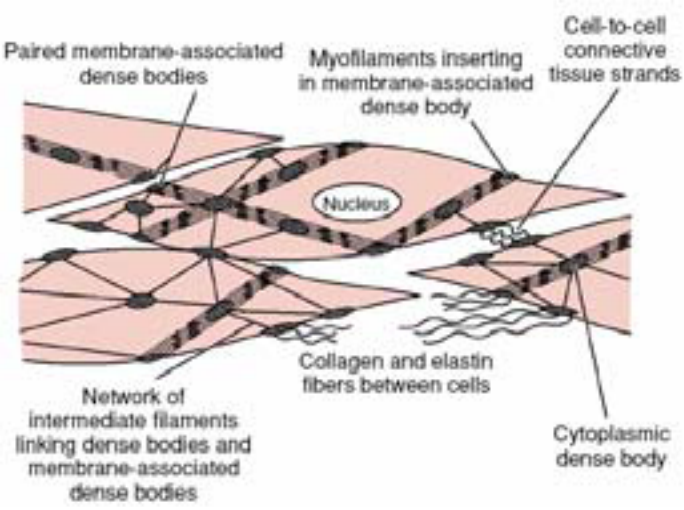


Force transmission from cell to cell

Membrane-associated dense bodies are opposite one another in adjacent cells and may provide continuity of force transmission between the contractile apparatus in each cell

Short strands of connective tissue link adjacent cells

Cells are joined to the collagen and elastin fibers running throughout the tissue



Types of smooth muscle

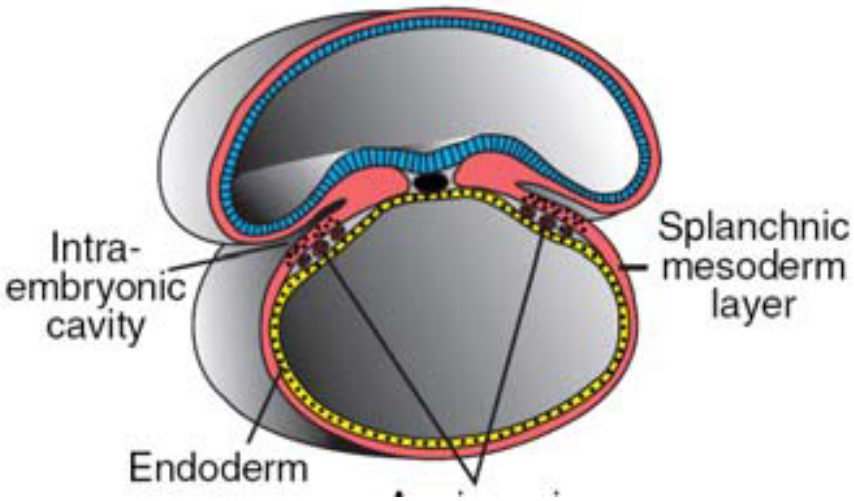
- **Multi-unit** smooth muscle
  - each muscle cell receives its own nerve supply
  - little cell-to-cell communication
  - locations: iris of the eye, vas deferens

Single-unit smooth muscle →functional syncytium via gap junctions

- nerve fibers pass through the tissue without synapsing with any specific muscle cell→axons have many (up to 20,000) beadlike swellings called **varicosities** along its length →the nerve fiber passes amid several myocytes and stimulates all of them

- ➢ muscle cells do not have motor end plates or any other specialized area of sarcolemma to bind the neurotransmitter → diffusely distributed receptor
- ➢ visceral organs

Development of smooth muscle



- ➢ Smooth muscle in the wall of the gut and gut derivatives is derived from **splanchnic mesoderm** surrounding the endoderm of these structures
- ➢ Vascular smooth muscle differentiates from **mesoderm** adjacent to vascular endothelium
- ➢ Sphincter and dilator muscles of the pupil and muscle tissue in the mammary gland and sweat glands originate from **ectoderm**

Smooth muscle cell regeneration

Preexisting smooth muscle cells retain mitotic capability to form more smooth muscle cells → pregnant uterus

Differentiation of relatively undifferentiated pericytes accompanying some blood vessels

Dispersed cells with contractile function

Myofibroblasts
Myoepithelial cells
Myoid cells (testis)
Cells of perineurium

Originate from ectoderm

Myofibroblasts

- ➢ Fibroblasts with contractile functions
  - retain ECM (e.g. collagen) production
  - express contractile proteins
- ➢ Location
  - alveolar septa (lung)
  - crypts of Lieberkühn (intestine)
  - healing wounds

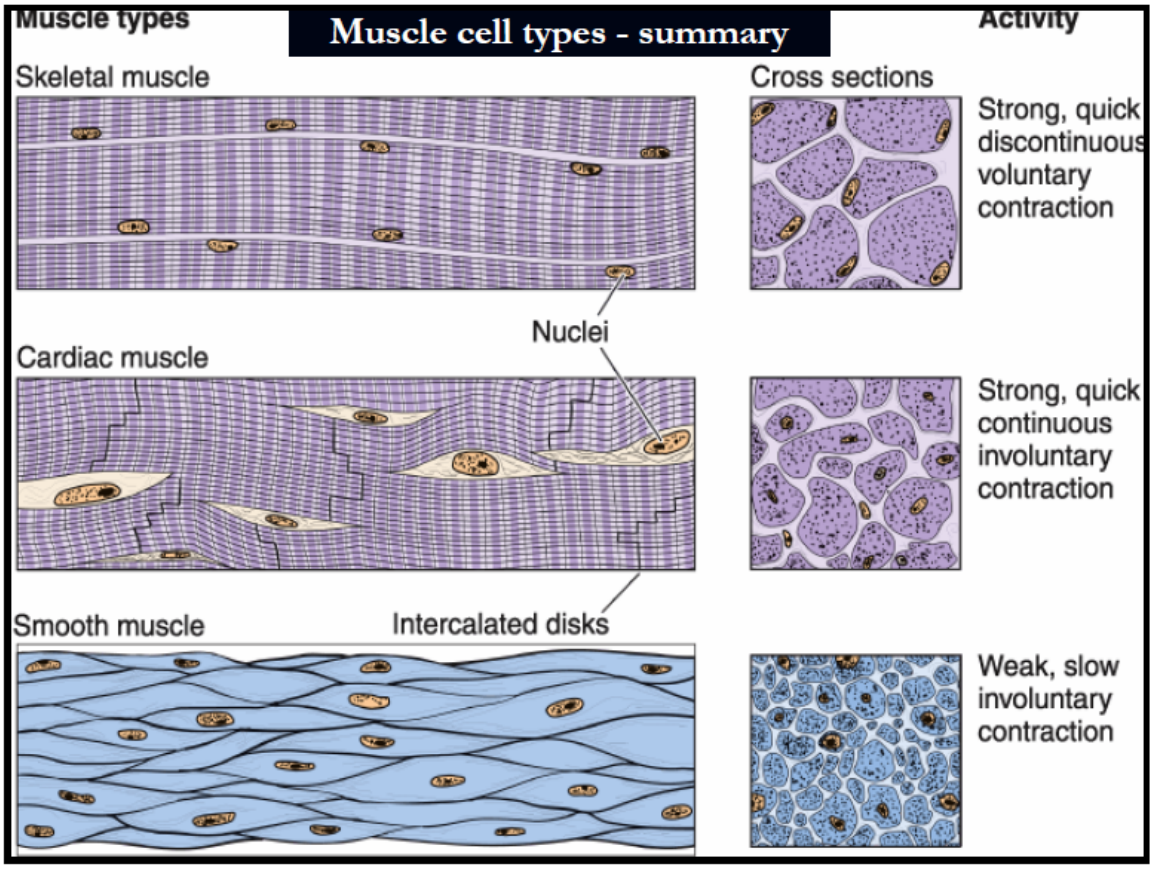
Myoepithelial cells

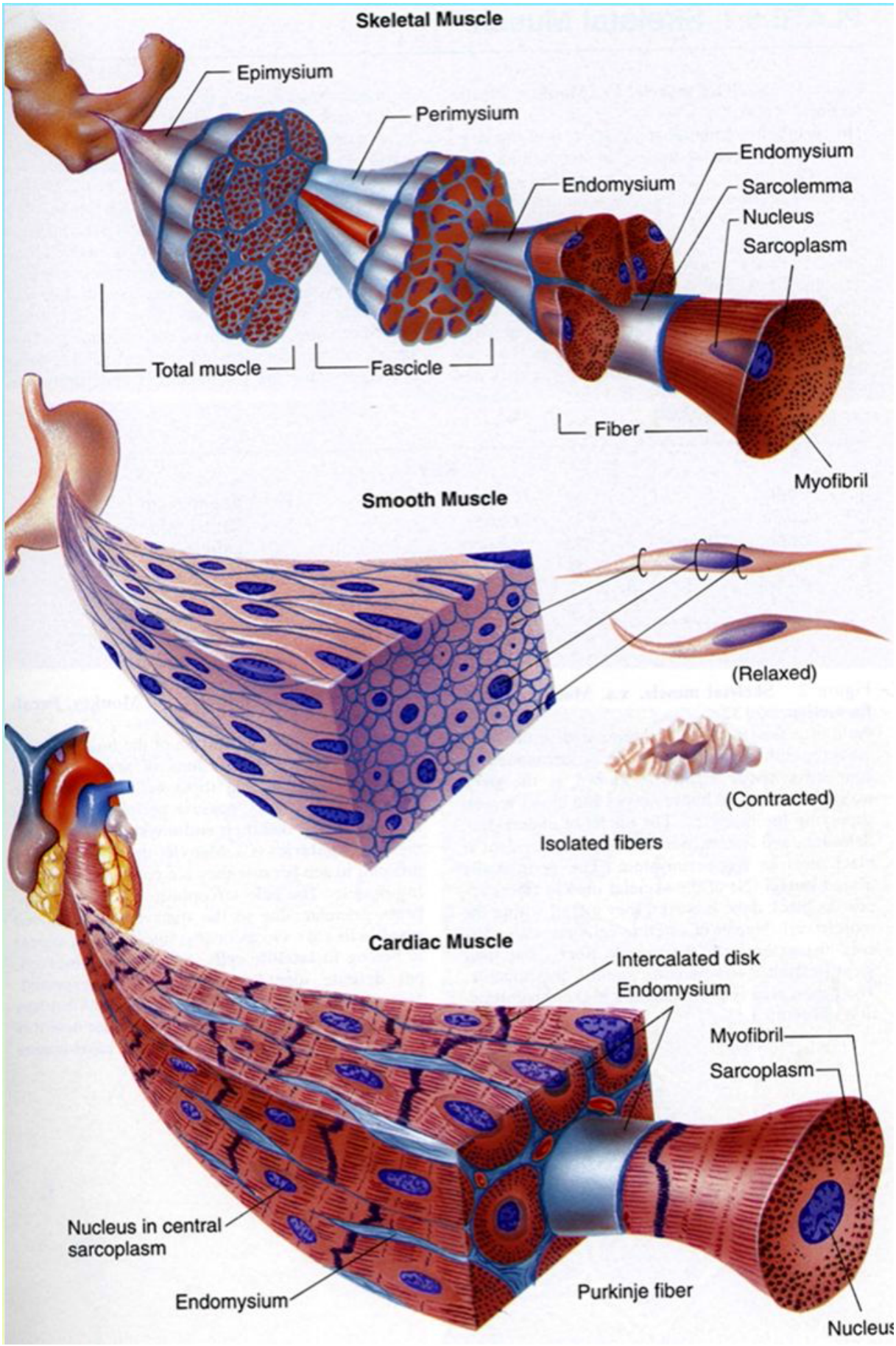
- ➢ Epithelial cells with contractile functions
  - retain secretion ability
  - express contractile proteins

- ➢ Location
  - sweat glands
  - salivary glands
  - mammary glands

- ➢ Function: assist in expressing the fluid from the gland

Skeletal/Cardiac/Smooth Muscle – same mechanisms of contraction regulation


Muscle types
Muscle cell types - summary
Activity
Skeletal muscle
Cross sections
Strong, quick discontinuous voluntary contraction
Nuclei
Cardiac muscle
Strong, quick continuous involuntary contraction
Smooth muscle
Intercalated disks
Weak, slow involuntary contraction


Skeletal Muscle
Epimysium
Perimysium
Endomysium
Endomysium
Sarcolemma
Nucleus
Sarcoplasm
Total muscle
Fascicle
Fiber
Myofibril
Smooth Muscle
(Relaxed)
(Contracted)
Isolated fibers
Cardiac Muscle
Intercalated disk
Endomysium
Myofibril
Sarcoplasm
Nucleus in central sarcoplasm
Endomysium
Purkinje fiber
Nucleus

Muscle tissue

Cardiac muscle

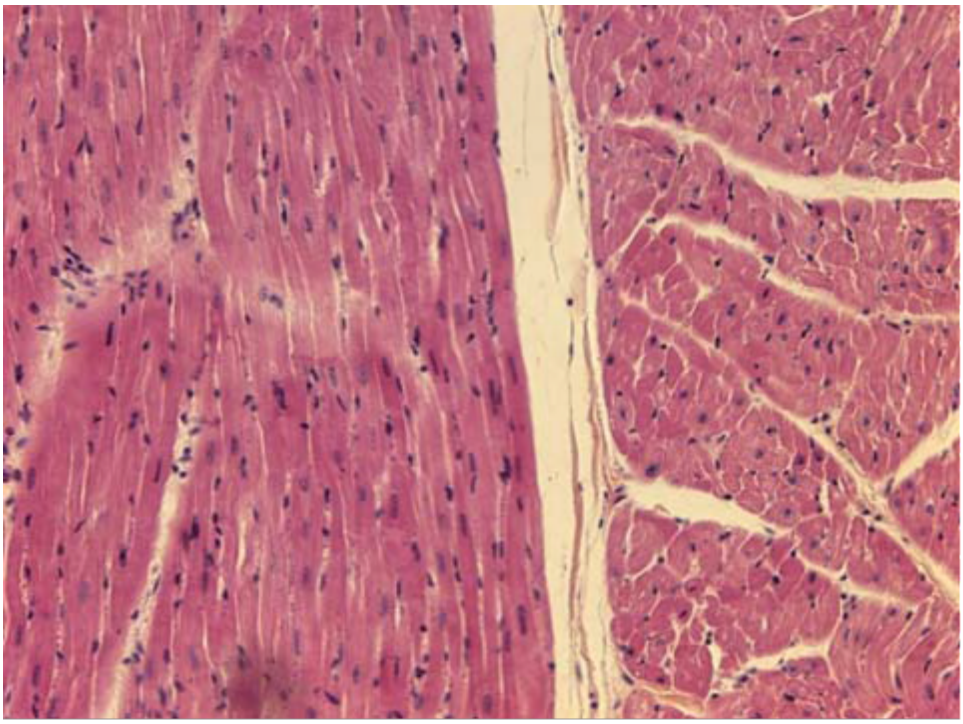
CARDIAC MUSCLE

Cardiac muscle is **nonvoluntary** striated muscle limited to the heart and the proximal portions of the pulmonary veins

- Exhibit a cross-striated banding pattern identical to that of skeletal muscle
- Size: 15 µm in diameter, 80-100 µm in length
- Possess only 1 or 2 centrally located nuclei
- Surrounded by a delicate sheath of endomysium
- Joined at intercalated disks →unique to cardiac muscle

Like skeletal, cardiac muscle cell organelles have specific names

- **Sarcoplasm**(Gr. *sarkos,* flesh, + plasma, thing formed)→cytoplasm (excluding the myofibrils)
- **Sarcoplasmic reticulum** →smooth endoplasmic reticulum
- **Sarcolemma** (*sarkos* + Gr. *lemma,* husk) →cell membrane, plasmalemma



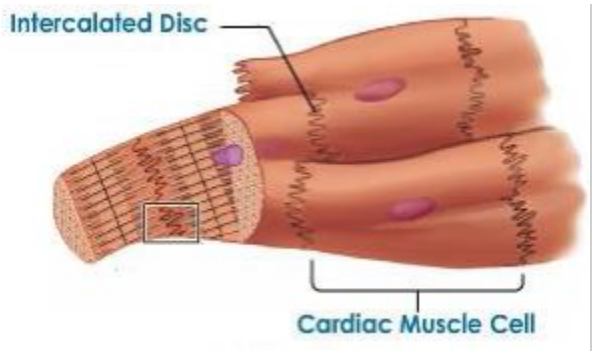
Longitudinal Crosssection

Cardiomyocytes are branched cells joined to make a fiber

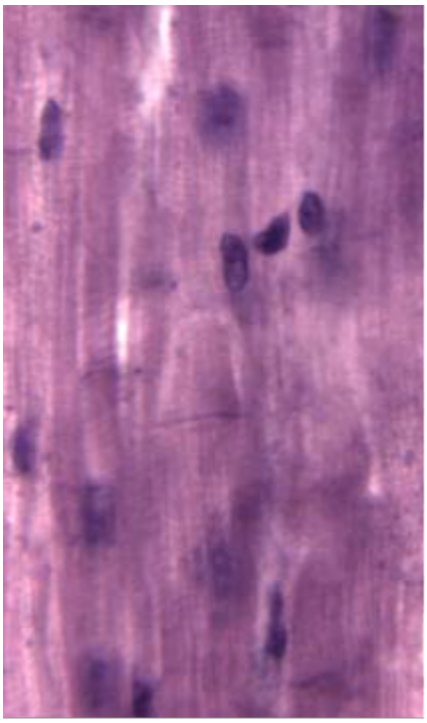
In the heart: “fiber” = long row of joined cardiac muscle cells →the fibres of cardiac muscle are not single syncytial cells with a common cytoplasm (as in skeletal muscle)

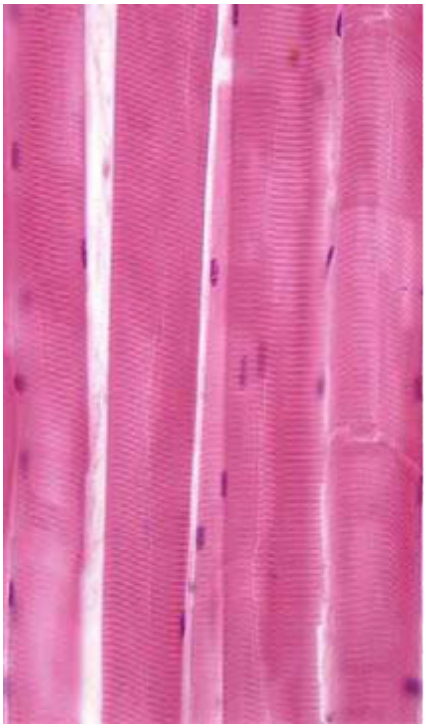
Cardiomyocytes have specific junctional complexes found at the interface between adjacent cells

Intercalated disks



Cardiac Skeletal





Component	Skeletal Muscle	Cardiac Muscle
Membrane channel	**Dihydropyridine Receptor (DHPR)**	**Voltage-gated Ca2+ channles**
SR channel	**Ryanodine Receptor (RyR1)** **IP3 Receptor (IP3R1)**	**Ryanodine Receptor (RyR2)** **IP3 Receptor (IP3R2)**
Reuptake	**SarcoEndoplasmic Reticulum Ca2+ ATPase (SERCA) – 70%** **Sodium-Calcium exchanger (NCX) – 28%** **Mitochondrial Ca2+ uptake** **Sarcolemmal Ca2+ ATPase**	**SarcoEndoplasmic Reticulum Ca2+ ATPase (SERCA) – 70%** **Sodium-Calcium exchanger (NCX) – 28%** **Mitochondrial Ca2+ uptake** **Sarcolemmal Ca2+ ATPase**

Dilated Cardiomyopathy (DCM) characterized by:

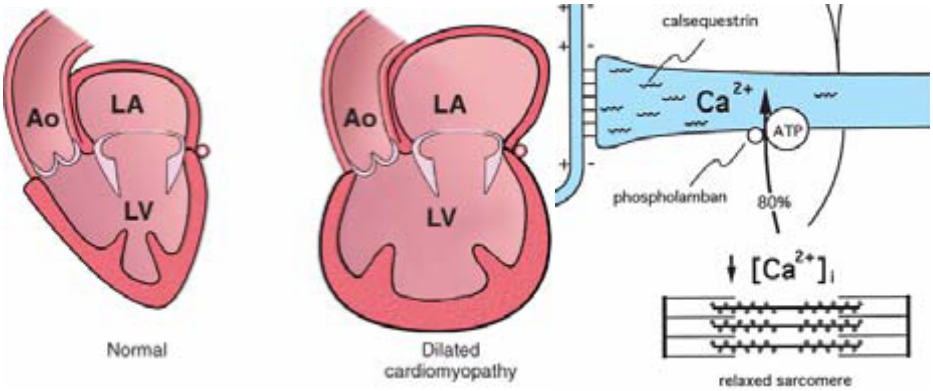
• Dilated and poorly functioning left ventricle

• Absence of other abnormal conditions (hypertension, ischemic heart)

• Global systolic impairment

DCM is often initiated by environmental stimuli on a background of genetic susceptibility.

