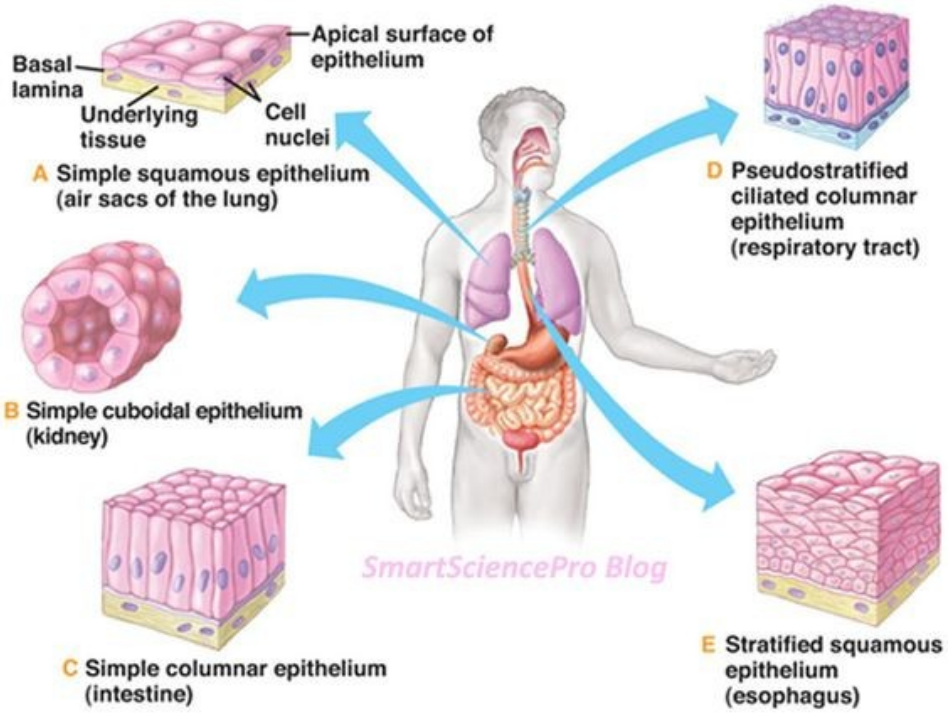



Radhika Reddy, PhD

# CHAPTER 4-7: EPITHELIAL, CONNECTIVE, ADIPOSE, CARTILAGE

# Tissues

Cells work together in functionally related groups called tissues

Types of tissues:

1. Epithelial – lining and covering
2. Connective – support
3. Muscle – movement
4. Nervous – control

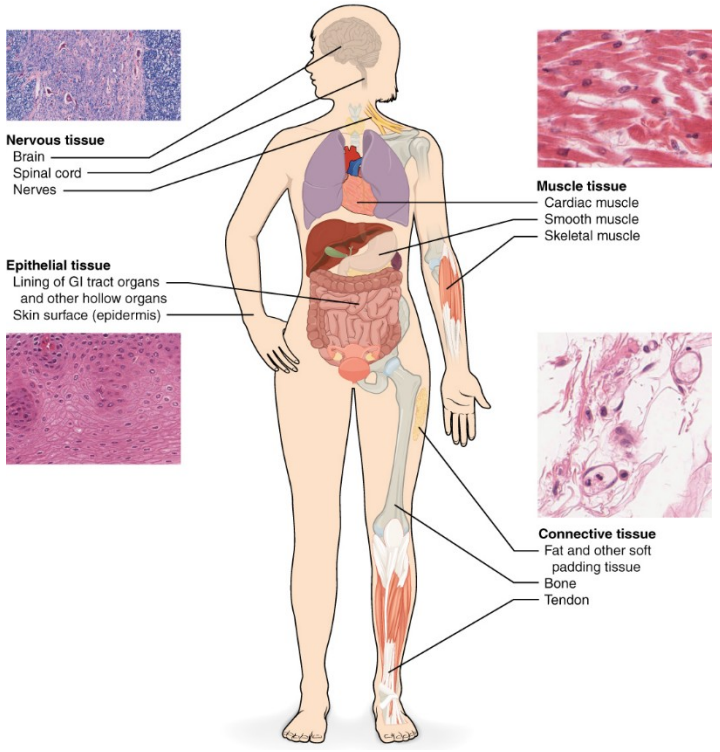
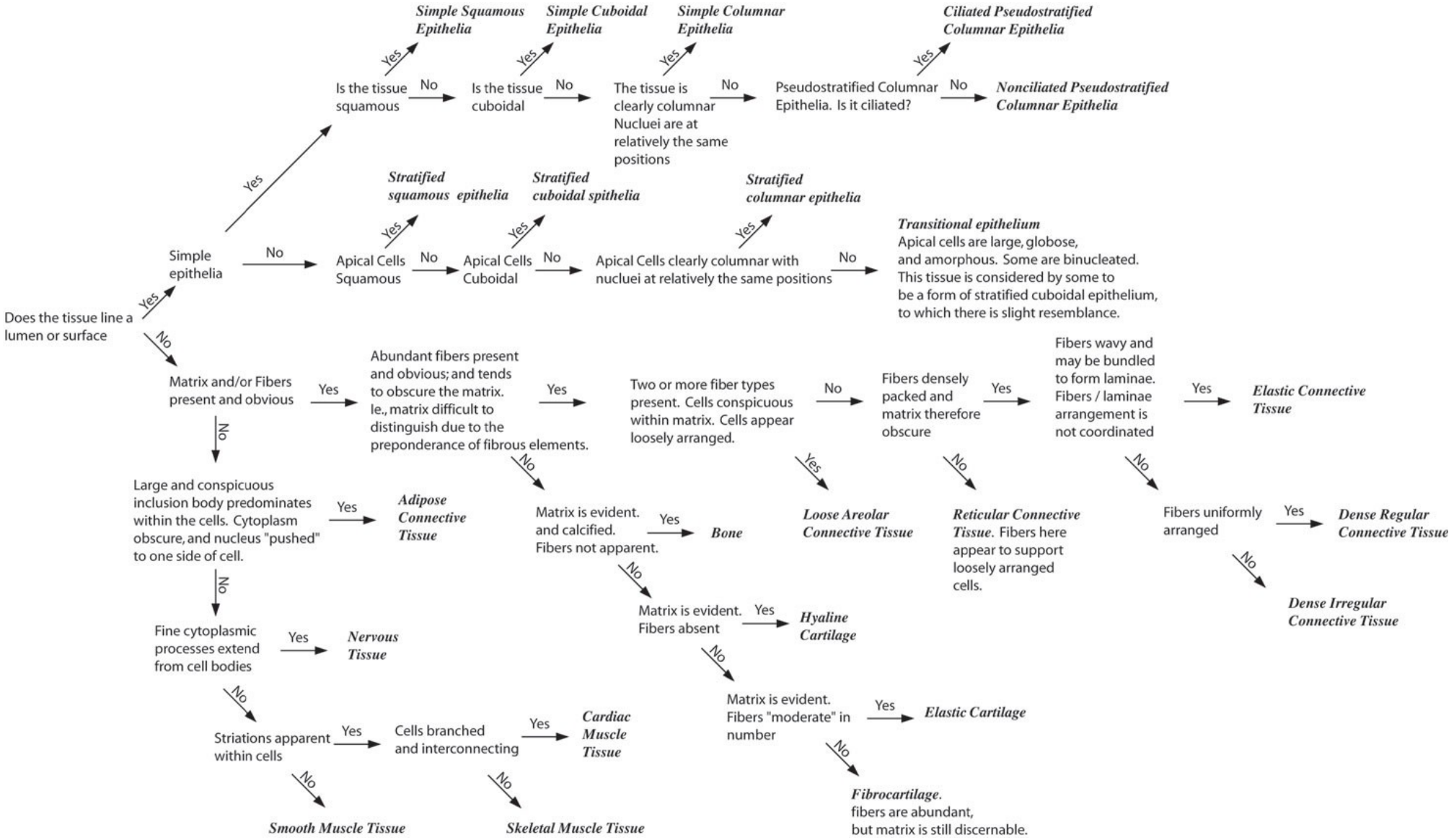