Dilated Cardiomyopathy (DCM)



- Decreased SERCA activity
- Decreased sequestration of Ca2+ in SR
- Decreased Ca2+ SR content
- Decreased Ca2+ release from SR
- Decrease in the peak calcium transient →defect in EC coupling
- Progressive contractile dysfunction

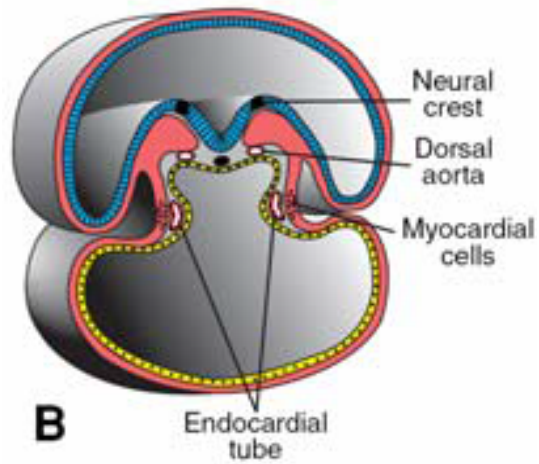
Development of cardiac muscle

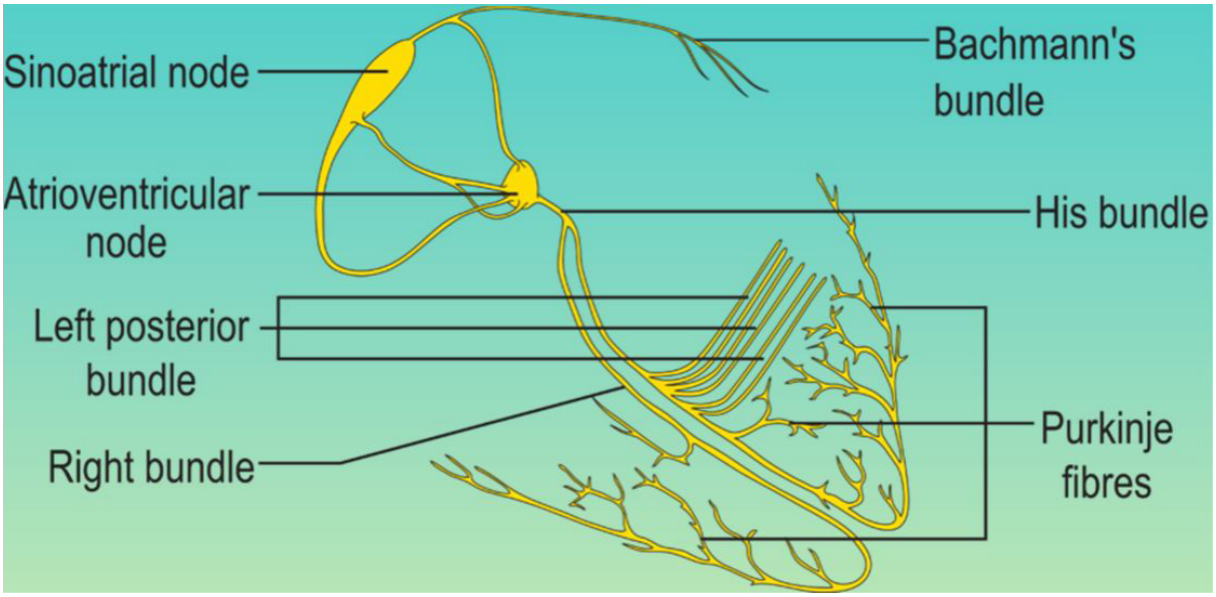
Cardiac muscle develops from **splanchnic mesoderm** surrounding the endothelial heart tube

Myoblasts adhere to one another by special attachments that later develop into intercalated discs, but **do not fuse**

During later development, a few special bundles of muscle cells with irregularly distributed myofibrils become visible. These bundles, the **Purkinje fibers,** form the conducting system of the heart

Cardiomyocytes do not regenerate




Sinoatrial node
Bachmann's bundle
Atrioventricular node
His bundle
Left posterior bundle
Right bundle
Purkinje fibres

The Blood

Blood = formed elements + plasma

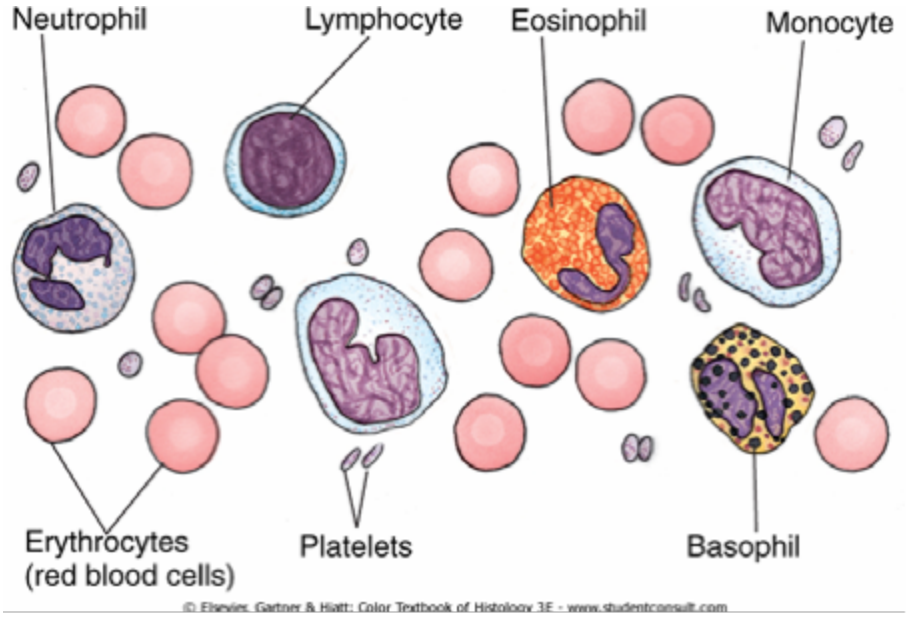
If blood is removed from the circulatory system, it will clot.

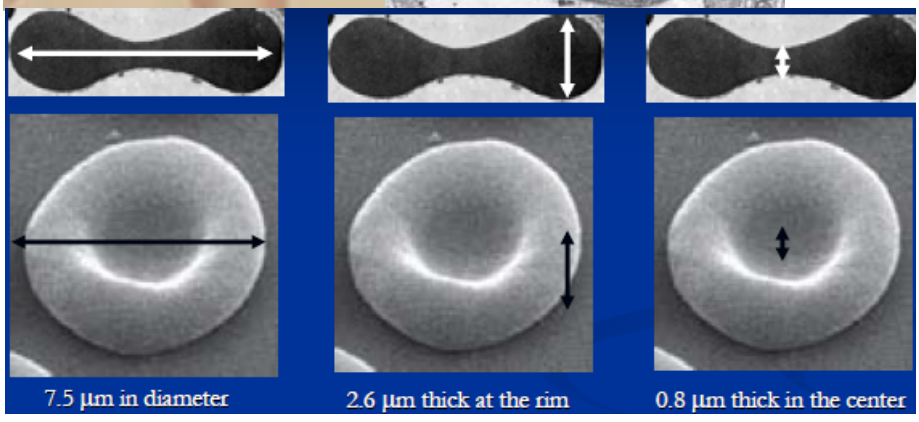
This clot contains **formed elements** and a clear yellow liquid called **serum,** which separates from the coagulum.

The **hematocrit** - the volume of packed erythrocytes per unit volume of blood.

The normal value is 40–50% in men and 35– 45% in women.

Humans contain about 5 liters of blood, accounting for 7% of body weight

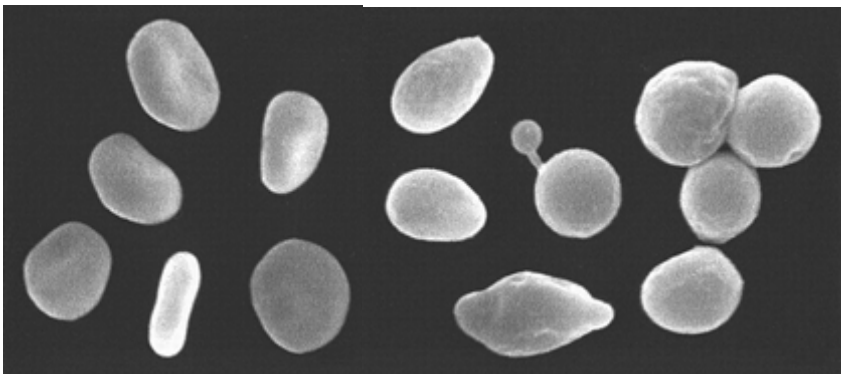




RBC life cycle

Human erythrocytes survive in the circulation for **about 120 days**. Worn-out erythrocytes are removed from the circulation mainly by macrophages of the spleen and bone marrow.

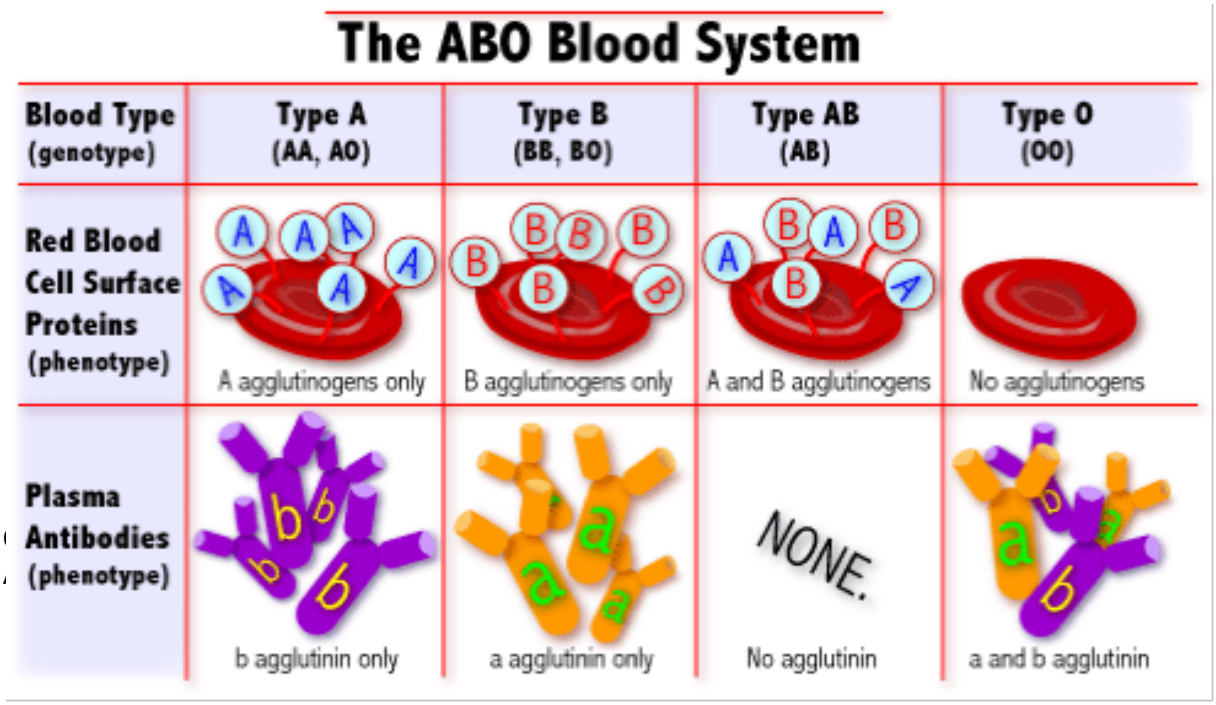
Hereditary Spherocytosis (HS)



Normal RBC HS RBC

ABO blood group system

The extracellular surface of the red blood cell plasmalemma has **specific inherited carbohydrate chains** that act as antigens and determine the blood group of an individual for the purposes of blood transfusion.



Granulocytes - nuclei with two or more lobes

Granulocytes (L. *granulum,* granule, + Gr. *kytos*)

Contain 2 types of granules

specific granules →specific functions

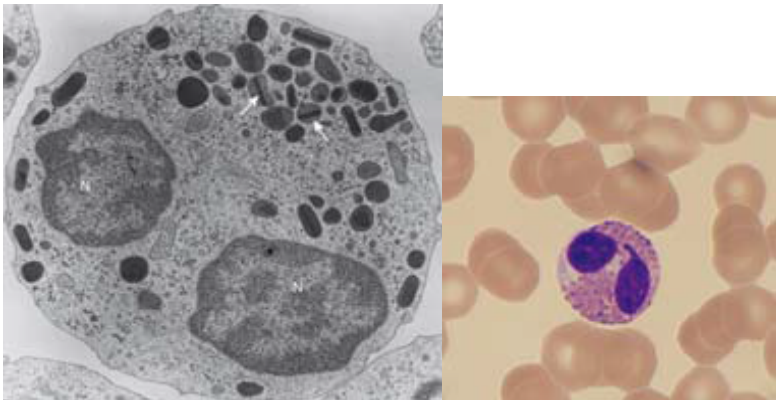
azurophilic granules →lysosomes

- Nondividing terminal cells with a life span of a few days
- Die by apoptosis (programmed cell death) in the connective tissue
- Few mitochondria (low energy metabolism) → depend mostly on glycolysis

Neutrophilic granulocyte

- 12–15 microm in diameter
- 2-5 lobes linked by fine threads of chromatin
- short-lived cells with a half-life of 6-7 h in blood and a life span of 1-4 days in connective tissues

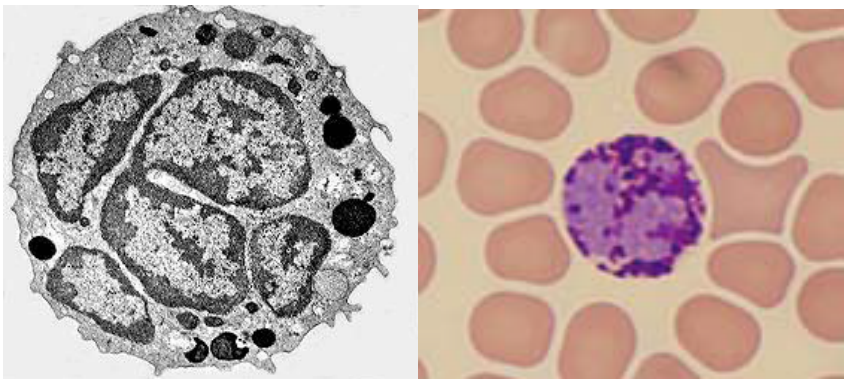
Eosinophilic granulocyte



The specific granules have a crystalline core (**internum**) & outer **externum,** or **matrix**.

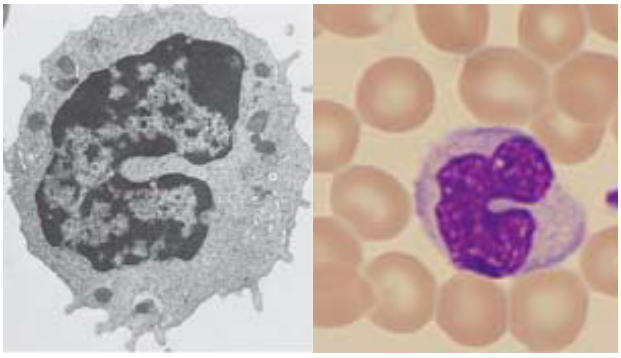
The internum contains a protein called the **major basic protein** to which the eosinophilia accounts.

Basophilic granulocyte



The lobulated nucleus appears as several separated portions. Note the basophilic granule (arrows).

Monocyte



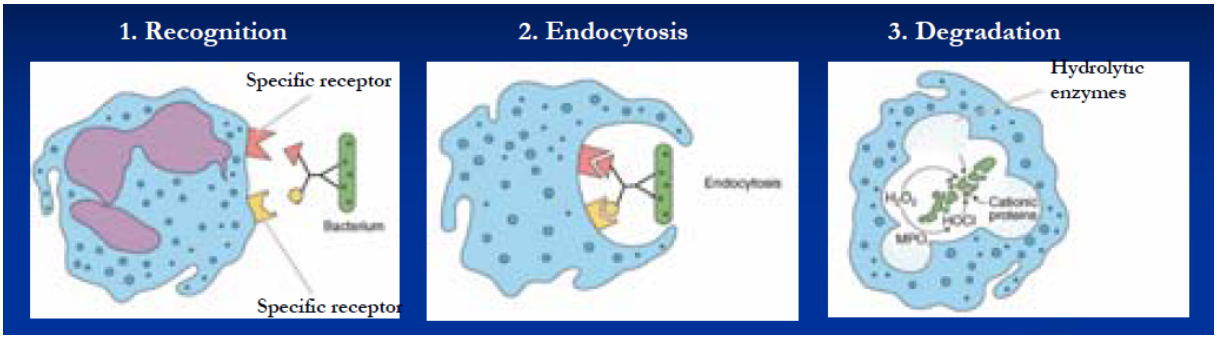
Kidney-shaped nucleus. Azurophilic granules (arrows).

Monocyte differentiation in various tissues

Cell Type	Location	Main Function
Monocyte	Blood	Precursor of macrophages
Macrophage	Connective tissue, lymphoid organs, lungs, bone marrow	Inflammation (defense), antigen processing and presentation
Kupffer cell	Liver	Same as macrophages
Microglia cell	Nerve tissue of the central nervous system	Same as macrophages
Langerhans cell	Skin	Antigen processing and presentation
Dendritic cell	Lymph nodes	Antigen processing and presentation
Osteoclast	Bone (fusion of several macrophages)	Digestion of bone
Multinuclear giant cell	Connective tissue (fusion of several macrophages)	Segregation and digestion of foreign bodies

Phagocytes participate in the anti-bacterial immunity

1. **Penetration of bacterial cells releases chemotactic factors**
2. **Chemotactic factors activate phagocytes**
3. **Diapedesis – phagocytes migrate from blood to tissue**
4. **Phagocytes engulf bacteria**



Leukocyte Extravasation

Leukocyte extravasation is the movement of leukocytes out of the circulatory system, towards the site of tissue damage or infection.

Main Steps

• Rolling (tethering)

reversible binding of leukocytes to endothelial cells

mediated by selectins and glycosylated ligands

• Activation

stimulation of the leukocyte by chemokines

result – increase in integrin alpha4beta1 (VLA-4) activity

binding of integrin to its endothelial partner (VCAM-1)

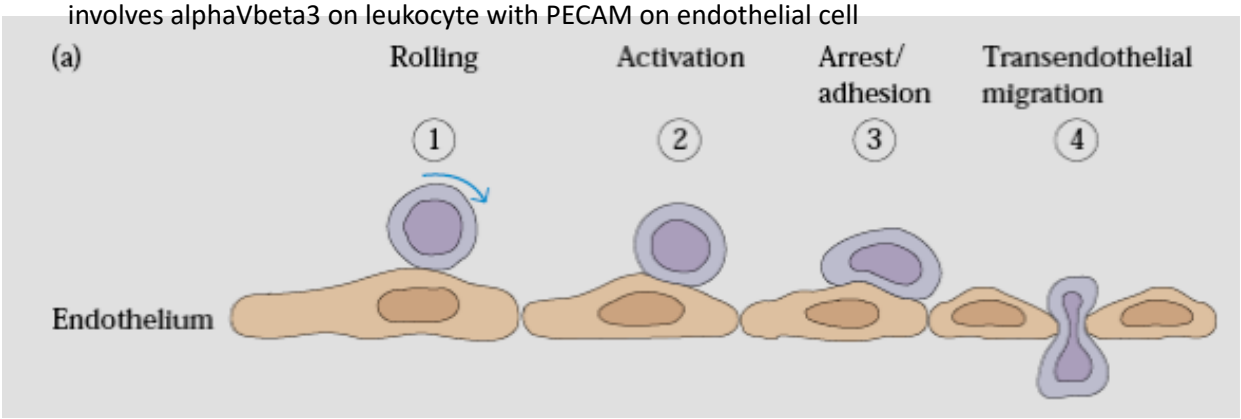
• Adherence (tight adhesion)

irreversible adhesion mediated by integrins & Ig family on leukocyte with ICAM-1 on endothelial cell

• Diapedesis (extravasation)

transmigration of leukocyte between endothelial cells

involves alphaVbeta3 on leukocyte with PECAM on endothelial cell



Lymphocyte

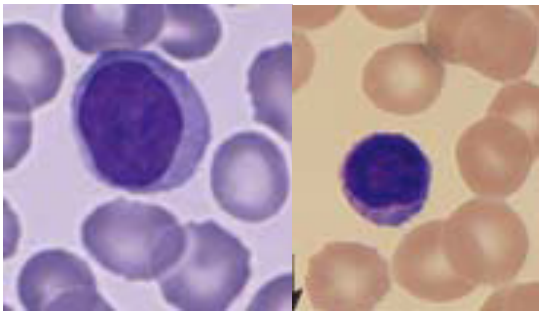
larger lymphocytes →cells activated by specific antigens

scant cytoplasm, a few azurophilic granules

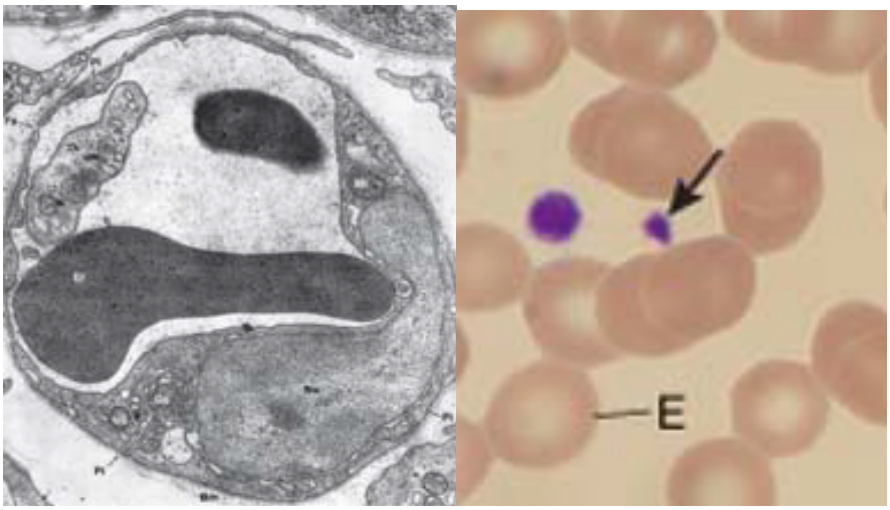
the only type of leukocytes that return from the tissues back to the blood

variable life span: days – years

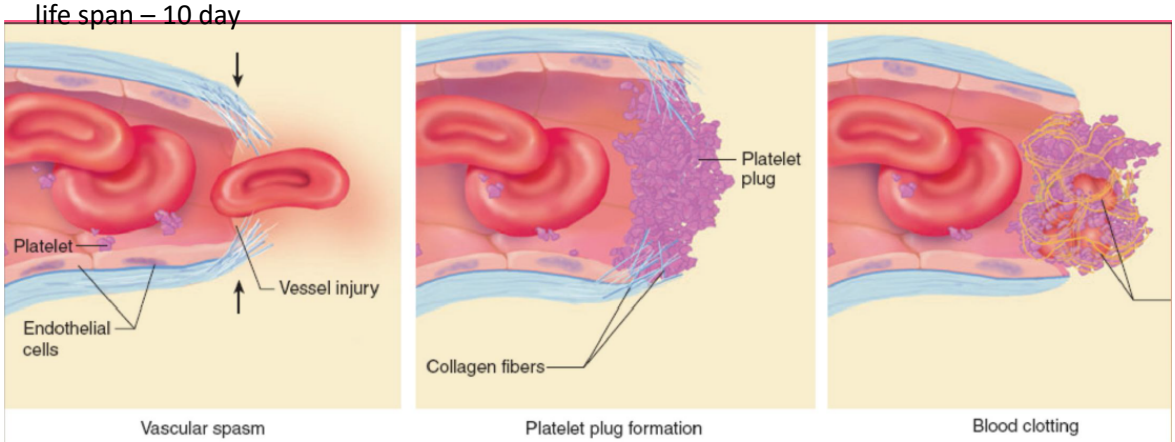
80% of the circulating lymphocytes are T cells, 15% are B cells, and the remainder are null cells (NK or circulating stem cells)



Thrombocyte (platelet)



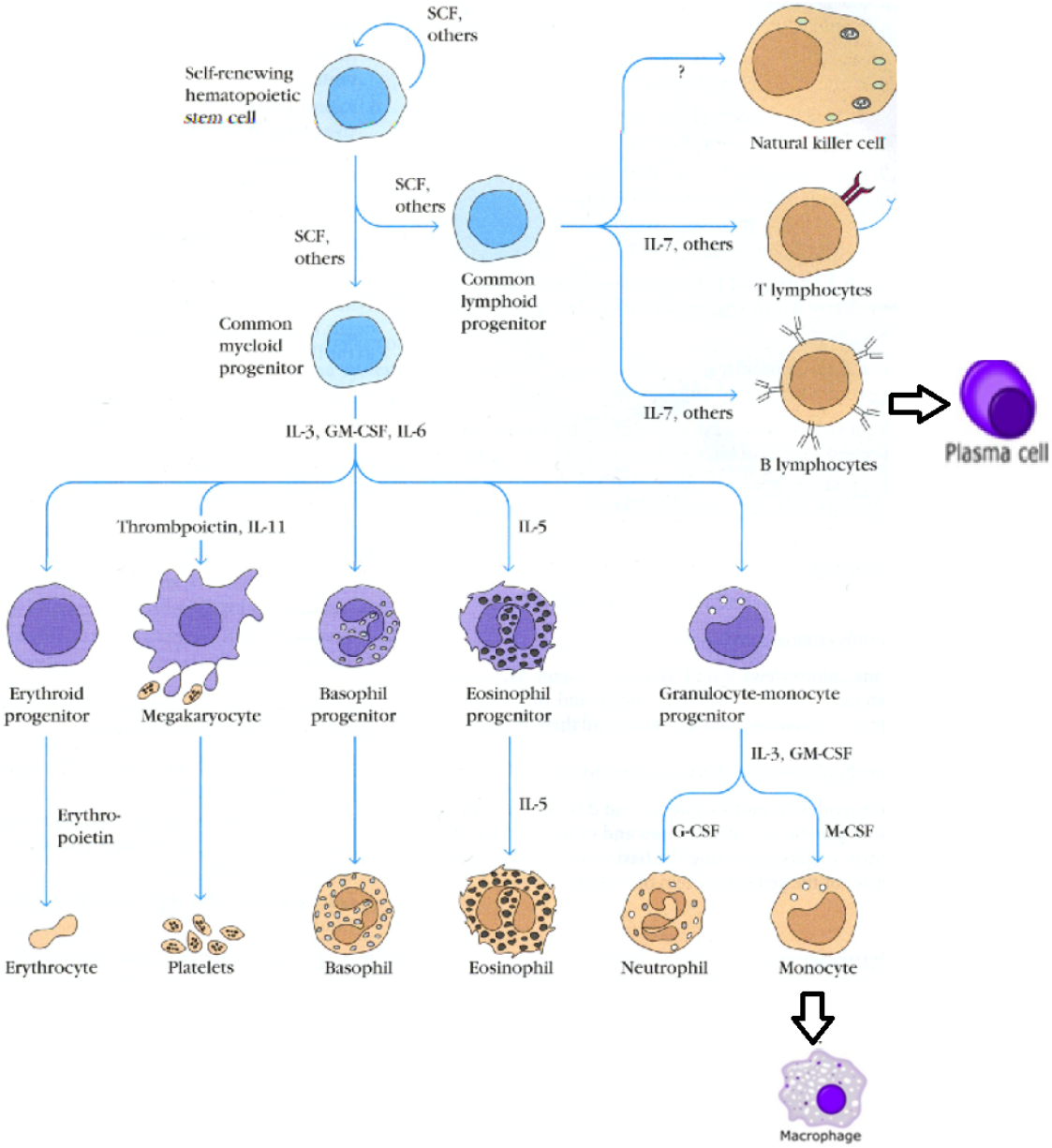
- nonnucleated, disk-like, 2-4 mm in diameter
- 2 main regions
- peripheral →**hyalomere**
- **central →granulomere**
- participate in the clotting of the blood
- life span – 10 day



Hemopoiesis

(Gr. *haima,* blood, + *poiesis,* a making)

Stem **C**ell **F**actor (**SCF**)



Prenatal hemopoiesis:

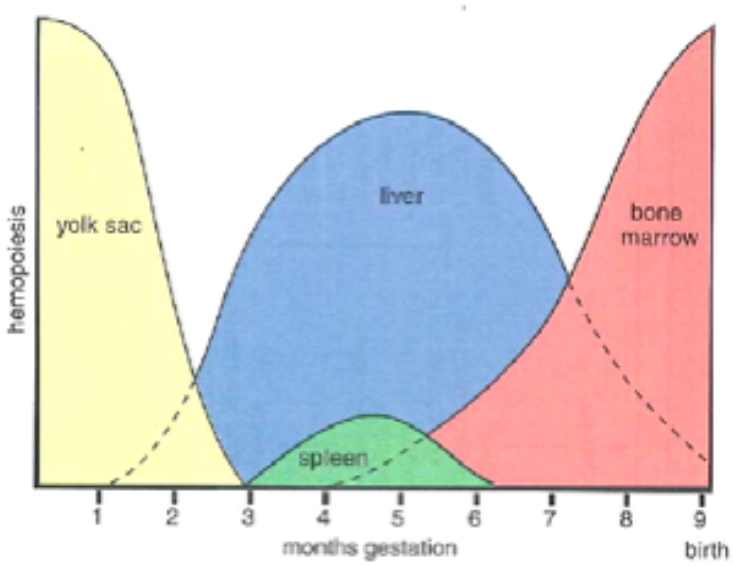
> **Mesoblastic** phase (2 weeks after conception) – *blood islands* in the mesoderm of the yolk sac; only RBC

Hepatic phase (6th week of gestation) - leukocytes appear by the 8th week

Splenic phase (2nd trimester)

Myeloid phase (end of 2nd trimester) – bone marrow

Postnatal hemopoiesis - occurs almost exclusively in bone marrow, but the liver and the spleen can revert to forming new blood cells if the need arises



Stem cell populations in the bone marrow

Pluripotential hemopoietic stem cells (PHSCs)

about 0.1% of the nucleated cells in bone marrow

can produce themselves or multipotential hemopoietic stem cells (MHSCs)

Multipotential hemopoietic stem cells (MHSCs)

responsible for the formation of various progenitor cells

CFU-GEMM cells – colony forming unit for granulocyte, erythrocyte, monocyte, megakaryocyte

CFU-Ly cells – colony forming unit for lymphocytes

PHSCs & MHSCs are morphologically indistinguishable, resemble lymphocytes and constitute a small fraction of the null-cell population of circulating blood

CD34+ colonies of progenitors

Researchers studying hemopoiesis have isolated individual lymphocyte-like cells that, under proper conditions, occasionally give rise to groups (*colonies*) of cells composed of granulocytes, erythrocytes, monocytes, lymphocytes, and platelets →such cells are called *colony-forming units*

Progenitor cell populations in the bone marrow

- Morphologically indistinguishable from stem cells, resemble lymphocytes like stem cells
- Can be differentiated only by CD expression
- **Unipotential** →committed to forming a single cell line, responsible for the formation of various progenitor cells
- Limited capacity for self-renewal →depend on stem cells for renewal

Hemopoietic Growth Factors

- Glycoproteins acting on specific stem cells, progenitor cells, and precursor cells, generally inducing rapid mitosis, differentiation, or both

- Routes to deliver growth factors to their target cells:
    - transport via the bloodstream (as endocrine hormones)
    - secretion by stromal cells of the bone marrow near the hemopoietic cells (as paracrine hormones)
    - direct cell-to-cell contact (as surface signaling molecules)

Precursor cell populations in the bone marrow

Arise from progenitor cells

Have **specific morphological** characteristics →permit them to be recognized as the first cell of a particular cell line

- (cell name)-blast: e.g. erythroblast, myeloblast
- pro-(cell name)-cyte
- (cell name)-cyte
- meta-(cell name)-cyte

Incapable of self-renewal

Undergo cell division and **differentiation**→give rise to a clone of mature cells

Changes in properties of hematopoietic cells during differentiation

cell volume decreases

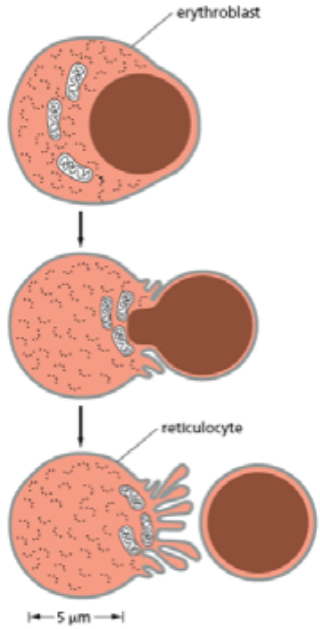
nucleoli diminish in size

nuclear diameter decreases

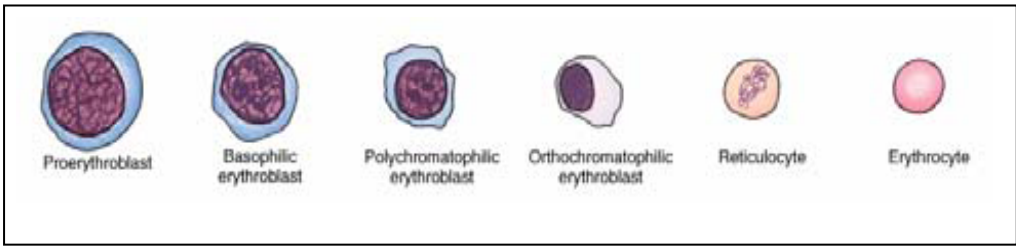
chromatin becomes more dense → pyknotic → extruded from the cell

mitochondria and other organelles gradually disappear

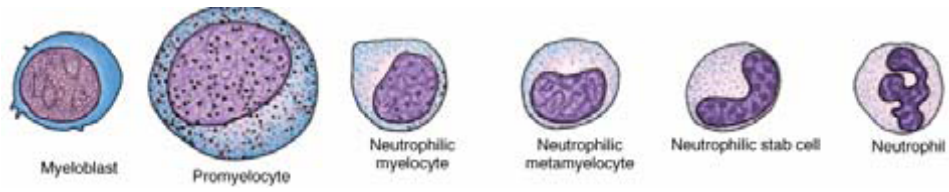
Erythroid cells

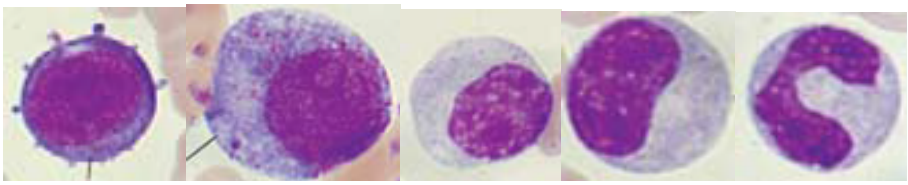


A developing red blood cell **(erythroblast)** extrudes its nucleus to become an immature erythrocyte (a **reticulocyte**), which then leaves the bone marrow and passes into the bloodstream



Neutrophilic lineages

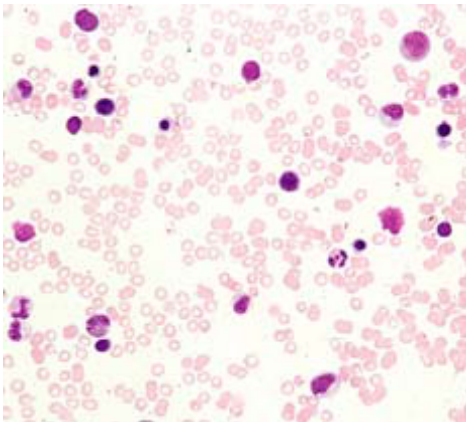


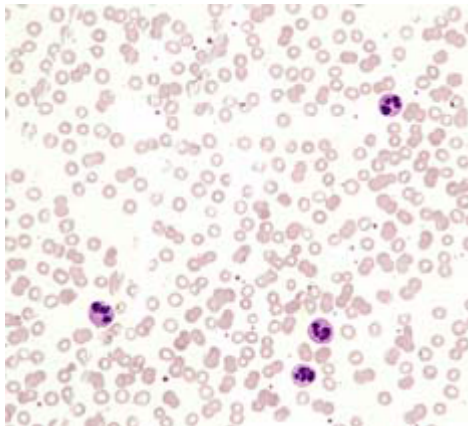


Myeloblast→the most immature recognizable cell

Myelocyte→first sign of Differentiation

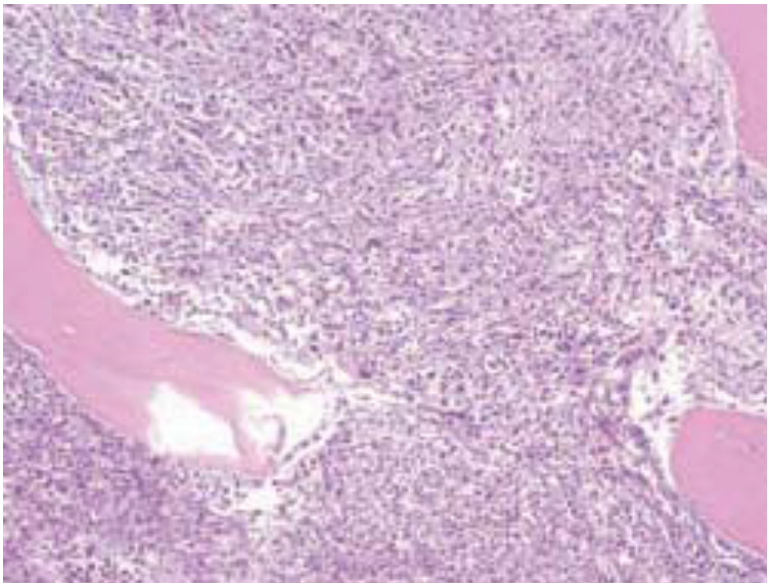
Smears from bone marrow vs peripheral blood



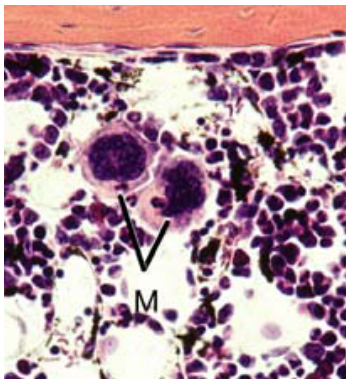


Leukemias – disorders of the hematopoietic progenitors

Acute myeloblastic leukemia results from uncontrolled mitosis of a transformed stem cell whose progeny do not differentiate into mature cells. The cells involved may be the CFU-GM, CFU-Eo, or CFU-Ba, whose differentiation stops at the myeloblast stage.