TABLE 4–1 Main characteristics of the four basic types of tissues.

| Tissue | Cells | Extracellular Matrix | Main Functions |
|---|---|---|---|
| Nervous | Elongated cells with extremely fine processes | Very small amount | Transmission of nerve impulses |
| Epithelial | Aggregated polyhedral cells | Small amount | Lining of surface or body cavities; glandular secretion |
| Muscle | Elongated contractile cells | Moderate amount | Strong contraction; body movements |
| Connective | Several types of fixed and wandering cells | Abundant amount | Support and protection of tissues/ organs |

http://www.bozemanscience.com/anatomy-and-physiology-introduction

Watch 3:25-9:25




Help with Histology: https://www.youtube.com/watch?v=ux9rvC5NvQ8

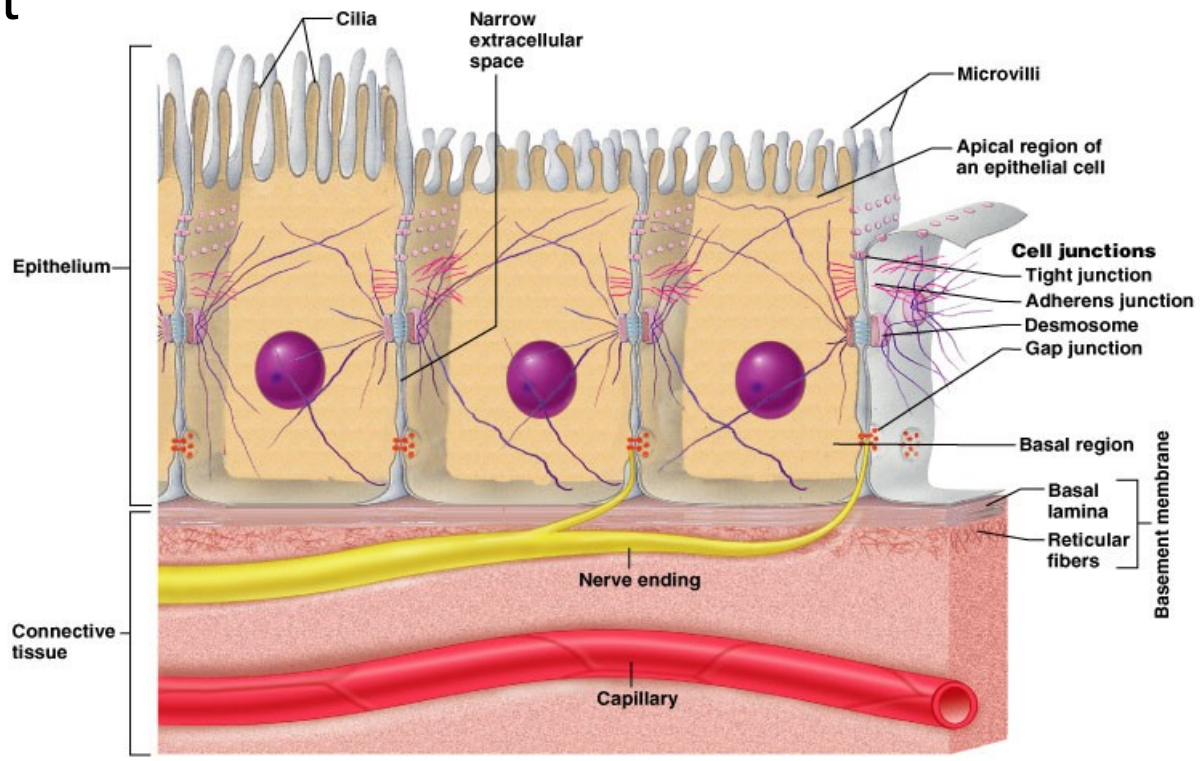
# Chapter 4 Epithelial Tissues Objectives

1. General Characteristics of epithelium
2. Basal domain: basement membrane, basal lamina, focal adhesions, hemidesmosomes
3. Lateral Domain: cell junctions and adhesions
4. Apical domain: microvilli and cilia
5. Glands: exocrine and endocrine
6. Classification of epithelium based on shape and complexity

# Epithelial Tissue: General Characteristics & Functions

Covers a body surface or lines a body cavity
Forms most glands
Functions of epithelium