Development of platelets



Megakaryoblasts

1 nucleus with many lobes & numerous nucleoli

undergo endomitosis→up to 64 N (polyploid)

Megakaryocytes (Gr. *megas,* big, + *karyon,* nucleus, + *kytos*)

giant cells (35-150 mm in diameter)

irregularly lobulated nucleus, coarse chromatin, and no visible nucleoli

numerous invaginations of the plasma membrane →areas that shed platelets

The Immune System

Innate immunity

Innate immune defenses are non-specific, meaning these systems respond to pathogens in a generic way. This system does not confer long-lasting immunity against a pathogen. The innate immune system is the dominant system of host defense in most organisms.

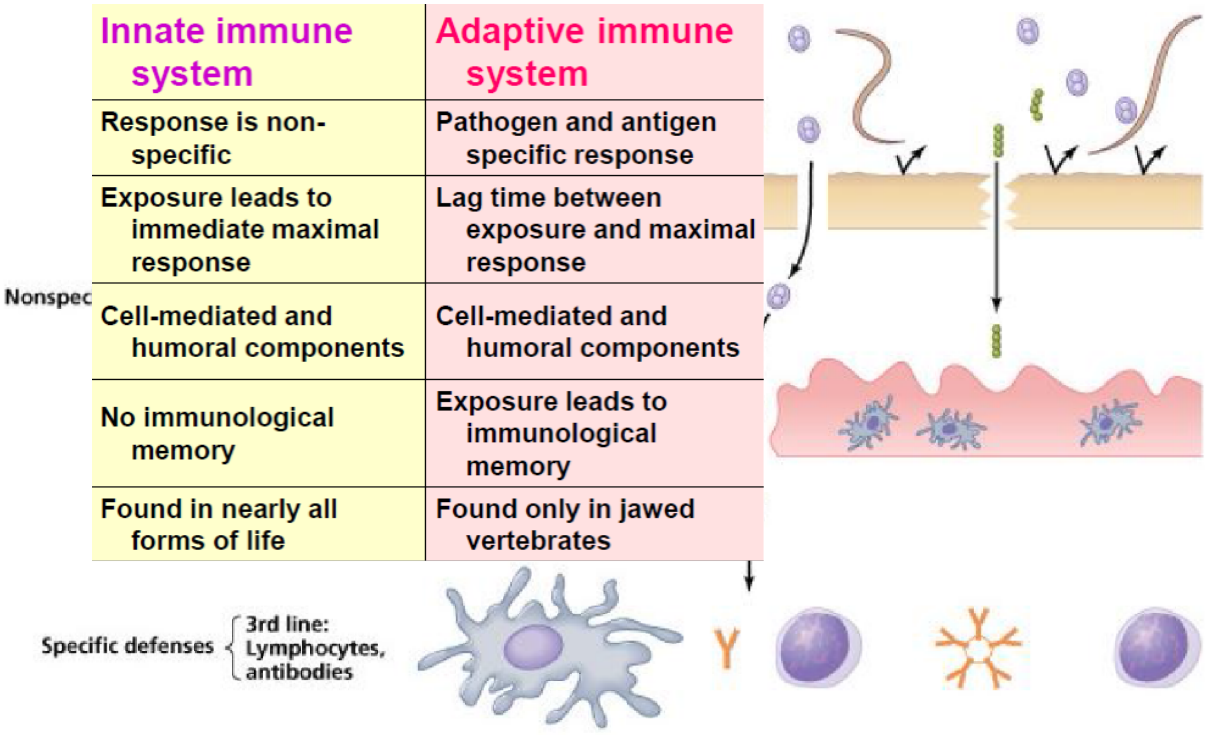
1. Inflammation (redness, swelling, heat and fever)
2. Complement system (is a **biochemical cascade** that attacks the surfaces of foreign cells.)
3. Cellular barriers (Leukocyten)

- activated immediately after an infection begins
- do not depend on the host's prior exposure to the pathogen
- present in all multicellular organisms
- components:
    - Skin (Barrier)
    - Mucus
    - Complement antimicrobial peptides
    - Macrophages
    - Neutrophils
    - NK cells, Toll-like receptors (TLRs)

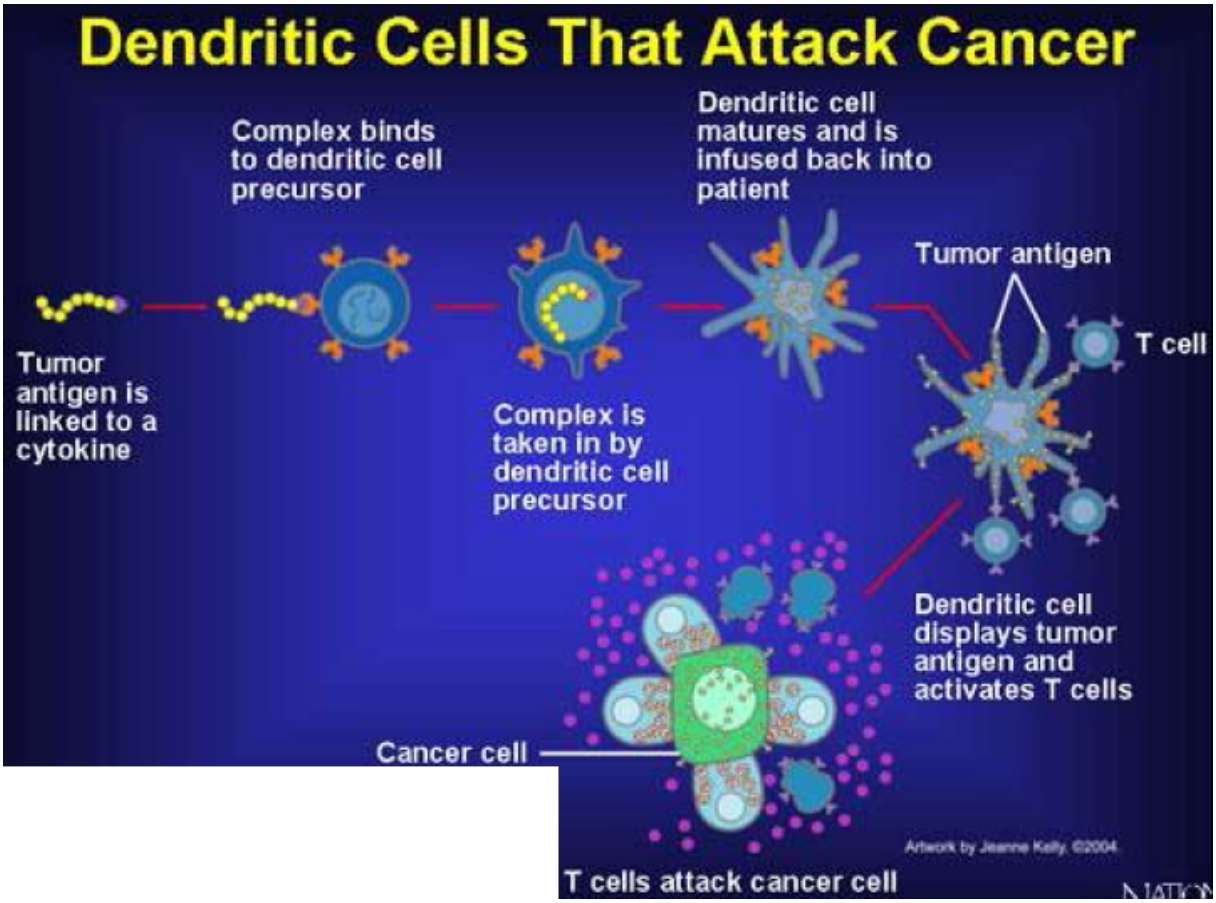
Adaptive immunity

- operate later than the innate response
- highly specific for the pathogen
- present only in vertebrates
- components:
    - T cells
    - B cells
    - antigen-presenting cells (APCs),
    - immunoglobulins
    - cell-mediated immunity component

Innate immune system	Adaptive immune system
Response is non-specific	Pathogen and antigen specific response
Exposure leads to immediate maximal response	Lag time between exposure and maximal response
Cell-mediated and humoral components	Cell-mediated and humoral components
No immunological memory	Exposure leads to immunological memory
Found in nearly all forms of life	Found only in jawed vertebrates

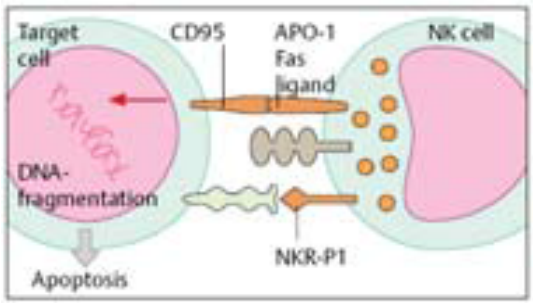


T cell activation by dendritic cell

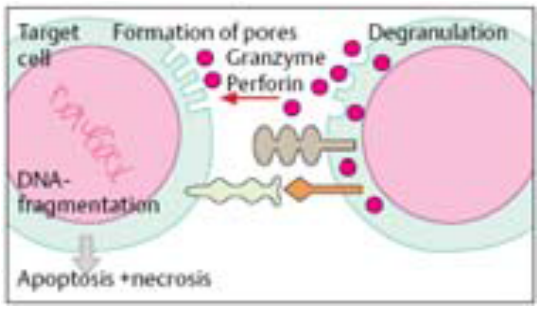


Cell mediated cytotoxicity

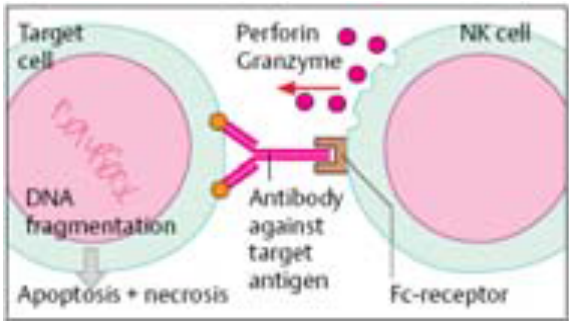
Nonsecretory lysis



Secretory lysis



ADCC (antibody dependent cellular cytotoxicity)



Immunological memory

When stimulated by their specific antigen, naïve cells proliferate and differentiate. Most become effector cells, which function and then usually die, while others become memory cells.

During a subsequent exposure to the same antigen, the memory cells respond more readily, rapidly, and efficiently than did the naïve cells: they proliferate and give rise to effector cells and to more memory cells.

Lymphatic Cells and Tissues

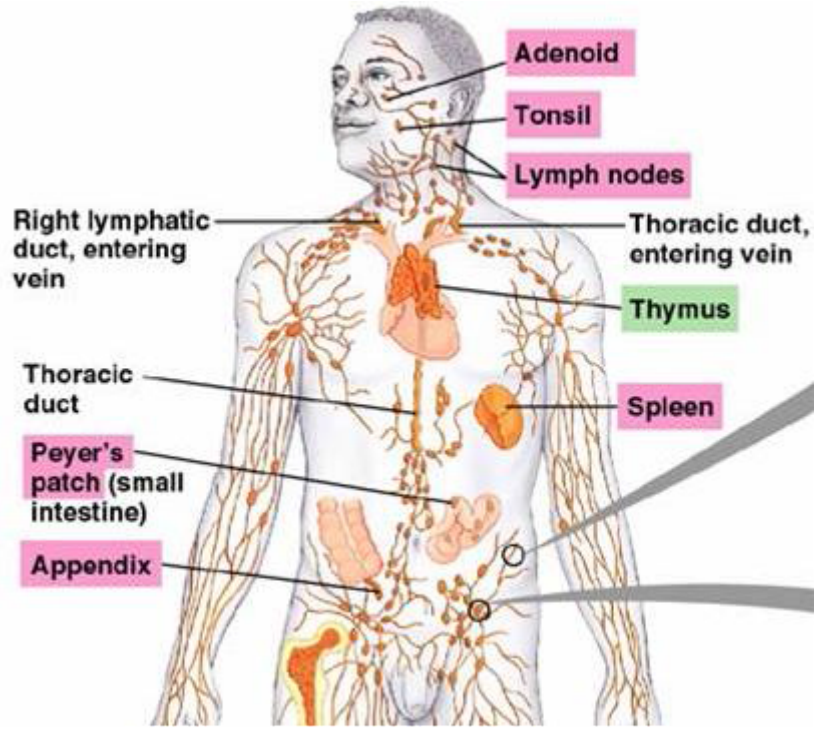
The lymphatic system is part of the circulatory system, comprising a network of conduits called lymphatic vessels that carry a clear fluid called lymph directionally towards the heart.

Lymphatic organs play an important part in the immune system, having a considerable overlap with the lymphoid system.

Lymph nodes act as filters or traps for foreign particles and are important in the proper functioning of the immune system. They are packed tightly with the white blood cells called lymphocytes and macrophages.

Functions

- It is responsible for the removal of interstitial fluid from tissues
- It absorbs and transports fatty acids and fats as chyle from the digestive system
- It transports white blood cells to and from the lymph nodes into the bones
- The lymph transports antigen-presenting cells (APCs), such as dendritic cells, to the lymph nodes where an immune response is stimulated.



Primary lymphatic organs:

- **Thymus**
- **Bone marrow**

Secondary lymphatic organs:

- **Tonsils**

- **Lymph nodes**
- **Spleen**

T-Lymphocytes (T cells)

Natural killer (NK) cells

Cytotoxic cells

Helper cells

Supressor cells

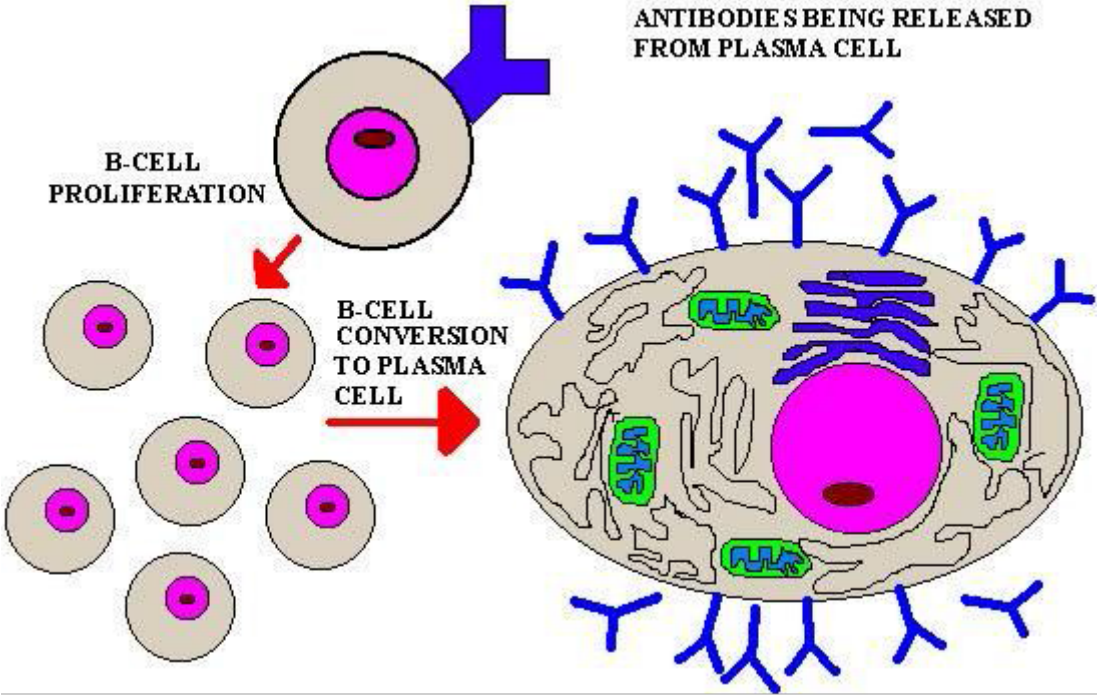
Amplifier cells

Memory cells

Natural killer and **cytotoxic cells** release a protein called **perforin**, which creates pores within the cell membranes, through which the **granzymes** (serine proteases) can enter, inducing **apoptosis** within virus-infected cells, thus destroying them.

B- Lymphocytes

The principal functions of B cells are to make antibodies against antigens, to perform the role of antigen-presenting cells (APCs), and to develop into memory B cells after activation by antigen interaction.



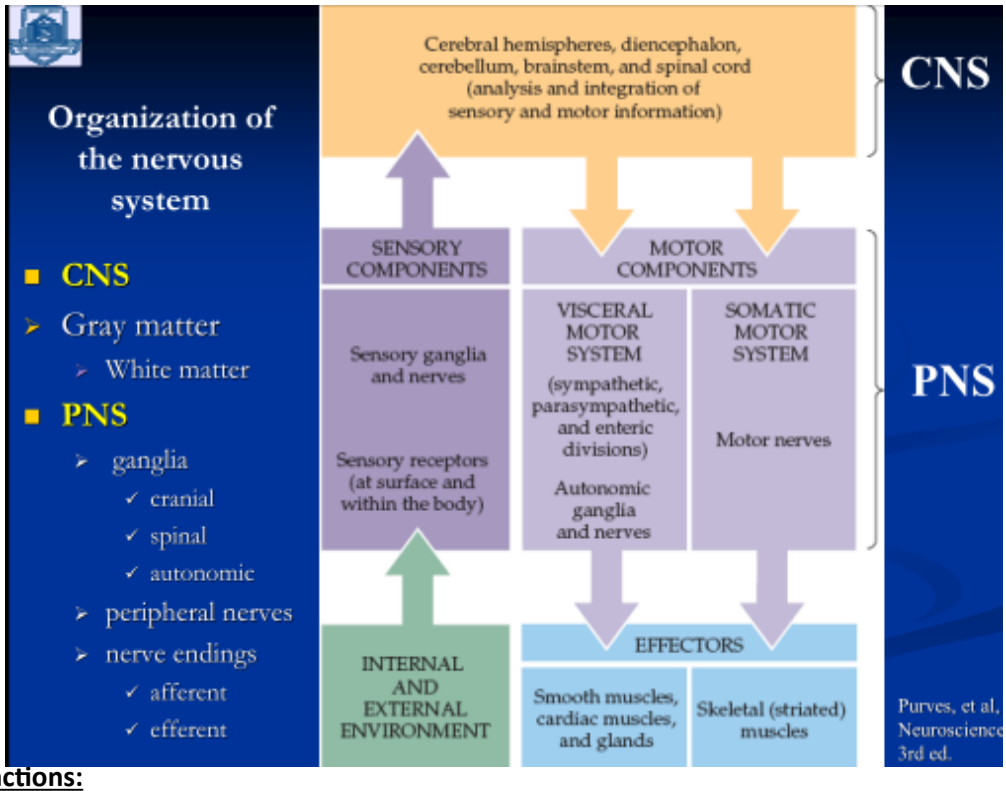
In general, an encounter with a given antigen triggers a response characterized as either a humoral immune response (antibody production) or a cell-mediated immune response. Typically, however, both humoral and cellular immune systems are involved, although one system generally predominates, depending on the stimulus.