1. Protection
2. Absorption, secretion, and ion transport
3. Filtration
4. Forms slippery surfaces



# Special Characteristics of Epithelia

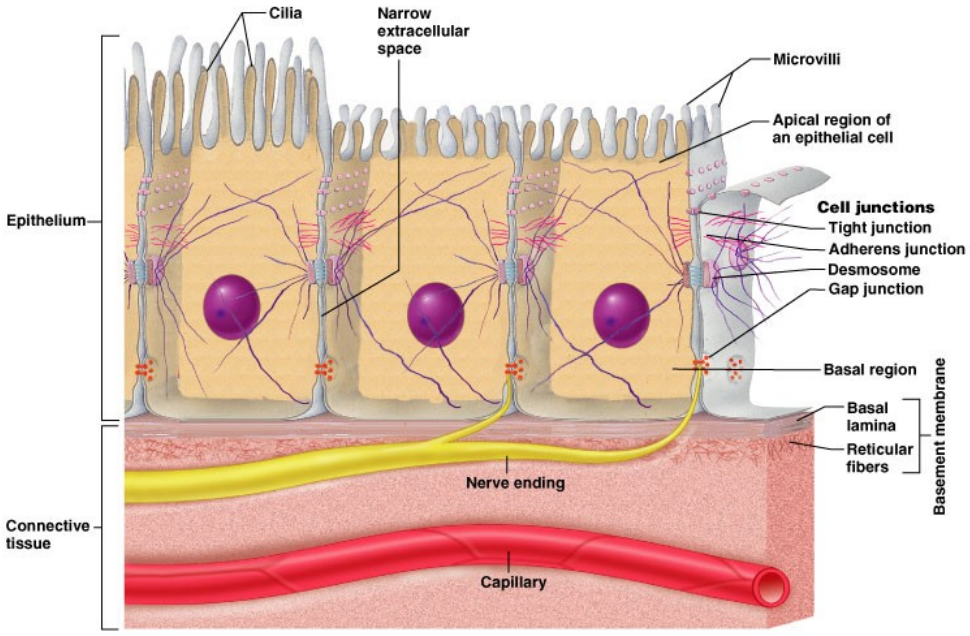
**Cellularity**: cells are in close contact with each other with little or no intercellular space between them
**Specialized contacts**: may have junctions for both attachment and communication
**Polarity:** epithelial tissues always have an **apical** and **basal surface**

**Support by connective tissue:** at the basal surface, both the epithelial tissue and the connective tissue contribute to the **basement membrane**

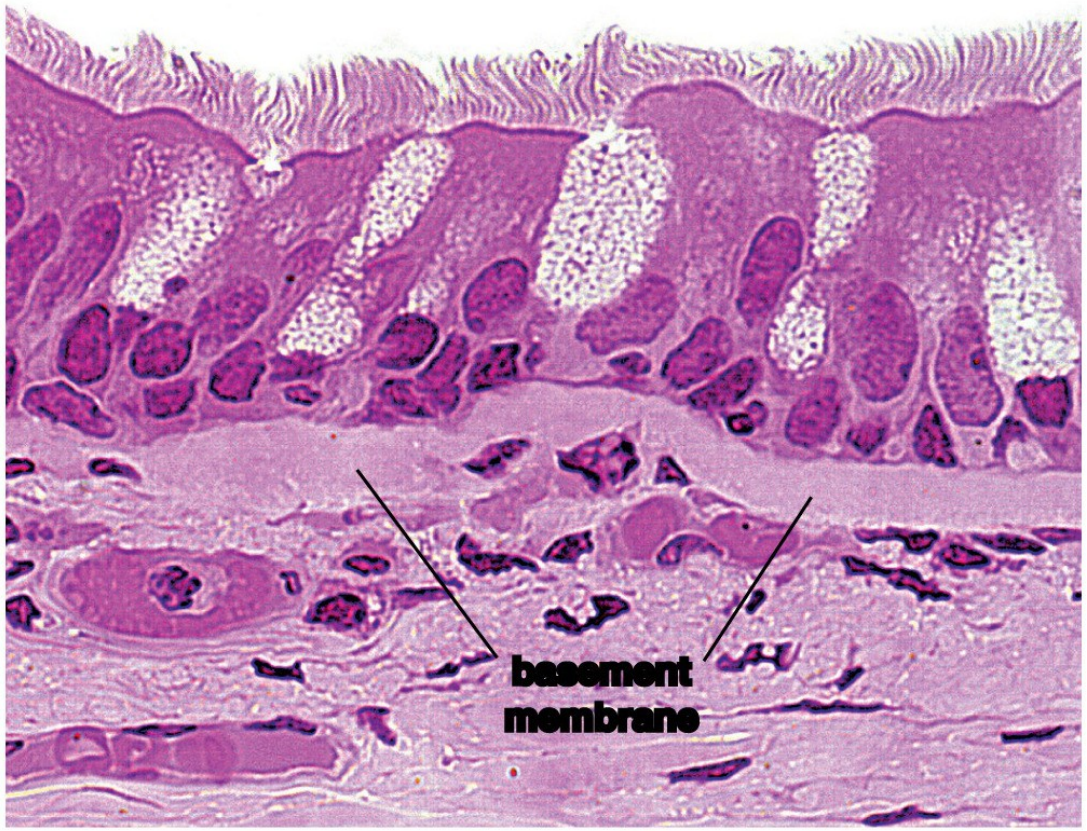
**Avascular:** nutrients must diffuse

**Innervated**

**Regeneration:** epithelial tissues have a high capacity for regeneration



# The basal domain of epithelial cells



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The **basement membrane** is a specialized structure located next to the basal domain of epithelial cells and the underlying connective tissue stroma.