Nervous tissue: Neurons

- The human nervous system is the most complex system in the human body a formed by a network of:

→ *neurons and associated glial cells*

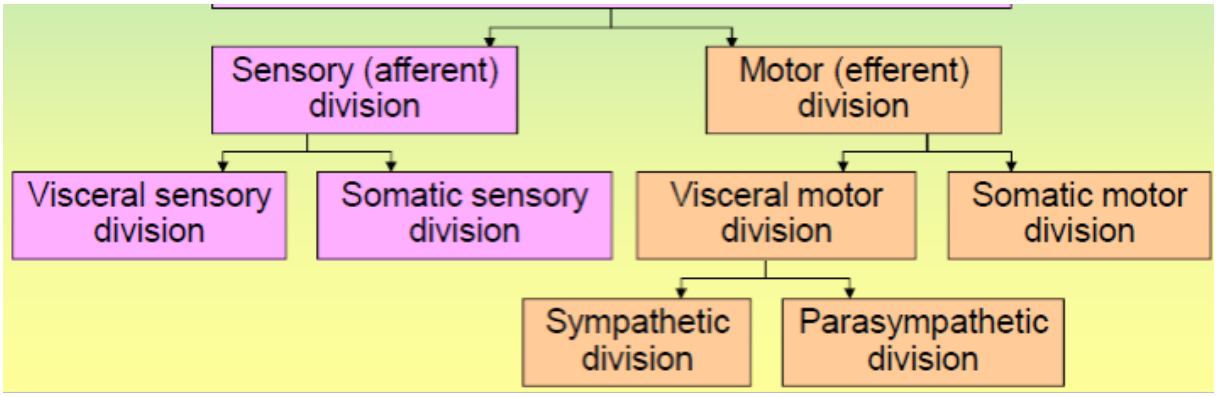
- Nerve tissue is distributed throughout the body as an integrated communications network



Main functions:

- The nervous system controls and integrates the functional activities of the organs of the body and play a central role in maintaining ist homeostasis.
- The PNS responds to stimuli and sends impulses to the CNS.
- These impulses are interpreted by the CNS and then other impulses initiated in the CNS travel back through the PNS to effector organs to produce the proper response.

Structural and functional organisation of N.S.



Gray matter

- contains neuronal bodies, dendrites, unmyelinated axons and glial cells – lack of myelin determine the gray colour in vivo.

White matter

- contains mainly myelinated and unmyelinated nerve fibers and glial cells – large amount of of myelin surrounding axons determines its white colour.

Major cell types of the nervous system

⇨ Neurons: ~ 10^11 in the human brain (Each neuron has, on average, at least 1000 interconnections with other neurons)

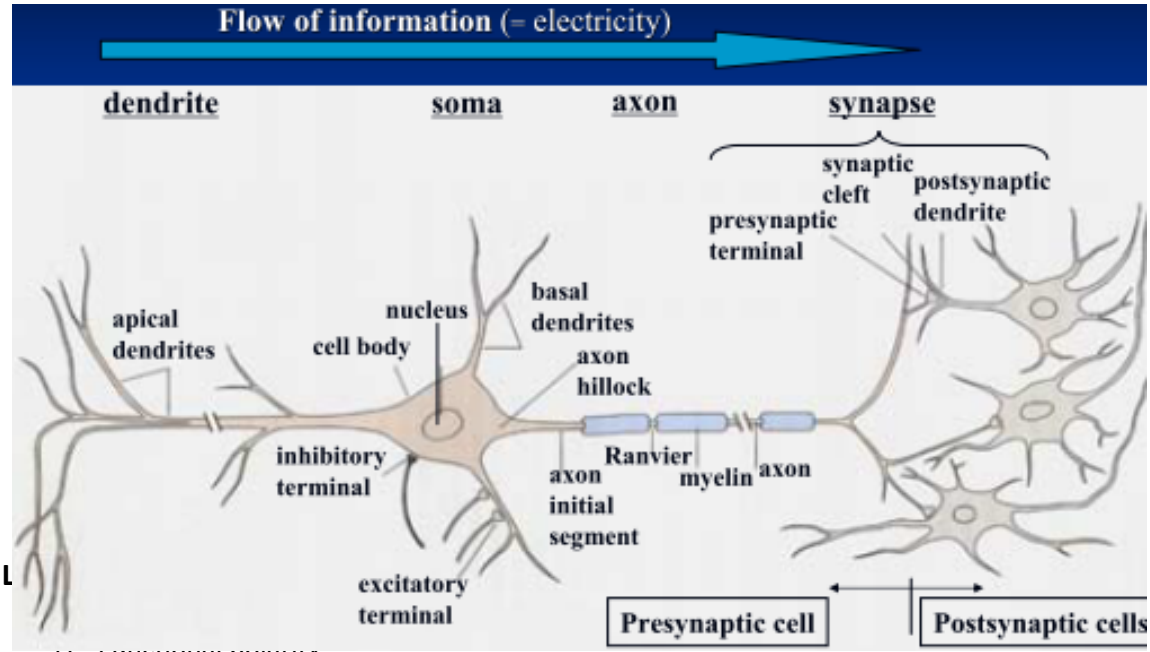
⇨ Glia: ~ 10^ 50 per neuron

1) macroglia
- Oligodendrocytes
- Schwann cells
- Astrocytes
- Ependymal cellsmicroglia

2) Microglia

The neuron

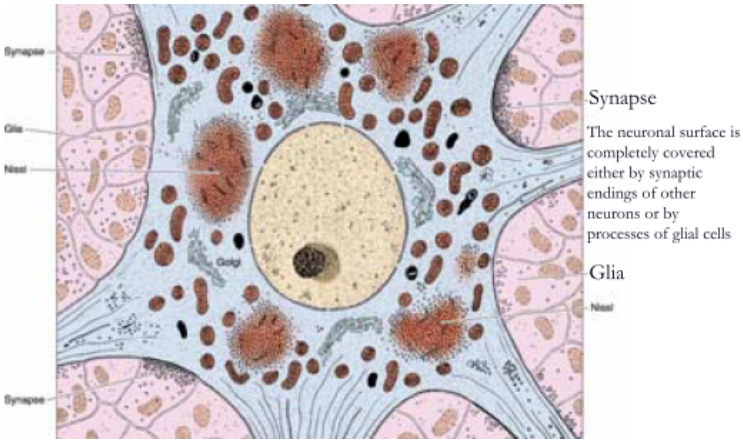
⇨ **The neurons is the structural and functional unit of the nervous system**



L

2) Anatomical polarity

3) Subcellular polarity



⇨ Soma = perikaryon = cell body

- The dilated region of the neuron – con
  →the neuronal nucleus
  →the perinuclear cytoplasm → abund

- Nissl bodies (stacks *[=Säule]* of RER), free ribosomes, and Golgi complex extend into the dendrites **but not into the axon**
  →(the organelle free area at the junction between perikaryon & axon → axon hillock *(=Hügelchen)*

⇨ Neurons are secretory cells

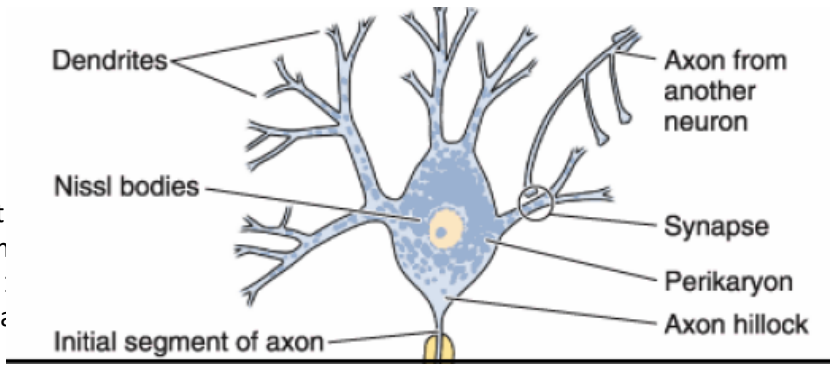
<u>Certain neuronal cell bodies contain pigments:</u>

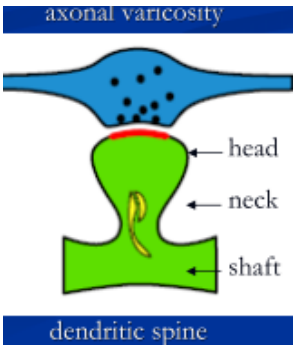
➔ Neuromelanin
- neurons of substantia nigra, locus ceruleus complexes of excess cytosolic neurotransmitters (e.g. dopamine) that are not accumulated by synaptic vesicles prevent neuronal damage of substance accumulation

➔ Lipofuscin → many neurons, particularly at older age →products of lysosomal processing

Dendrites

⇨ receptor processes that receive stimuli from other neurons or from the external environment
⇨ Dendrites are often multibranched (Gr. dendron, tree) → up to <u>200,000 axonal terminations</u> establish functional contact with the dendrites of a **Purkinje cell** of the cerebellum
⇨ They are arborized so that they can receive <u>multiple stimuli from many other neurons</u> simultaneously
⇨ The nerve impulses received by the dendrites are then transmitted toward soma

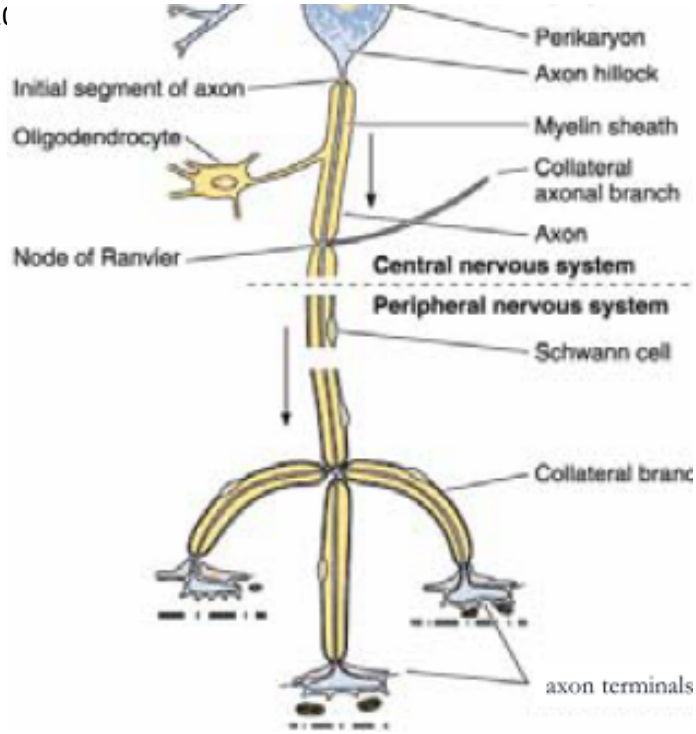




⇨ Most
⇨ Mush
⇨ Size:
⇨ Huma

➔ <u>Axon is a single process specialized in generating or conducting nerve impulses to other cells</u>

- Most neurons have only one axon (Gk. axis); a very few have no axon at all
- Axons are usually very long processes → up to 1(



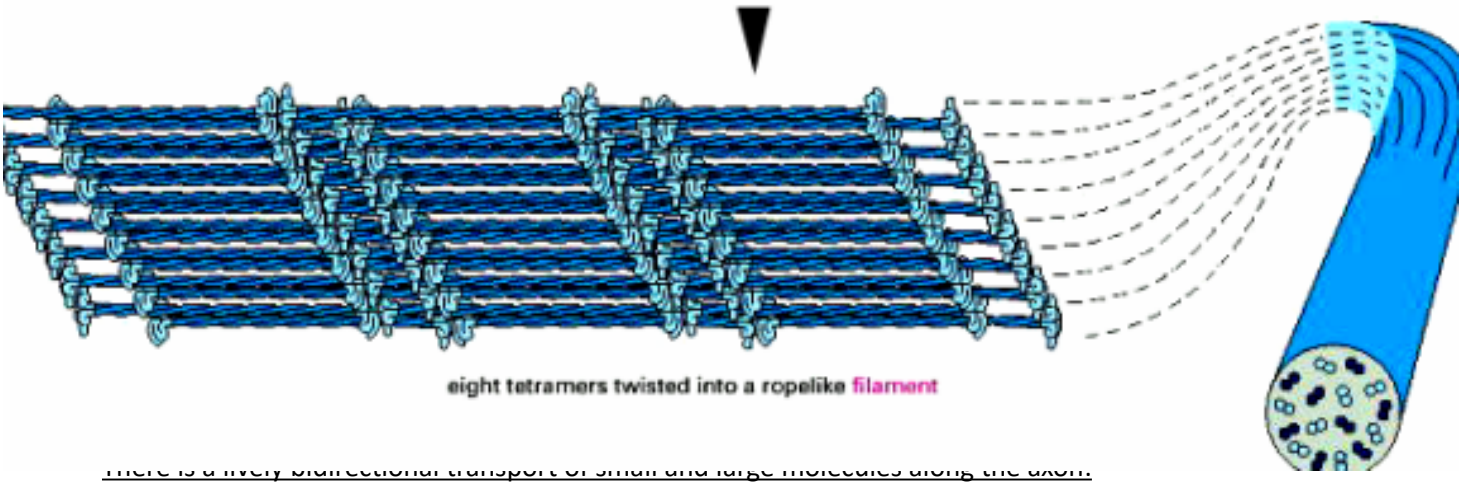
Terminology of axons:

- **axon hillock** -- initial segment (→arises from the perikaryon)
- **axolemma** (axon + Gr. eilema,sheath) (→plasma membrane)
- **axoplasm** –cytoplasm
- **initial segment** (only myelinated axons) → summation of excitatory & inhibitory stimuli
- **Collateral branches**
- Axon **terminals**

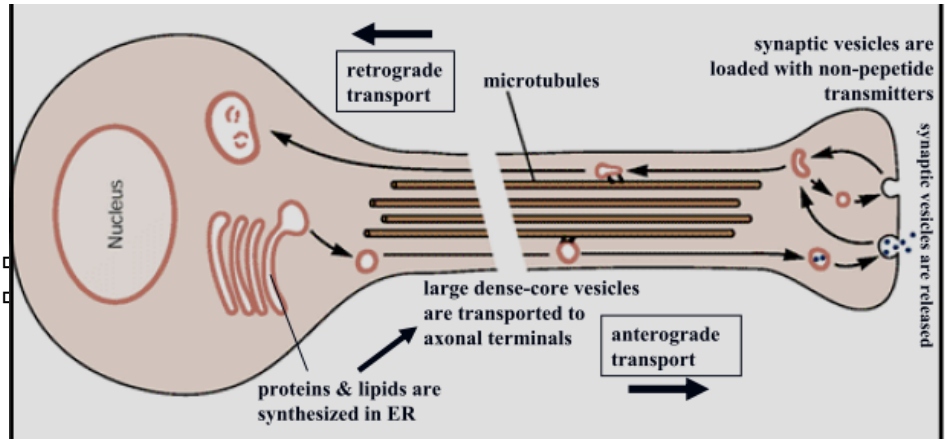
Axonal organelles

- Has **no RER** but preserves some SER → the absence of ribosomes & RER emphasizes the dependence of the axon on the perikaryon for its maintenance
- **Mitochondria** are especially abundant in the axon terminals
- Abundant in axons (also in soma) are **neurofilaments** → intermediate filaments

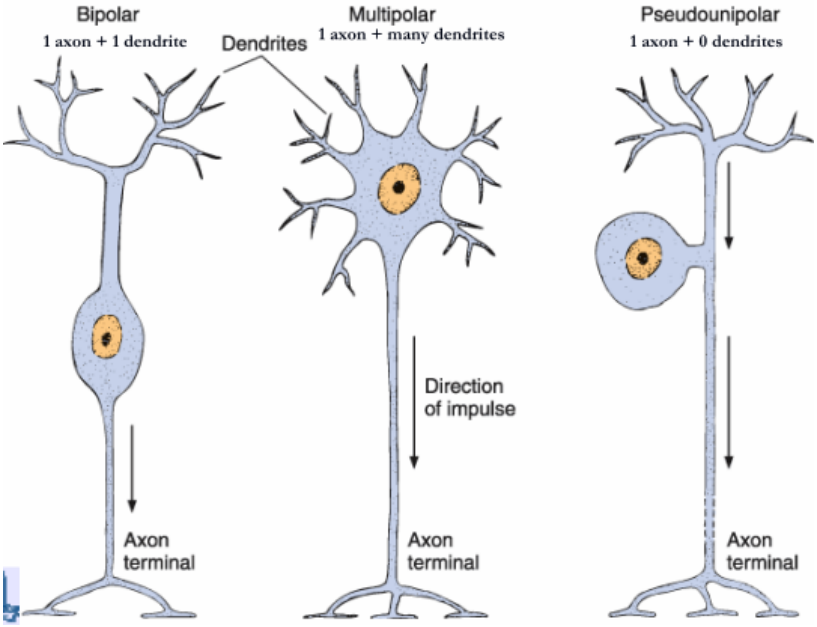
  → Neurofilaments are heteropolymers of proteins assembled from three polypeptide subunits



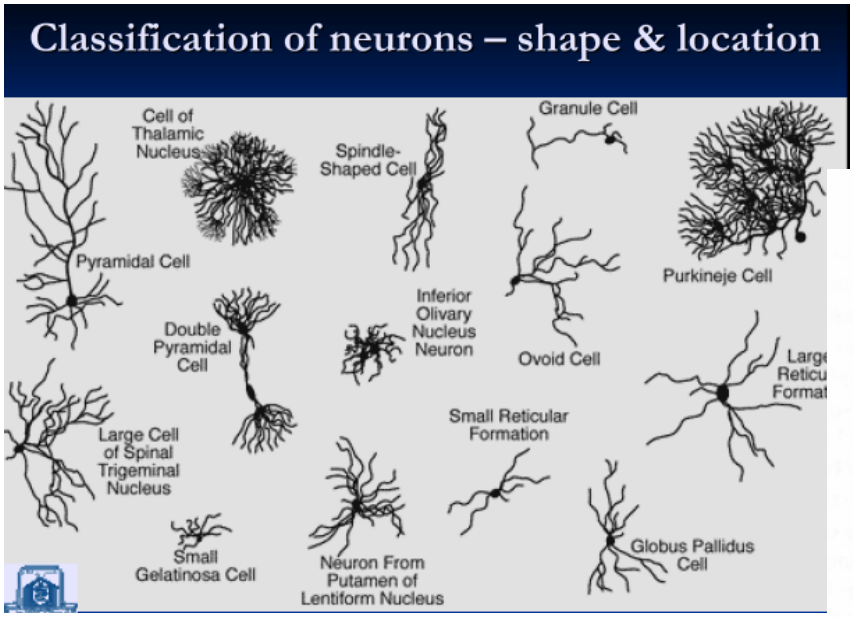
<u>There is a lively bidirectional transport of small and large molecules along the axon.</u>