**Cell-to-extracellular matrix junctions** anchor the cell to the extracellular matrix

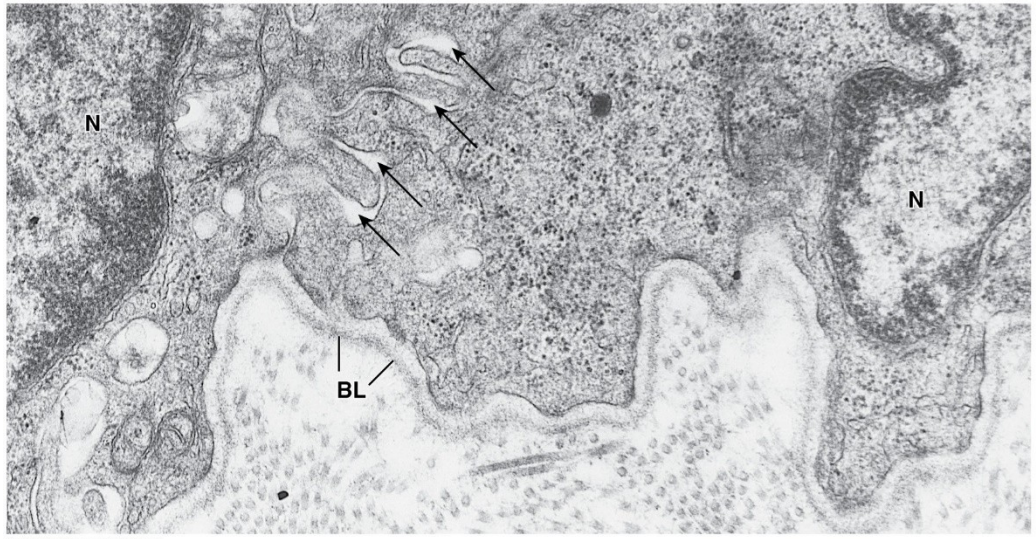
**Basal cell membrane infoldings** increase the cell surface area and facilitate morphologic interactions between adjacent cells and extracellular matrix proteins

# Basement Membrane = basal lamina + reticular lamina

**Basal lamina** (also called **lamina densa**): discrete layer of electron-dense matrix material 40- to 60-nm thick between the epithelium and the adjacent connective tissue

Composed of **laminins**, a **type IV collagen molecule**, and various associated **proteoglycans** and **glycoproteins**.

**Reticular lamina**: below basal lamina, more diffuse and fibrous



Nutrient Absorption in Small Intestine: https://www.youtube.com/watch?v=P1sDOJM65Bc

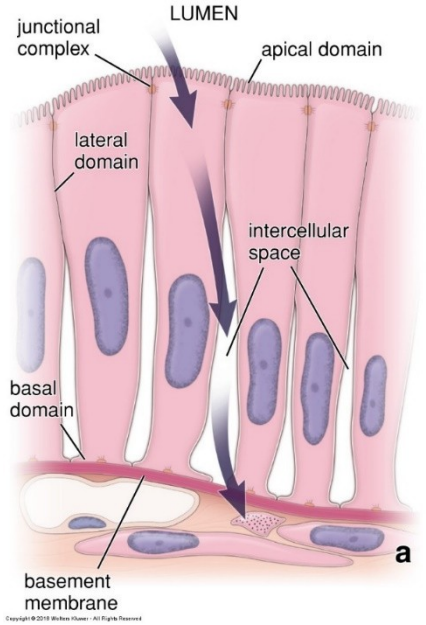
# Cellular domains of epithelia

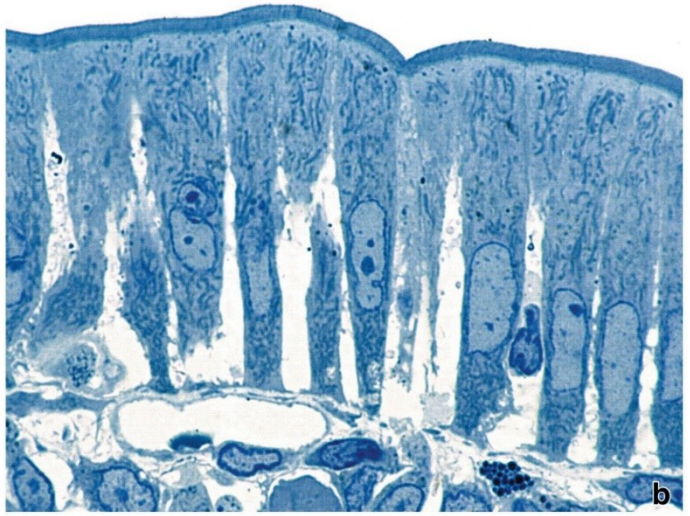
The **junctional complex** provides adhesion between adjoining cells and separates the luminal space from the intercellular space, limiting the movement of fluid between the lumen and the underlying connective tissue.

The **intracellular pathway** of fluid movement during absorption (*arrows*) is from the intestinal lumen into the cell, then across the lateral cell membrane into the intercellular space, and, finally, across the basement membrane to the connective tissue

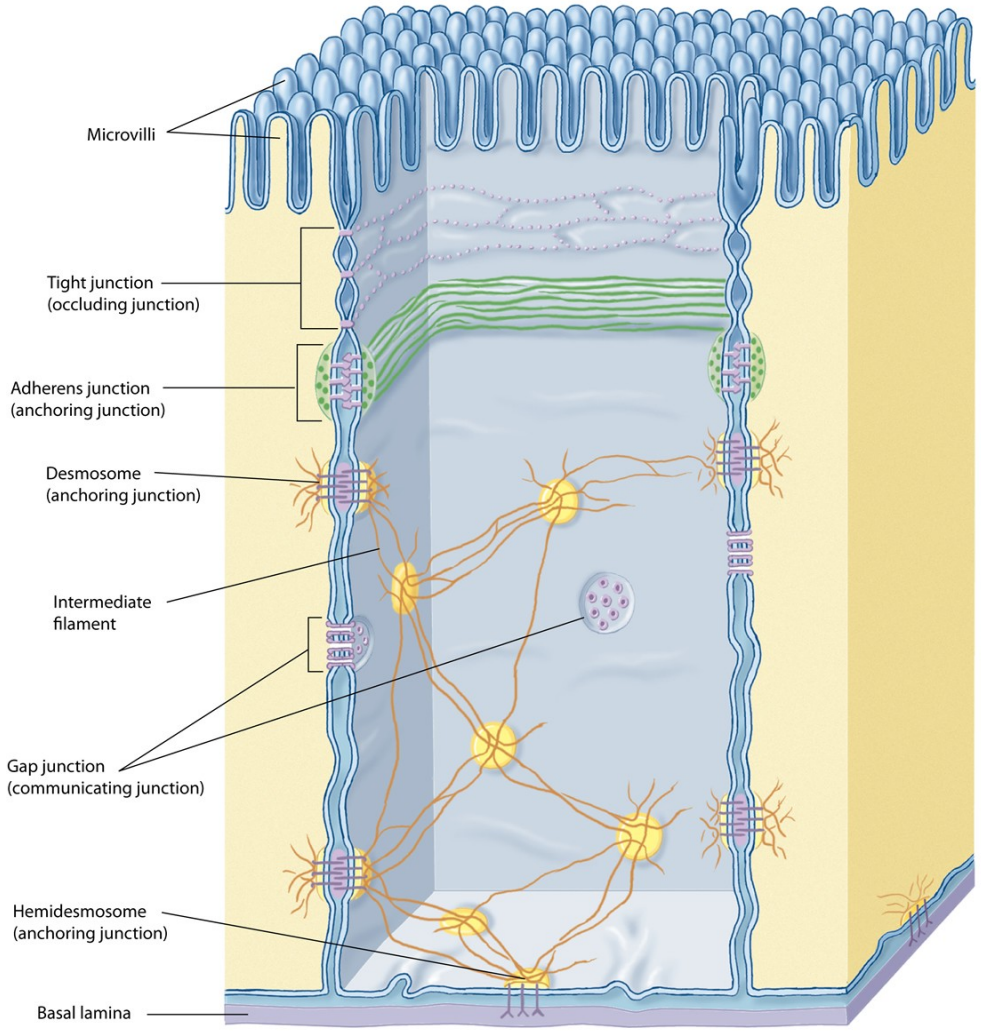
**❯❯ MEDICAL APPLICATION**

The enterotoxin secreted by *Clostridium perfringens*, which causes "food poisoning prevents maintenance of tight junctions, and causes loss of tissue fluid into the intestinal lumen via the intracellular pathway.



# Junctional complexes of epithelial cells.




**Tight Junctions:** prevent passive flow of material between the cells

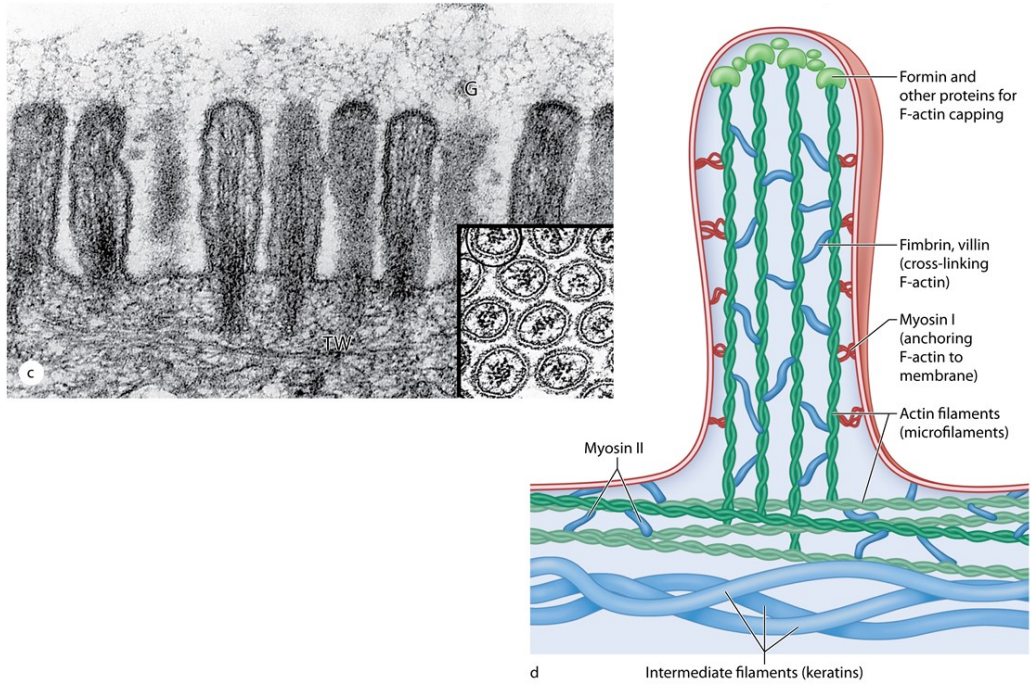
**Adhering junctions:** stabilize and strengthen the circular

**Desmosomes**: form very strong attachment points, play a major role to maintain the integrity of an epithelium.

**Gap junctions:** patch of many **connexons**, serve as intercellular channels for flow of molecules.

**Hemidesmosomes** bind epithelial cells to the underlying basal lamina

# Microvilli are fingerlike cytoplasmic projections on the apical surface of most epithelial cells.




**The internal structure of microvilli contains a core of actin filaments that are cross-linked by several actin bundling proteins.** Actin filaments (*arrows)*

Actin filament–bundling proteins: fimbrin, espin, and fascin

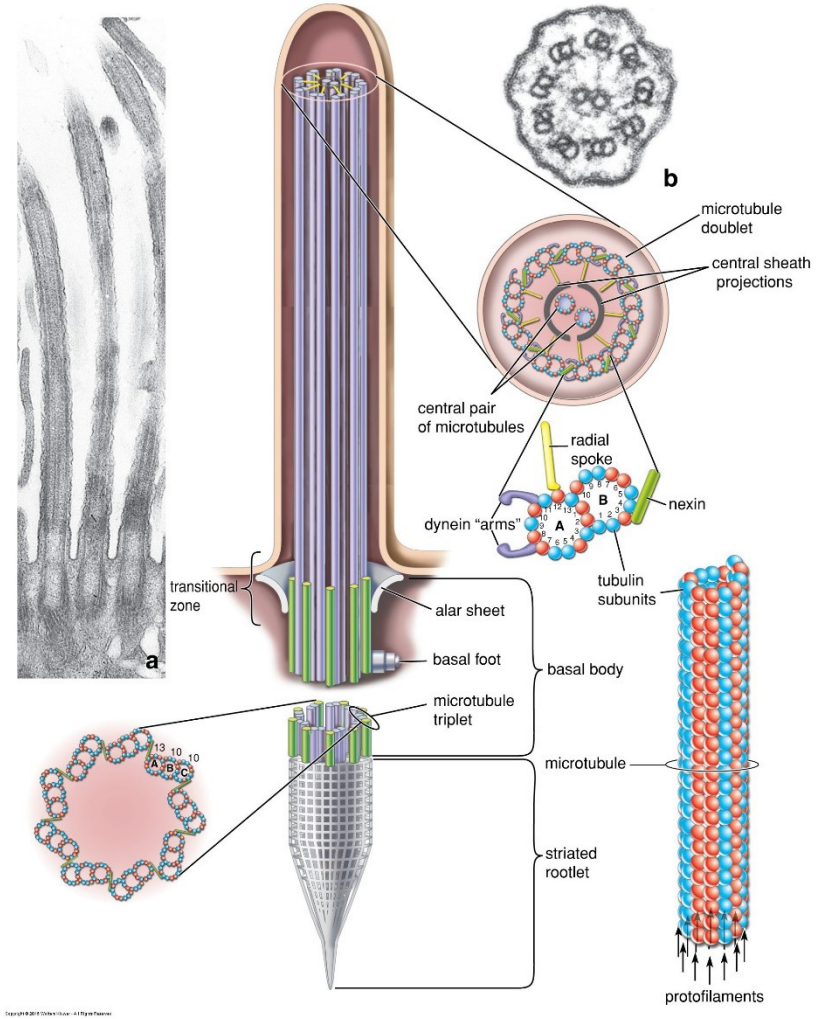
The spectrin molecules stabilize the actin filaments within the terminal web and anchor them into the apical plasma membrane.