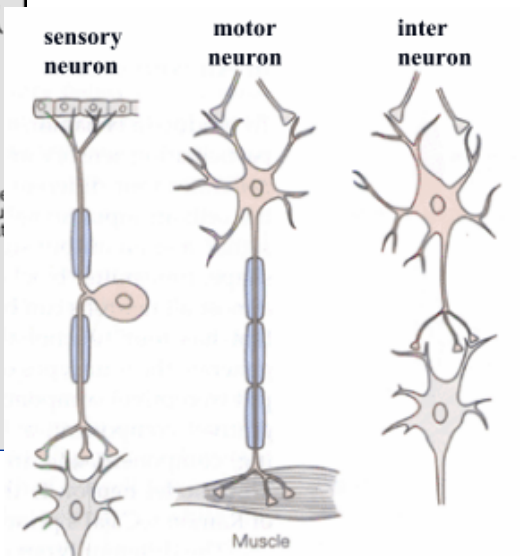


Types of neurons – basic morphological characteristics

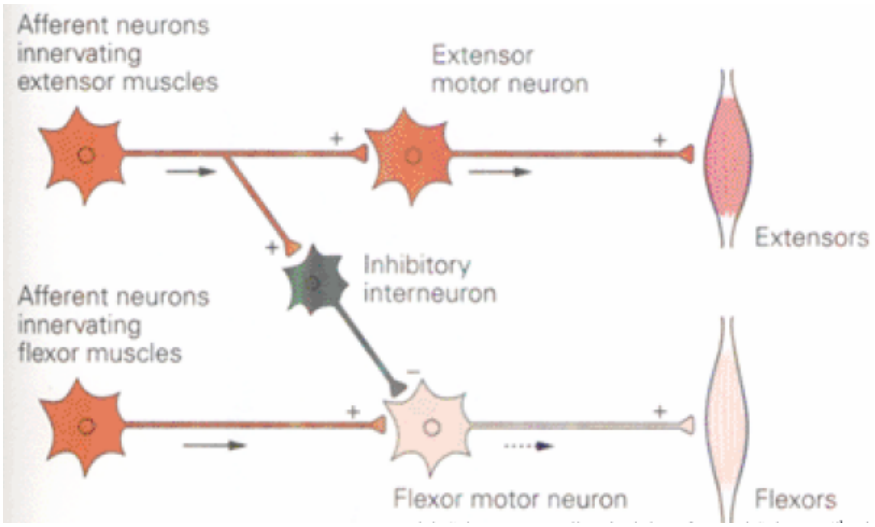


Neuronal type	% of neurons	Location
Pseudounipolar	0.5	Dorsal root ganglia of spinal cord Cranial nerve ganglia of brain stem Mesencephalic trigeminal nucleus in midbrain
Bipolar	0.5	Retina, inner ear, taste buds
Multipolar		
PNS	0.1	Autonomic ganglia
CNS	99.8	Brain and spinal cord

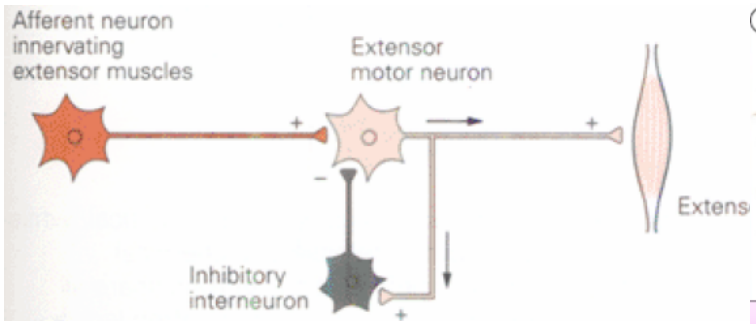


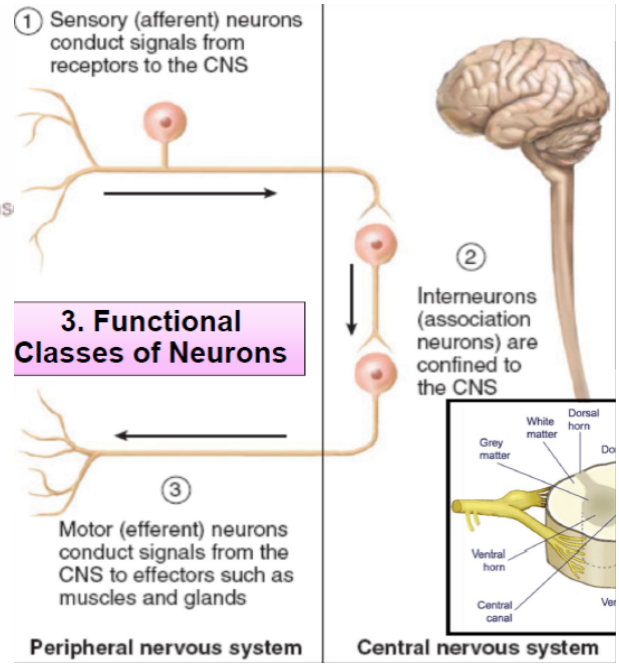


Inhibitory interneurons – feed forward inhibition



Inhibitory interneurons — feedback inhibition





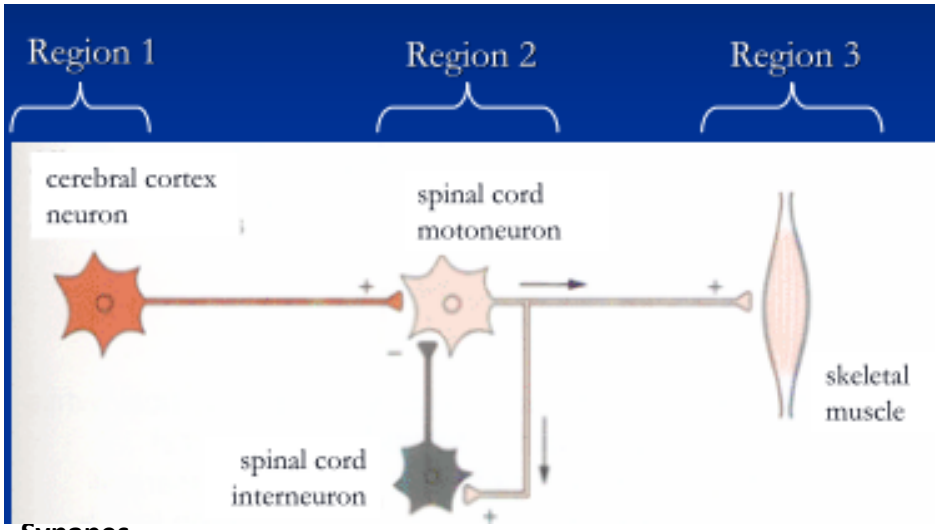
Functional classes of neurones

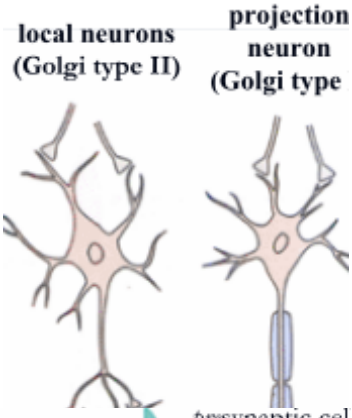
1) **Sensory** (**afferent**) **neurons**
- are specialized to detect stimuli such as light, heat, pressure, and chemicals, and transmit information about them to the CNS.
- afferent refers to signal conduction toward the CNS.
- Some sensory receptors, such as pain and smell receptors, are themselves neurons. In other cases, such as taste and hearing, the receptor is a separate cell that communicates directly with a sensory neuron.

2) **Interneurons** (association neurons) lie entirely within the CNS.
- The word interneuron refers to the fact that they lie between, and interconnect the incoming sensory pathways and the outgoing motor pathways of the CNS.
- About 90% of our neurons are interneurons. Functional Classes of Neurons

3) **Motor (efferent) neurons**
- send signals pre-dominantly to muscle and gland cells, the effectors that carry out the body's responses to stimuli.
- These neurons are called motor neurons because most of them lead to muscle cells, and efferent neurons to signify the signal conduction away from the CNS.

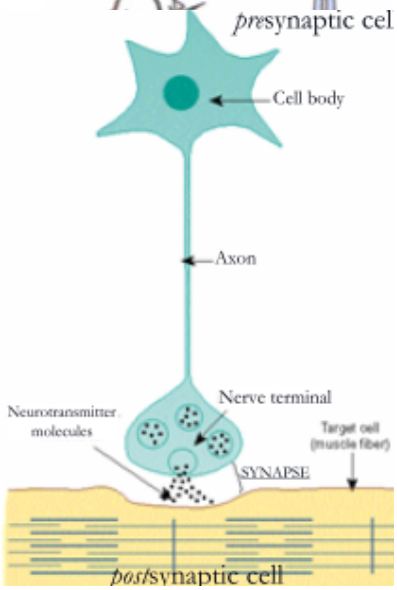
Classification of neurons –**region**alization





Synapes

- Synapses are specialized junction between neurons which facilitate transmission of information
- also occur between target organs (muscles, glands, etc.)

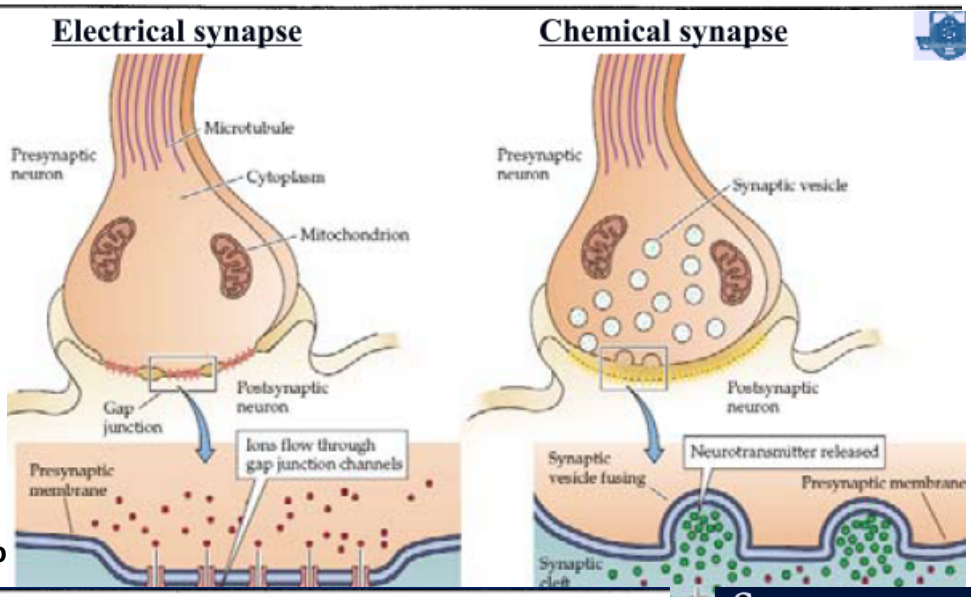


Challenges to the neuron doctrine

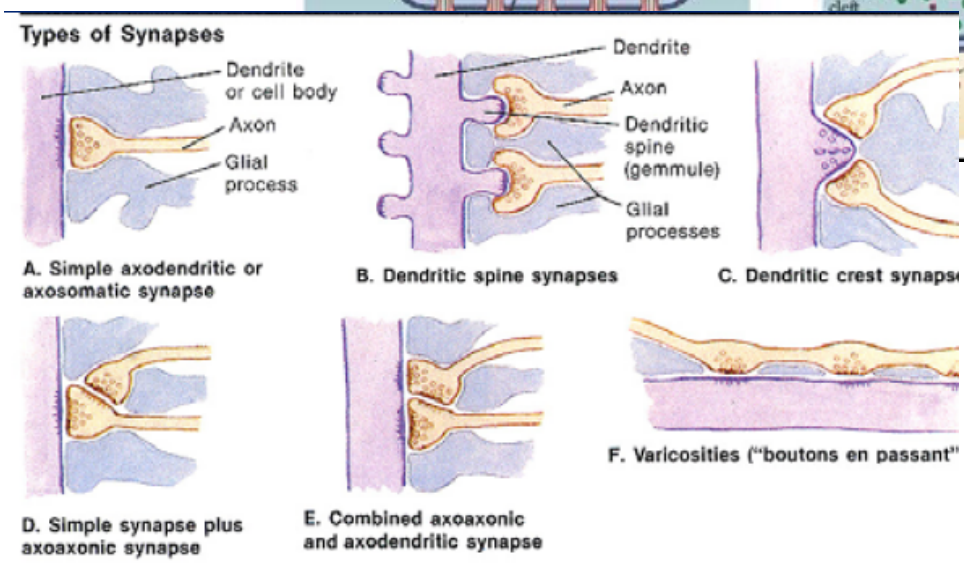
- Dendrites, like axons, also have voltage gated ion channels and can generate electrical potentials
  →which convey information to and from the soma
- Role of glia in processing neural information
  →<u>neurons may not be the sole information</u> processing cells in the nervous system

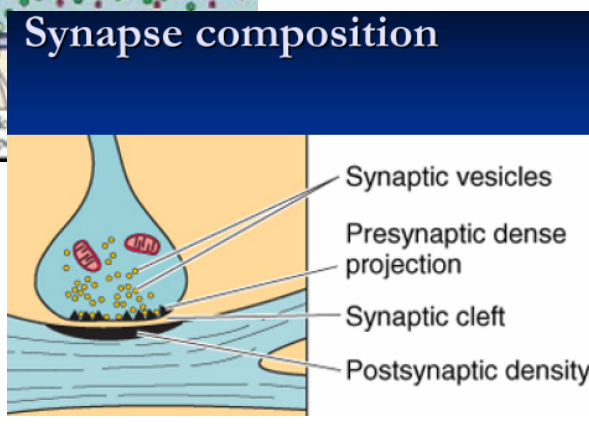
Classification of synapses — mechanisms of information transfer

Type of synapse	Distance between pre- and postsynaptic cell membranes	Cytoplasmic continuity between pre- and postsynaptic cells	Ultrastructural components	Agent of transmission	Synaptic delay	Direction of transmissior
Electrical	3.5 nm	Yes	Gap-junction channels	Ion current	Virtually absent	Usually bidirectional
Chemical	20–40 nm	No	Presynaptic vesicles and active zones; postsynaptic receptors	Chemical transmitter	Significant: at least 0.3 ms, usually 1–5 ms or longer	Unidirec-tional

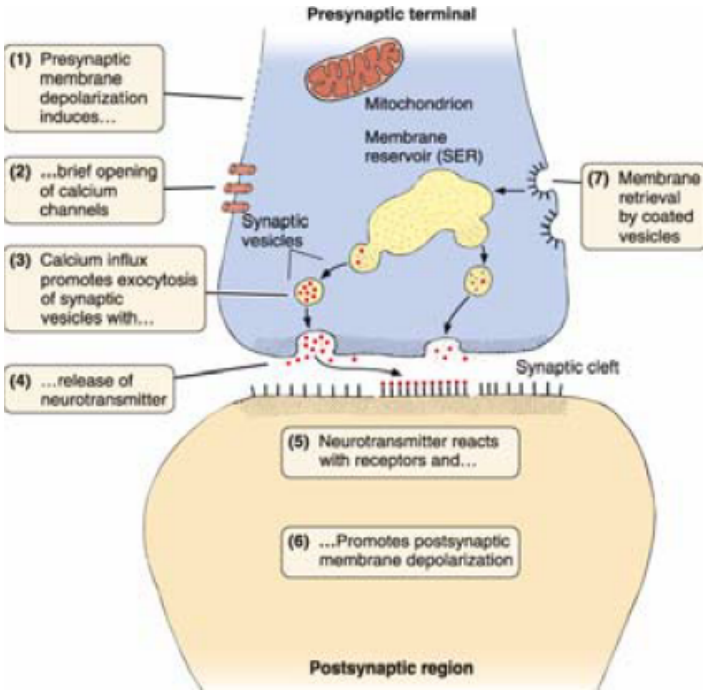


Morpho





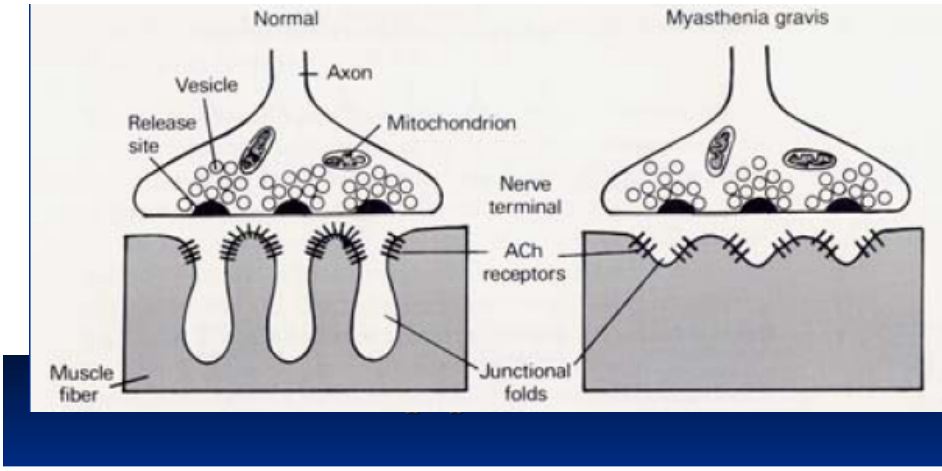
The synaptic vesicle cycle



Disease:

⇨ Bacterial toxins are proteases degrading membrane proteins

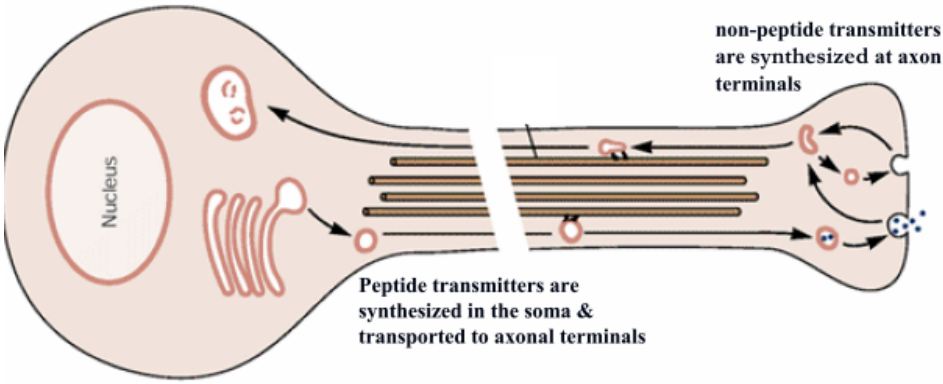
- Tetanus toxin → tetanus
- Botulinum toxins → botulism



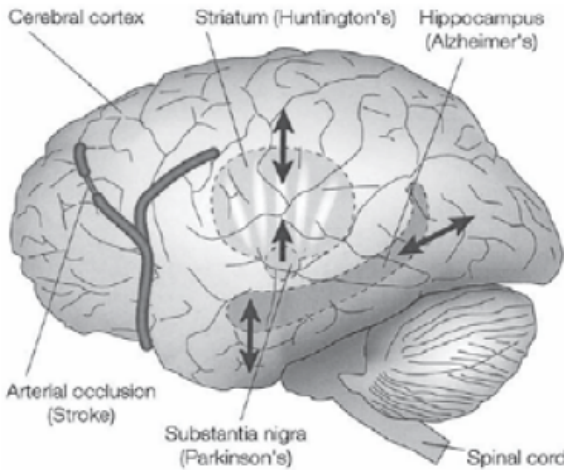
- Myasthenia gravis → (consequence: Ptosis *[Herabhängen eines oder beider oberen Augenlider]*

Classical neurotransmitters:

Neurotransmitter	*Postsynaptic effect*[a]	*Type of vesicle*
ACh	Excitatory	Small, clear
Glutamate	Excitatory	Small, clear
GABA	Inhibitory	Small, clear
Glycine	Inhibitory	Small, clear
Catecholamines (epinephrine, norepinephrine, dopamine)	Excitatory	Small dense-core, or large irregular dense-core
Serotonin (5-HT)	Excitatory	Large, dense-core
Histamine	Excitatory	Large, dense-core
ATP	Excitatory	Small, clear
Neuropeptides	Excitatory and inhibitory	Large, dense-core

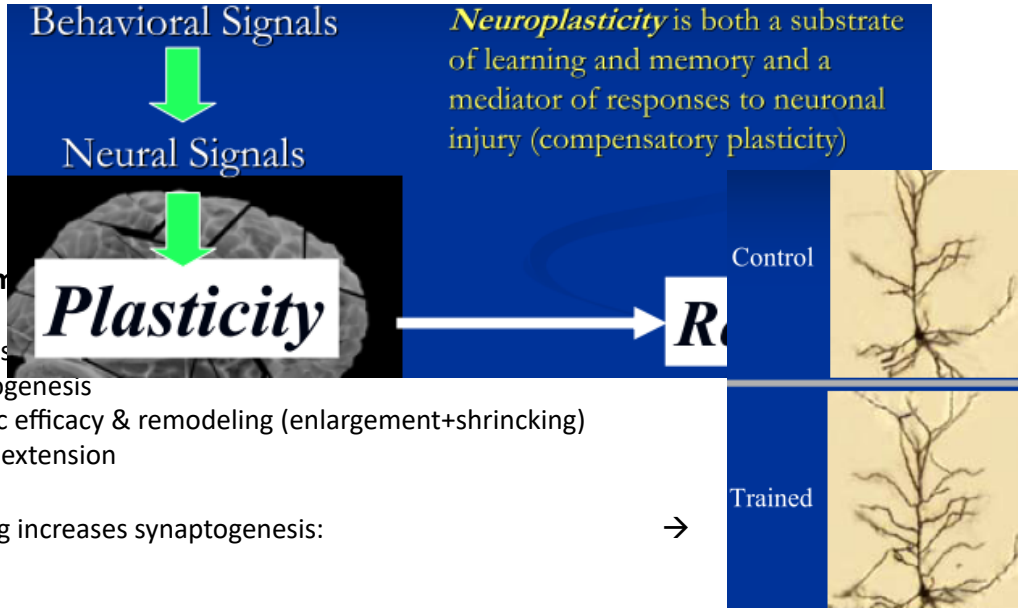


Selective vulnerability of certain neurons in disorders different neurodegenerative disorders



Neuroplasticity:

- is a continuous process in reaction to neuronal activity and neuron injury,
- which involves modulation of structural and functional processes of axons, dendrites, and synapses.