Endoscopy of Celiac Disease (0-1:00): https://www.youtube.com/watch?v=WStdJSgf-LQ

**❯❯ MEDICAL APPLICATION**

Celiac disease: loss of microvilli in brush border of the absorptive cells of small intestine, caused by immune reaction against the wheat protein gluten during its digestion, which produces diffuse enteritis (intestinal inflammation), changes to the epithelial cells leading to malabsorption, and eventually to pathologic changes in the intestinal wall.

# Cilia are long projecting structures, larger than microvilli, which contain internal arrays of microtubules




Epithelial cilia exhibit rapid beating patterns of movement
that propel a current of fluid and suspended matter in one direction over the epithelium

**Axoneme:** The nine doublets form an array around two central microtubules; the 9 + 2 assembly of microtubules

# Primary Ciliary Dyskinesia (Immotile Cilia Syndrome)

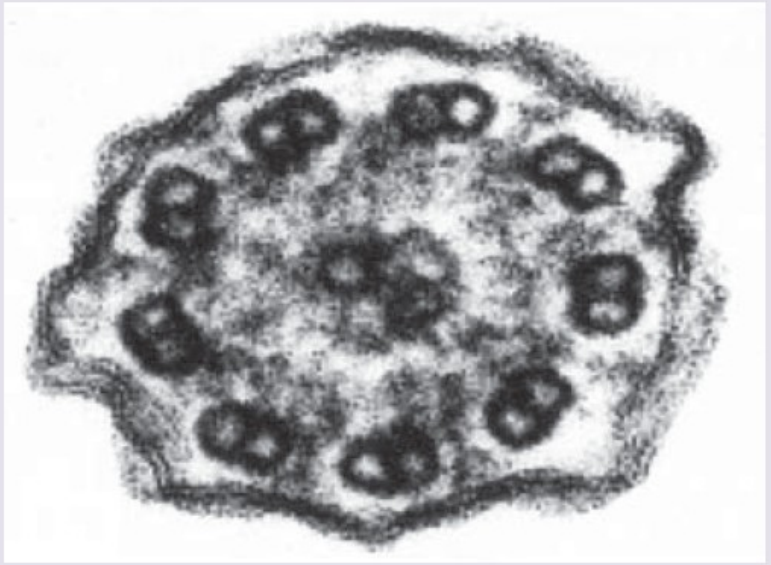
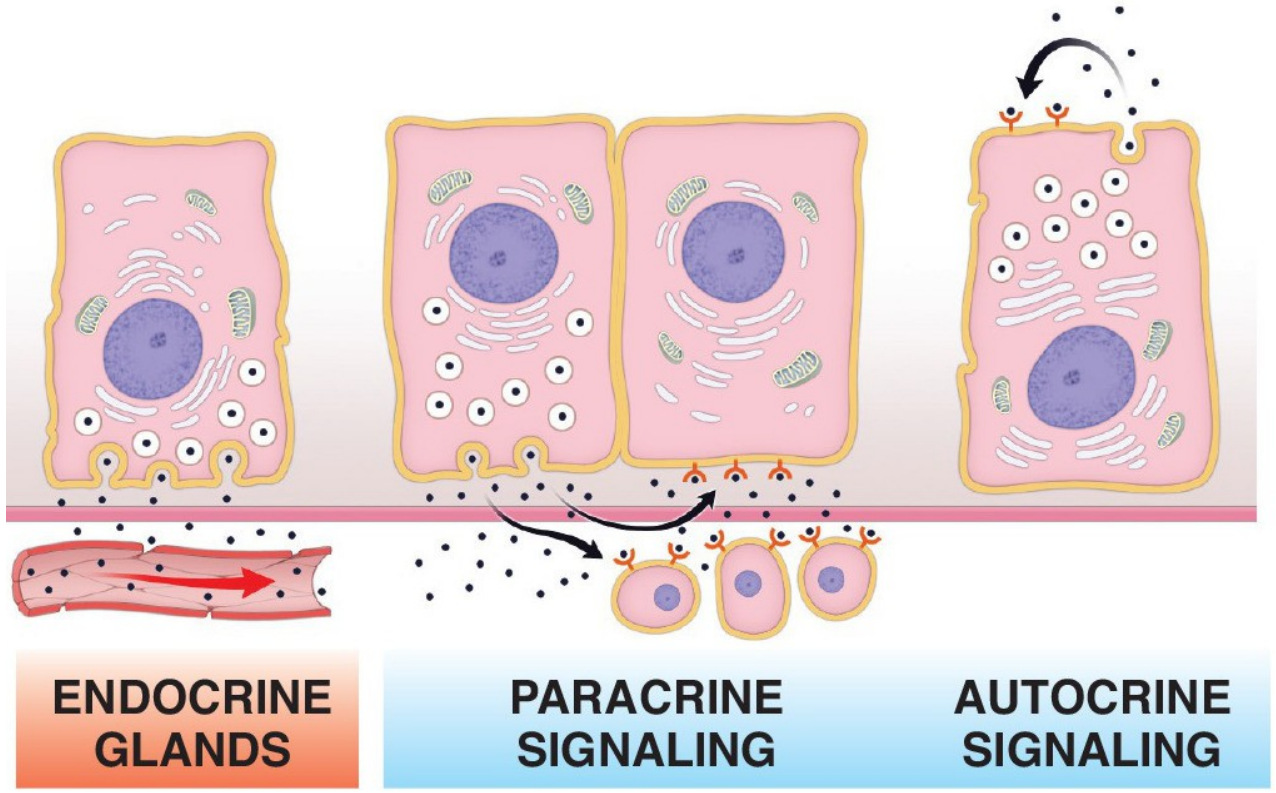


FIGURE F5.2.1 • **Electron micrograph of the cilium from an individual with primary cilary dyskinesia (PCD).** Note the absence of dynein arms on microtubule doublets. ×180,000. (Courtesy of Patrice Abell-Aleff.)

**MEDICAL APPLICATION**

Kartagener syndrome: muations in proteins of cilia, whose symptoms are chronic respiratory infections caused by the lack of the cleansing action of cilia in the respiratory tract and immotile spermatozoa, causing male infertility

# Types of glands and their mechanism of secretion




**Endocrine glands** lack a duct system. They secrete their products into the connective tissue, from which they enter the bloodstream to reach their target cells. The products of endocrine glands are called **hormones**.

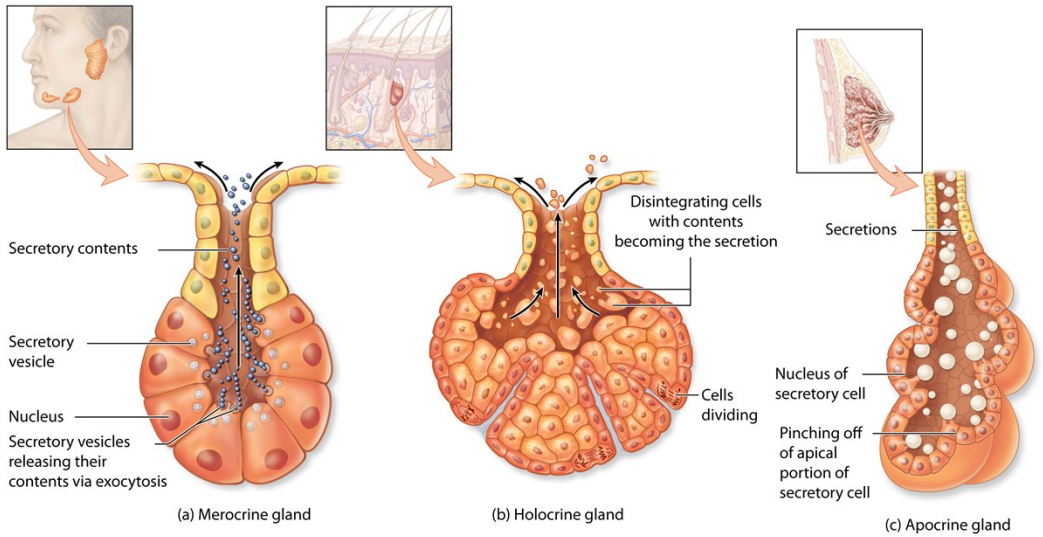
# Types of glands and their mechanism of secretion

**Exocrine glands** secrete their products onto a surface directly or through epithelial ducts or tubes that are connected to a surface.

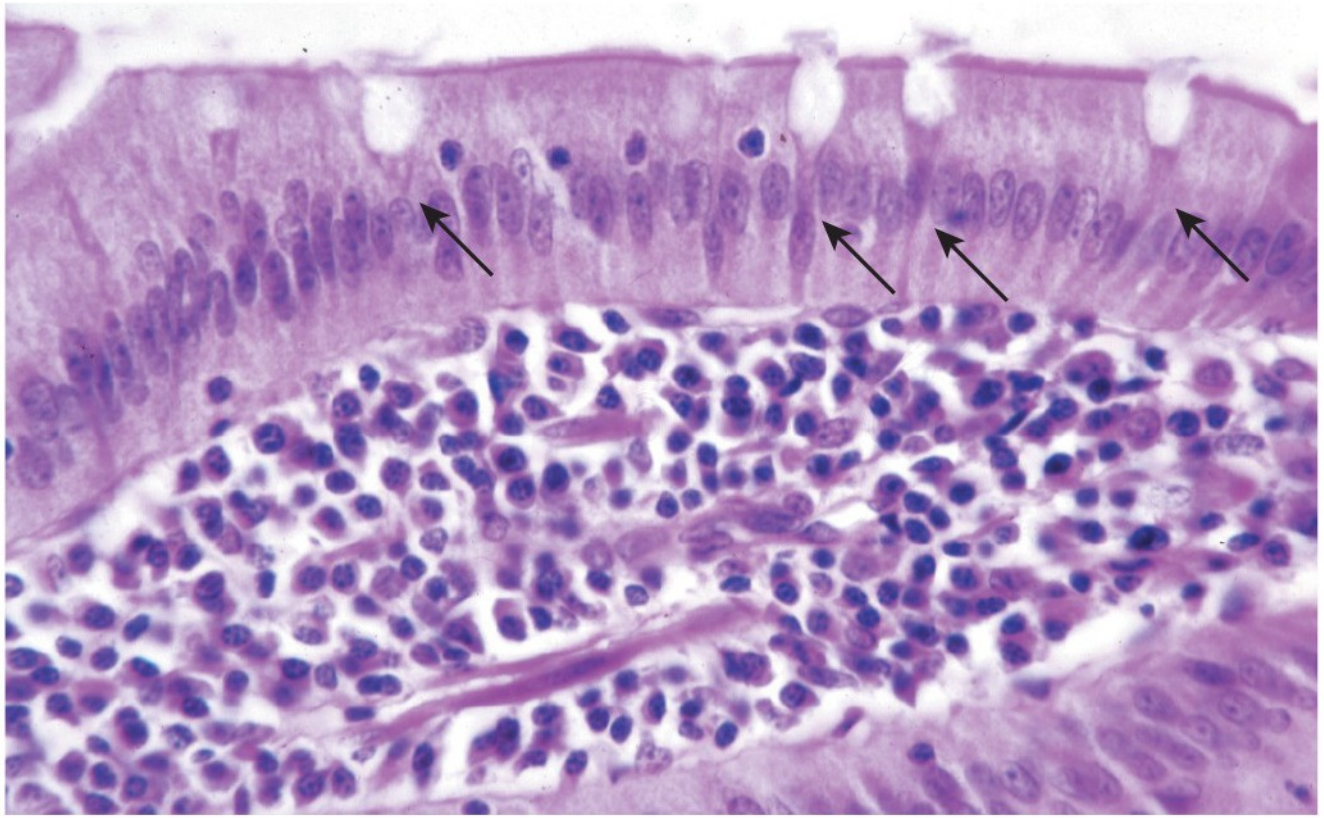
**Merocrine secretion**. This secretory product is delivered in **membrane-bounded vesicles** to the apical surface of the cell and extrude their contents by exocytosis.