Structural elem

- Cell divis
- Synaptogenesis
- Synaptic efficacy & remodeling (enlargement+shrincking)
- neurite extension

⇨ Learning increases synaptogenesis: →

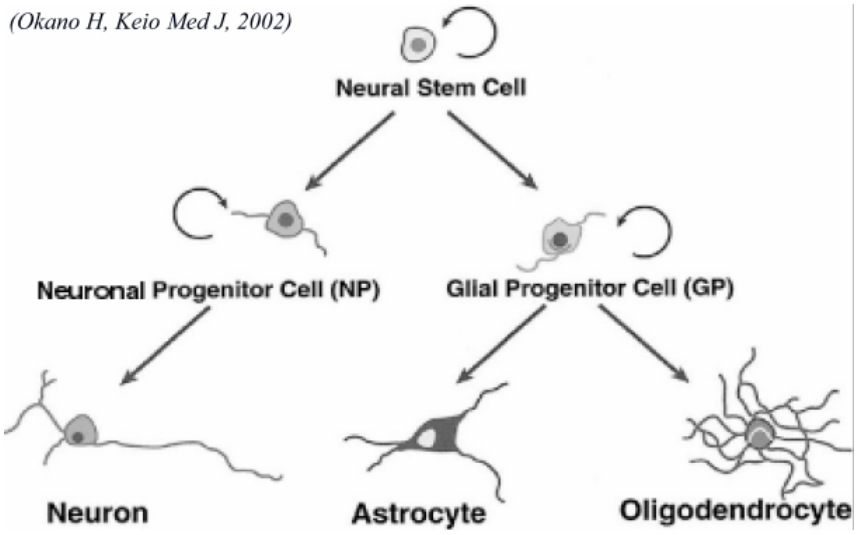
⇨ Targets secrete trophic factors for innervating structures

- ⇨ The neural tube is composed of stem cells which generate all neurons & glia (except microglia)
- ⇨ Microglia have bone marrow origin (derive from monocytes)
- ⇨ Neural induction is orchestrated by signals from adjacent tissue

Neurogenesis

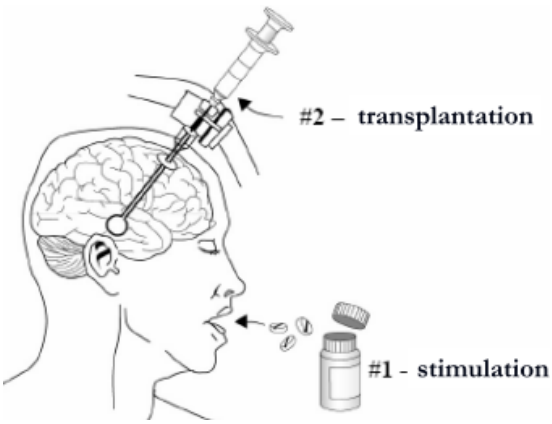
Neurons can can not undergo mitosis -- Only their progenitors can!

The concept of neural stem cells in adult mammalian brain

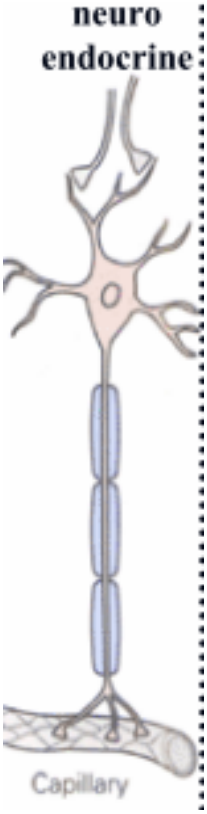


- ⇨ Stem cells in adult human brain are in the periventricular subependymal zone

Stem cell-based therapeutic approaches



Neuroendocrine cells (*endokrin* „nach innen abgebend“)



Hormones:

- Oxytocin
- Vasopressin

Diffuse Neuroendocrine System (DNES)

- Synonyms: APUD (Amine Precursor Uptake and Decarboxylation) paraneurons cells;
- Not designated as neurons, but closely related to neurons on the basis of:

  → fine structure (possession of synaptic vesicle--like granules)
  →metabolism (production of neurotransmitter like substances)
  →origin (neural crest)

- **Apudomas** are <u>tumors</u> derived from polypeptide secreting cells of the DNES.
  →Clinical symptoms depend on the specific chemical messenger produced

Nervous tissue

Glia

Neuroglia (= glia)

Numerous cells which surround both cell bodies and processes of neurons and occupy the interneuronal spaces; function in the physical and metabolic support of neurons

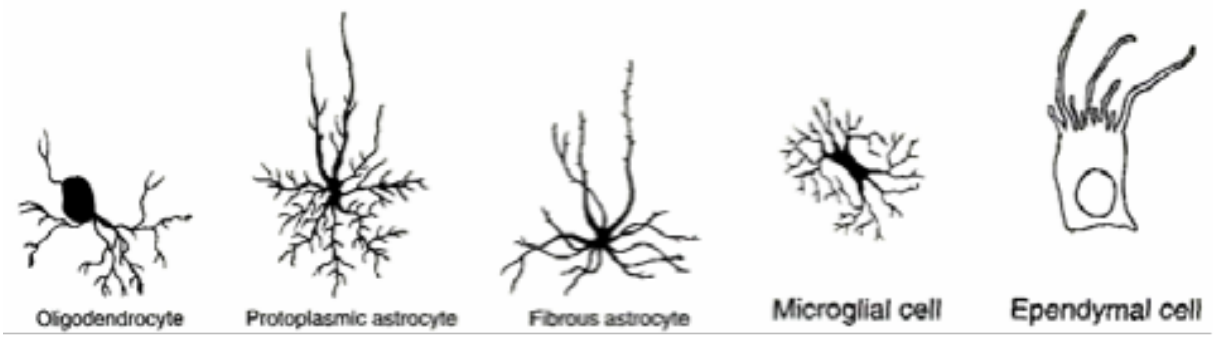
Major cell types of the nervous system

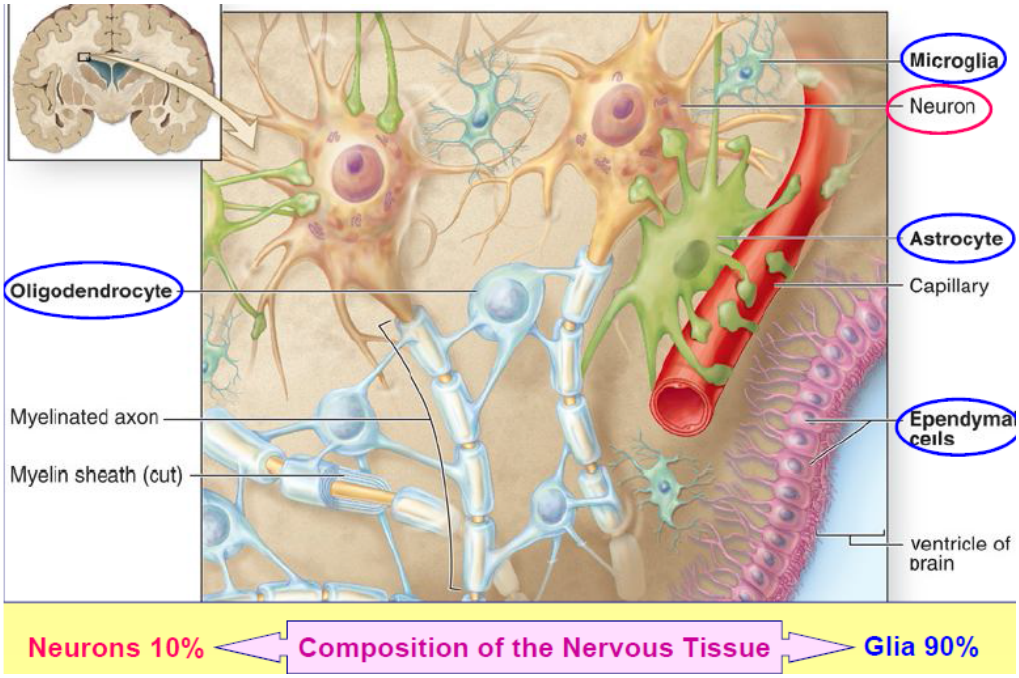
Neurons: **10^{11} in the human brain**

Glia: **10-50 *per* neuron**

- **macroglia**
    - **Oligodendrocytes**
    - **Schwann cells**
    - **Astrocytes**
    - **Ependymal cells**
- **Microglia**

Major types of glia – Golgi stain



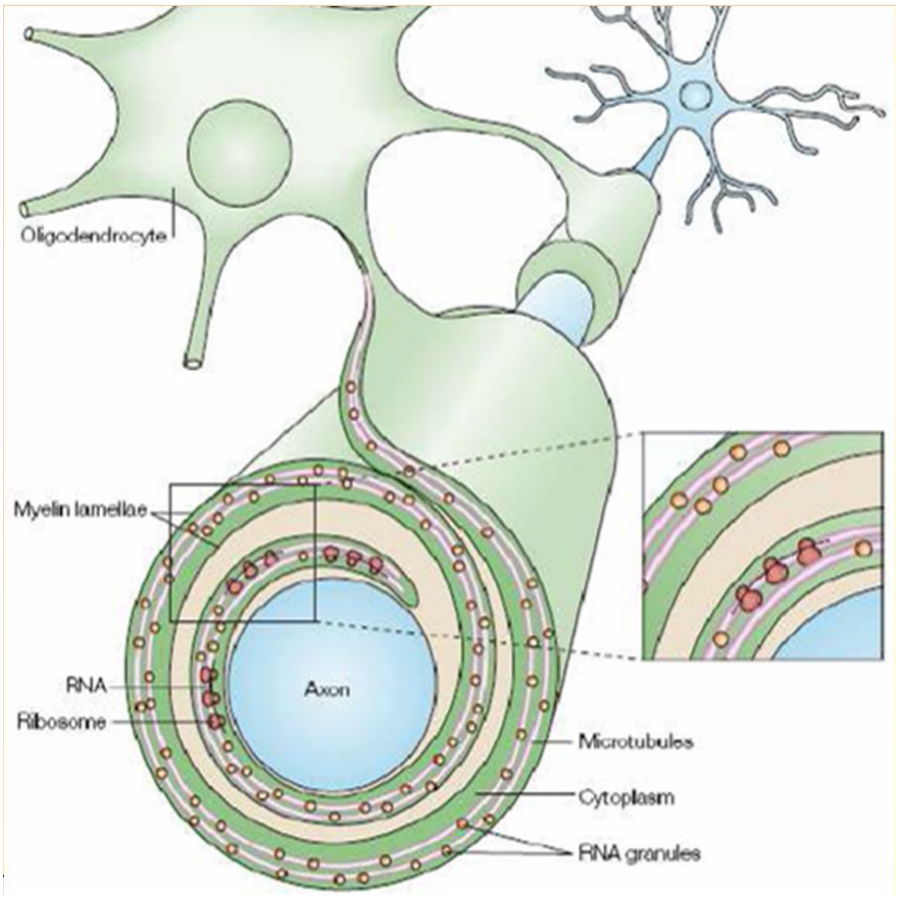


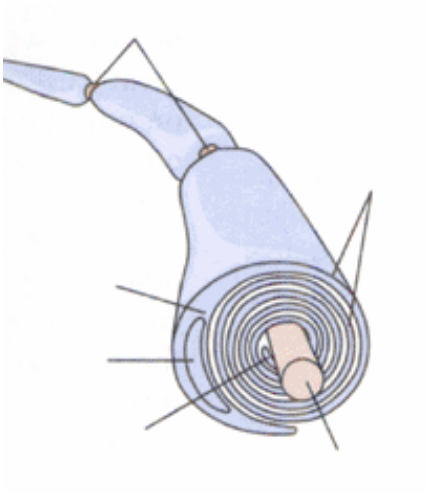
Oligodendrocytes

general features:

- **Contain fewer processes than astrocytes, with sparse branching (Gr. *oligos,* small, + *dendron* + *kytos,* cell)**
- **Smaller than astrocytes**
- **Location - CNS gray & white matter**
- **Abundant RER, Golgi; MT & Mit also present**
- **Types of oligodendrocytes**
  - **Interfascicular →myelin**
  - **Satellite →closely to cell bodies of large neurons**

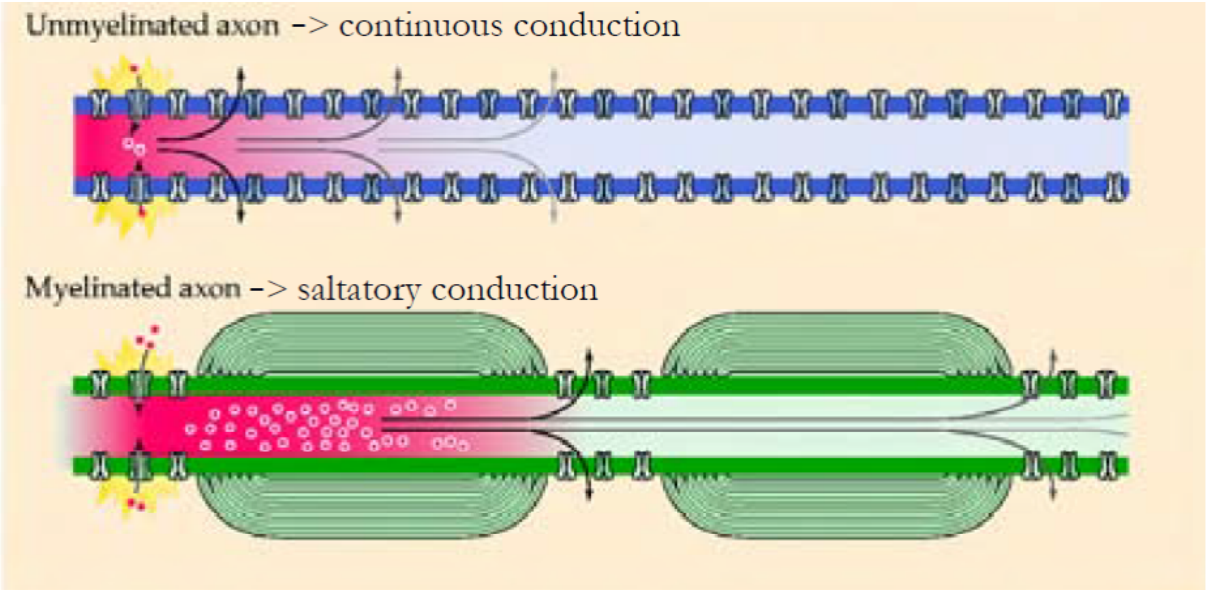
Oligodendrocyte *vs* Schwann cell





Myelin is the plasmalemma of OL organized into a sheath that is wrapped several times (up to 50) around the axon

What is the advantage of myelination?



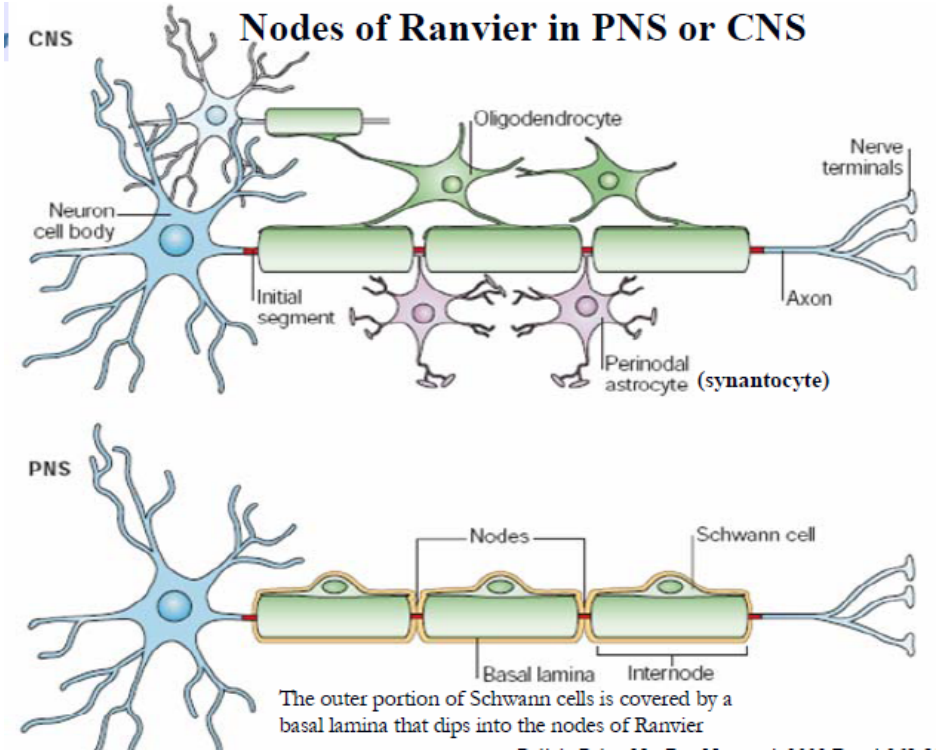
Functions of myelin

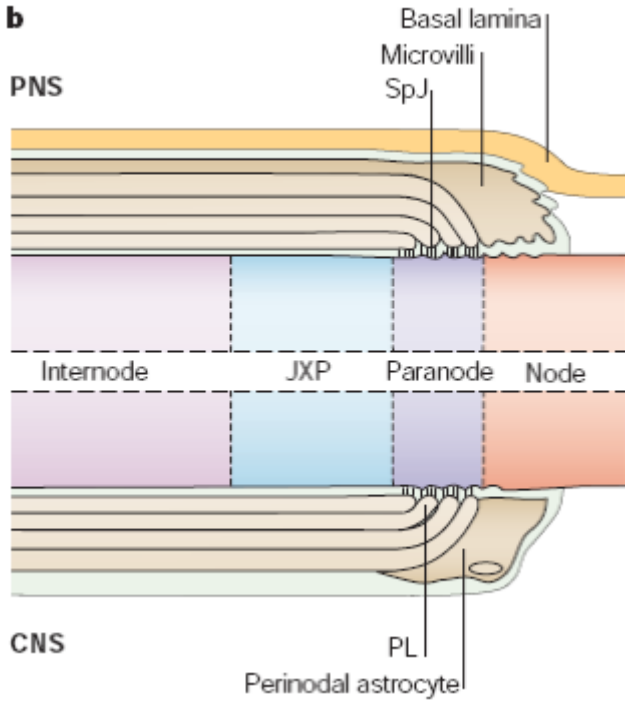
Prevents the outward movement of the excess Na+ in the axoplasm associated with the action potential

A track for regeneration – in PNS only (unmyelinated axons & CNS axons do not regenerate)

Nodes of Ranvier

- Interruptions in the myelin sheath at regular intervals along the length of the axon, exposing the axon
- Voltage-gated Na+ channels of the axolemma are clustered mostly at the nodes of Ranvier
- The distance between two nodes is called an **internode** and consists of one Schwann cell (in the PNS). The length of the internode varies between 1 and 2 mm

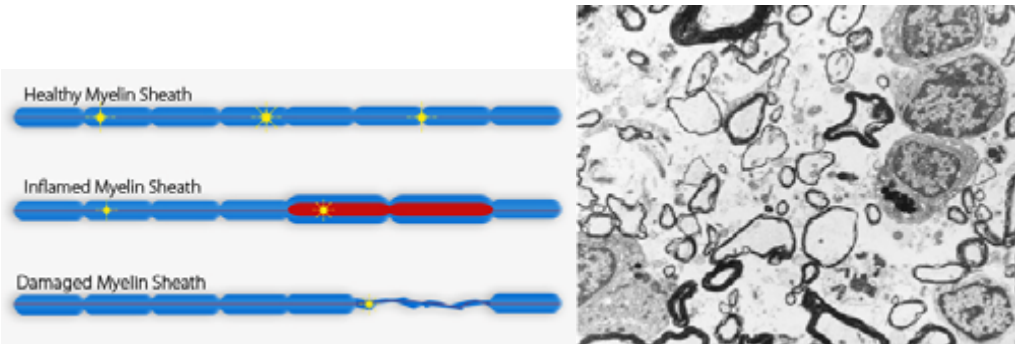




Myelinated fibers consist of molecular domains

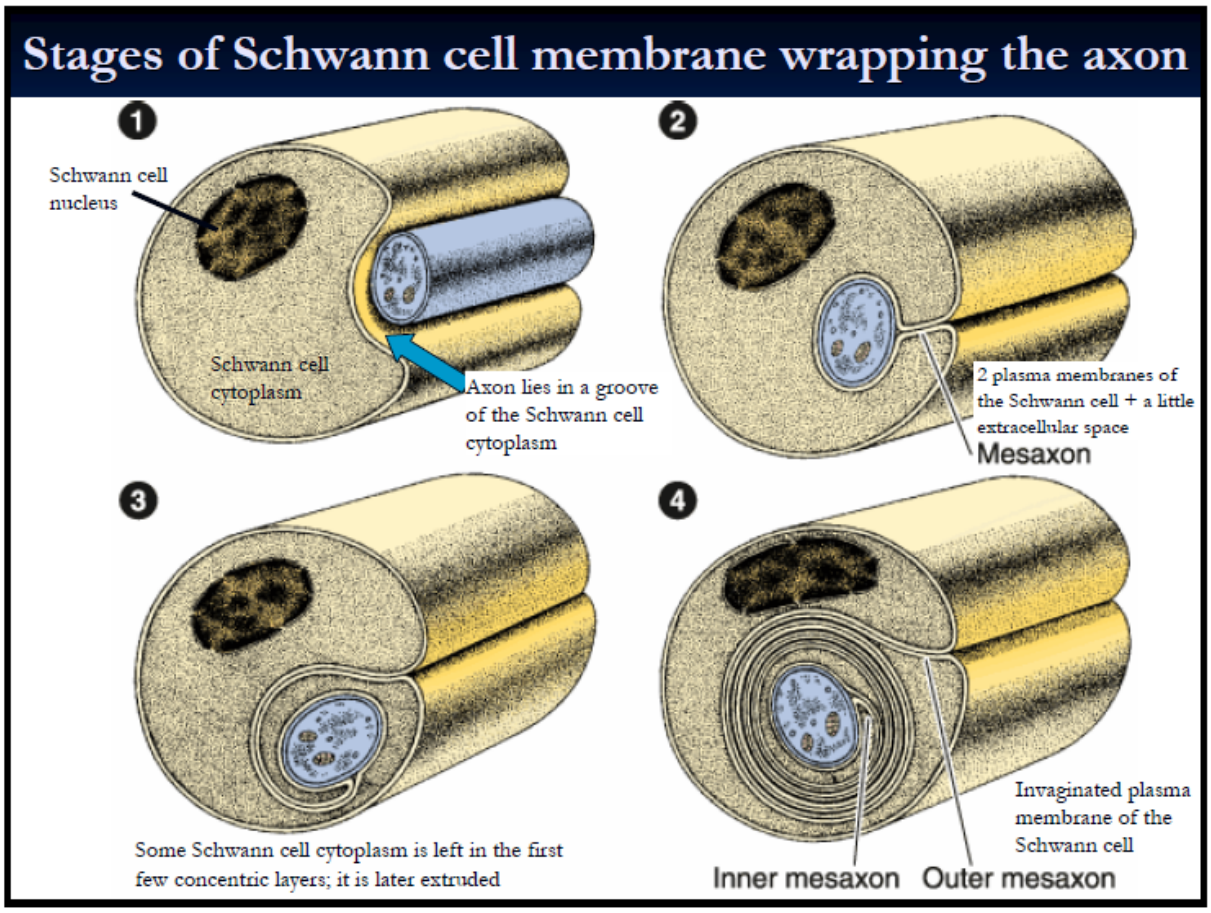
Internode
Paranode
Juxtaparanode
Node of Ranvier

Multiple sclerosis – demyelination in white matter



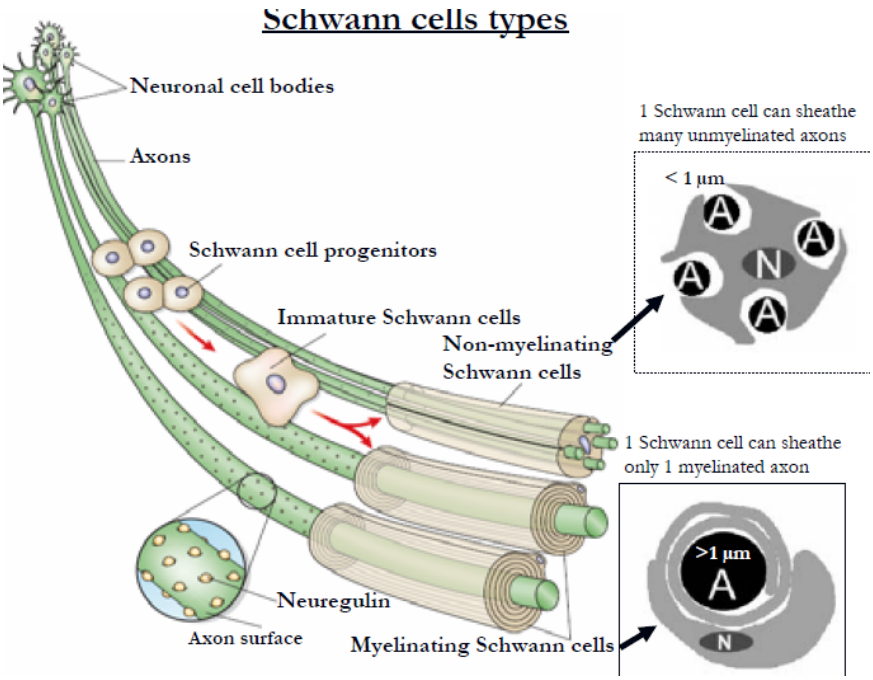
Schwann cells myelinate axons of the peripheral nervous system (PNS)

- ➢ Neurilemma – the layer of Schwann cell cytoplasm ensheathing the axon
- ➢ Schwann cells respond quickly to injury and aid axon regeneration
- ➢ Schwann cells are associated with a number of demyelinating disorders (Charcot–Marie-Tooth disease and Guillain–Barre Syndrome), infected during leprosy and are responsible for the tumors in both neurofibromatosis type 1 and type 2.



Nerve fiber

- ➢ Nerves are bundles of nerve fibers surrounded by connective tissue sheaths
- ➢ Nerve fibers = axons + myelin sheaths
  - myelinated nerve fibers
  - unmyelinated nerve fibers - do not have nodes of Ranvier
    - PNS - enveloped within simple clefts of Schwann cells
    - CNS - non-enveloped, i.e. run free among the other neuronal and glial processes



Peripheral nerve compartments Cellular elements of peripheral nerve compartments

Epineurium – collagen, some adipocytes, vessels

Perineurium – myoepitheloid cells (TJ - blood-nerve barrier), collagen

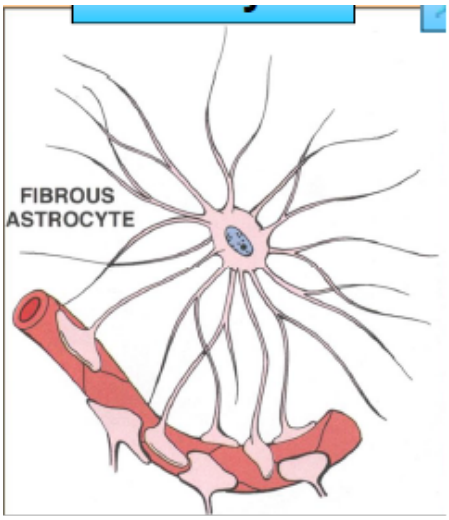
Endoneurium - 90% Schwann cells, 5% - fibroblasts, 5% - other cells

Astrocytes

Glial cells with multiple supportive and barrier functions in CNS

Morphological classification of astrocytes

- Protoplasmic – many short-branched processes
- Fibrous – few long processes
- Protoplasmic – many short-branched processes
- Fibrous – few long processes



Distribution of astrocytes

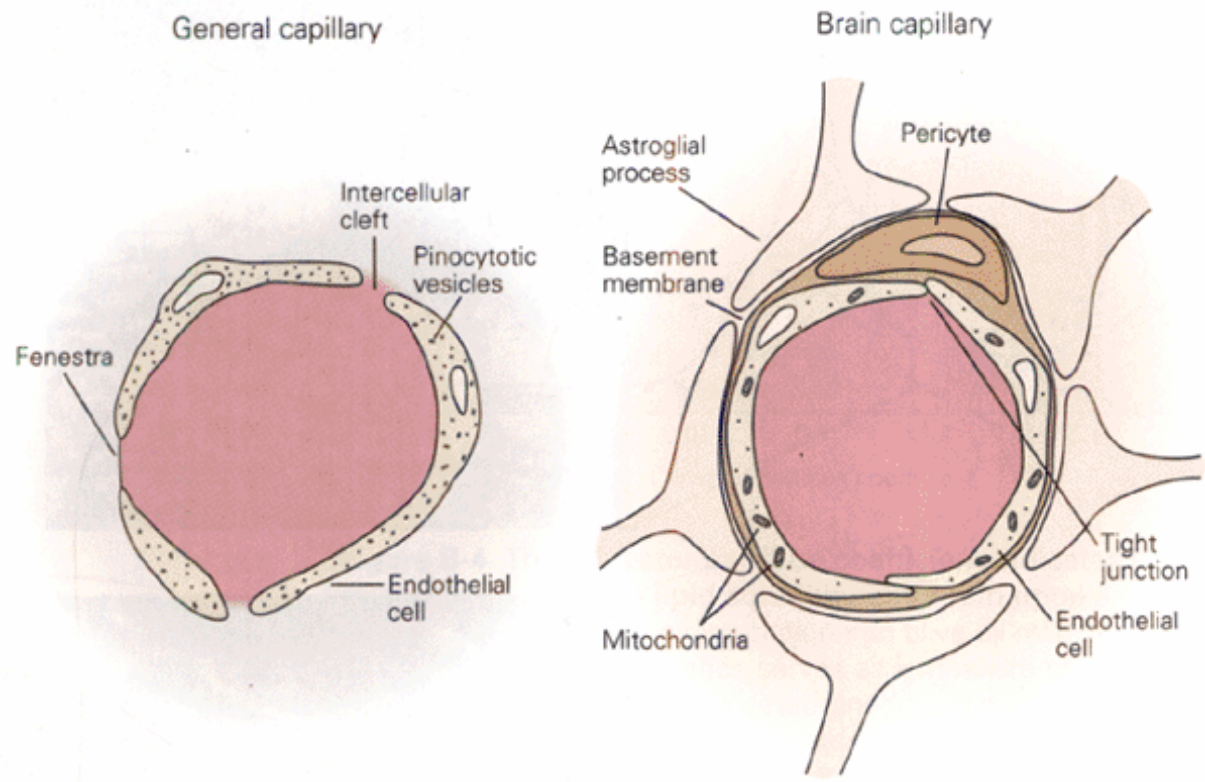
Protoplasmic – gray matter

Fibrous – white matter

Astrocyte Functions

- **Structural support of the brain**
- **Release trophic factors**
- **Maintain neuronal homeostasis – take up ions & tranmitters**
- **Participate in blood-brain barrier**
- **Modulate synaptic function**
- **Radial glia – guide neurons in development and perform the role of progenitors**

Astrocytes & Blood-Brain Barrier (BBB)



Agents modifying brain endothelial function and BBB tightness

Agents that impair BBB function

- **Bradykinin, histamine, serotonin, glutamate**
- **Purine nucleotides: ATP, ADP, AMP**
- **Adenosine, platelet-activating factor**
- **Phospholipase A2, arachidonic acid, prostaglandins, leukotrienes**
- **Interleukins: IL-1α, IL-1β, IL-6**
- **Tumor necrosis factor-α (TNFα), macrophage-inhibitory proteins**
- **Complement-derived polypeptide C3a**
- **Free radicals, nitric oxide**

Agents that cause BBB tightening and improved function

- **Steroids**
- **elevated intracellular cyclic AMP**
- **Adrenomedullin**
- **noradrenergic agents**

Ependymal Cells

Line the fluid-filled spaces in the CNS

- **Gr. *epi* + *endynein* (sink into)**
- **Line the ventricular walls, separate cerebrospinal fluid from white matter**
- **Ciliated**
- **Types**
    - **“classical” ependymocyte**
    - **Tanycyte**

Choroid plexus

Invaginated folds of pia mater, rich in dilated fenestrated capillaries, that penetrate the interior of the brain ventricles

Composed of loose connective tissue (pia mater) covered by cuboidal or columnar epithelium made of ion-transporting cells

Main function - elaborate cerebrospinal fluid

Microglia (Gr. *micros,* small, + *glia*)

Phagocytes that are mobilized after injury - clear debris and damaged structures in the CNS

Derived from fetal monocytes, or their precursors, which invade the developing nervous system

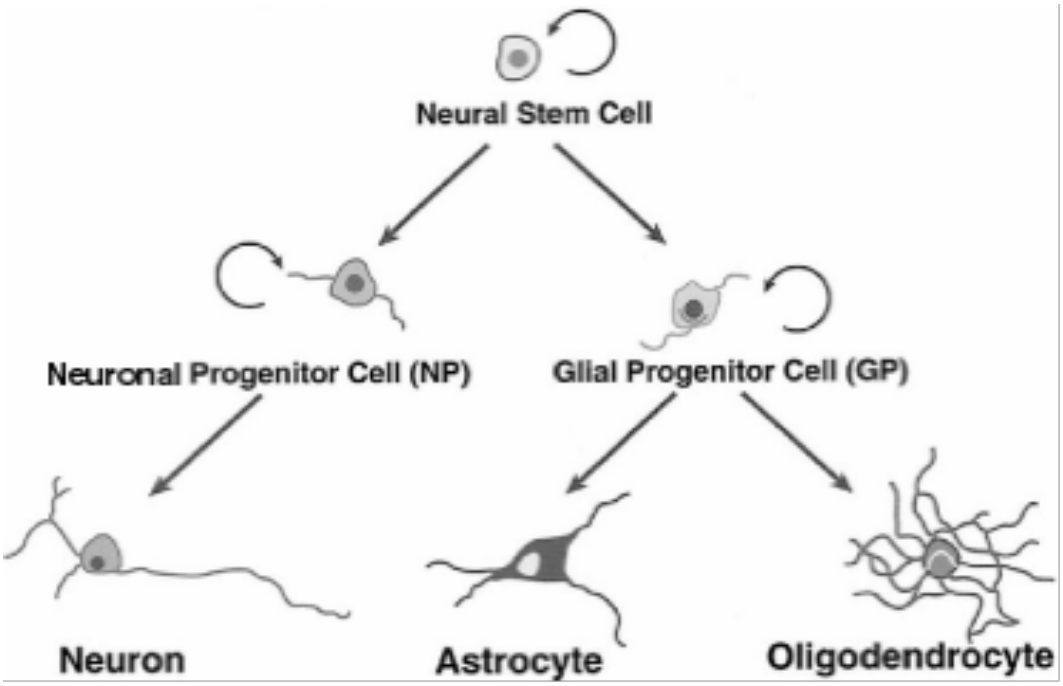
Derivation of glia

- **Neural tube derivatives**
  - Astrocytes
  - Oligodendrocytes
  - Ependymal cells
- **Neural crest derivatives**
  - Schwann cells
  - Satellite cells of peripheral ganglia
  - Cells of the arachnoid and pia mater

Gliogenesis

Generation of glia from stem/progenitor cells

Glial cell can undergo mitosis!



Sensory skin nerve endings

- **The skin is the most extensive sensory receptor**
- **Types of receptors**
  - free nerve endings - epidermis, hair follicles, and cutaneous glands
  - encapsulated and expanded receptors - dermis and subcutaneous tissue
- **Encapsulated corpuscles are not necessary for cutaneous sensation**
  - they act as mechanoreceptors

Free endings are mainly *thermo*- and *noci*receptors

- **Thermoreceptors -respond to temperature differences of about 2° C**
  - **warmth receptors**
  - **cold receptors**
  - **temperature-sensitive nociceptors**
- **Nociceptors - responsible for pain perception**
  - **mechanical stress or damage**
  - **extremes in heat or cold**

- **chemical compounds such as bradykinin, serotonin, and histamine**

Skin mechanoreceptors

(sensory skin nerve endings)

- **Meissner's corpuscles**
  - **the most mechanoreceptors of hairless skin (40% of hand)**
  - **connective tissue capsule + Schwann cell lamellae**
  - **low-frequency vibrations (30–50 Hz) – rough objects**
- **Pacinian corpuscles**
  - **less frequent (20% of hand)**
  - **inner core of membrane lamellae →fluid →outer lamella**
  - **high-frequency vibrations (250–350 Hz) – fine textures**
- **Merkel's disks**
  - **epidermal (20% of hand)**
  - **Light pressure - discrimination of shapes, edges**
- **Ruffini's corpuscles**
  - **deep in the skin + in ligaments & tendons**
  - **sensitive to the cutaneous stretching produced by digit or limb movements**