**Apocrine secretion**. The secretory product is released in the apical portion of the cell, surrounded by a thin layer of cytoplasm within an envelope of plasma membrane. Ex **mammary gland**, where it is responsible for releasing large lipid droplets into the milk. It also occurs in the **apocrine glands** of skin, **ciliary (Moll's) glands** of the eyelid, and the **ceruminous glands** of the external auditory meatus.

**Holocrine secretion**. **Programmed cell death**. Both secretory products and cell debris are discharged into the lumen of the gland. This mechanism is found in sebaceous glands of skin and the tarsal (Meibomian) glands of the eyelid.



# Unicellular glands



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**Unicellular glands.** Photomicrograph of intestinal epithelium showing single goblet cells (*arrows*) dispersed among absorptive cells. Each goblet cell may be regarded as a unicellular gland—the simplest exocrine type gland.

### ❯❯ MEDICAL APPLICATION

In chronic bronchitis, common among habitual smokers, the number of goblet cells in the lining of airways in the lungs often increases greatly. This leads to excessive mucus production in areas where there are too few ciliated cells for its rapid removal and contributes to obstruction of the airways. The ciliated pseudostratified epithelium lining the bronchi of smokers can also be transformed into stratified squamous epithelium by metaplasia.

**TABLE 4–4** Structural classes of exocrine glands, features of each class, and examples.

***SIMPLE Glands*** **(Ducts Do Not Branch)**

| Class | Simple Tubular | Branched Tubular | Coiled Tubular | Acinar (or Alveolar) | Branched Acinar |
|---|---|---|---|---|---|
| |   | | | | |
| Features | Elongated secretory portion; duct usually short or absent | Several long secretory parts joining to drain into 1 duct | Secretory portion is very long and coiled | Rounded, saclike secretory portion | Multiple saclike secretory parts entering the same duct |
| Examples | Mucous glands of colon; intestinal glands or crypts (of Lieberkühn) | Glands in the uterus and stomach | Sweat glands | Small mucous glands along the urethra | Sebaceous glands of the skin |

***COMPOUND Glands*** **(Ducts from Several Secretory Units Converge into Larger Ducts)**

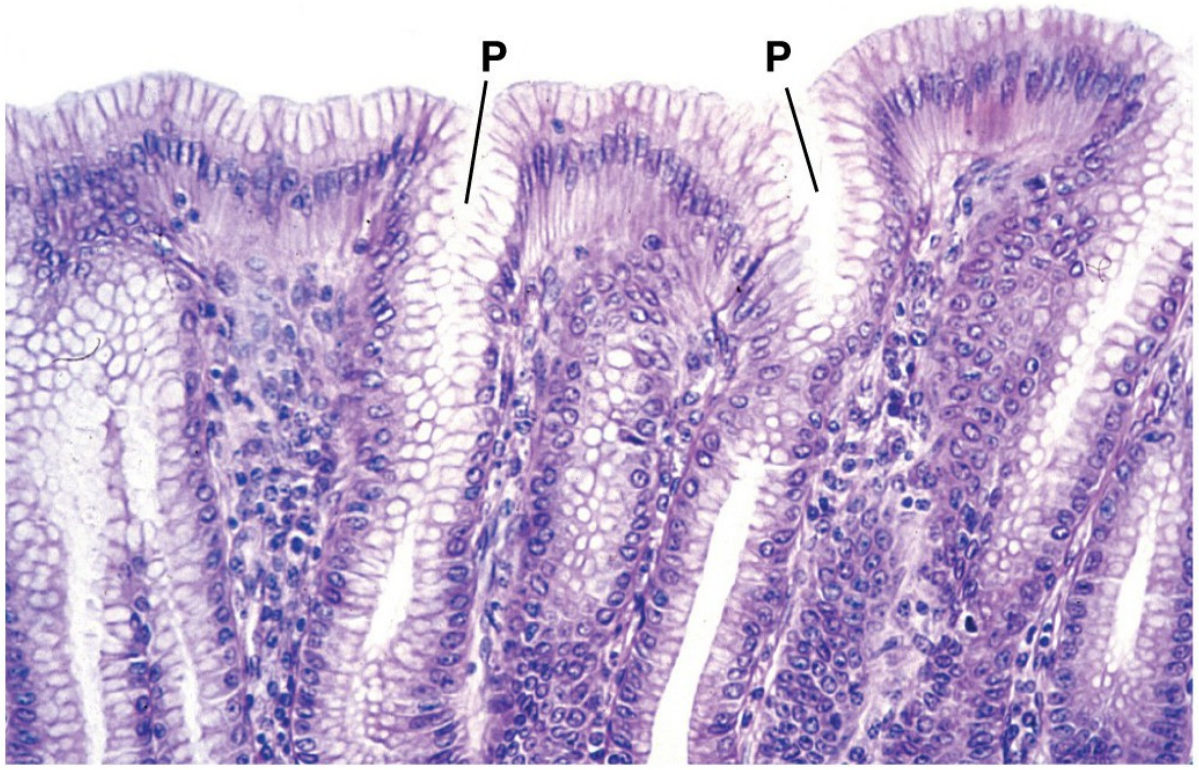
| Class | Tubular | Acinar (Alveolar) | Tubuloacinar |
|---|---|---|---|
| |   | | |
| Features | Several *elongated*, coiled secretory units and their ducts converge to form larger ducts | Several *saclike* secretory units with small ducts converge at a larger duct | Ducts of both tubular and acinar secretory units converge at larger ducts |
| Examples | Submucosal mucous glands (of Brunner) in the duodenum | Exocrine pancreas | Salivary glands |

**Multicellular glands** subclassification according to the arrangement of the secretory cells (parenchyma) and the presence or absence of branching of the duct elements.

**MEDICAL APPLICATION: Acne** Excessive holocrine secretion of sebum and keratin triggered by the surge of the steroid hormone testosterone. Activity of the normal commensal skin bacterium *Propionibacterium acnes* within the blocked duct commonly produces localized inflammation.

Is There A Pimple Cure? https://www.youtube.com/watch?v=CGvx4gl3D7w

# Mucus-secreting surface cells of stomach.



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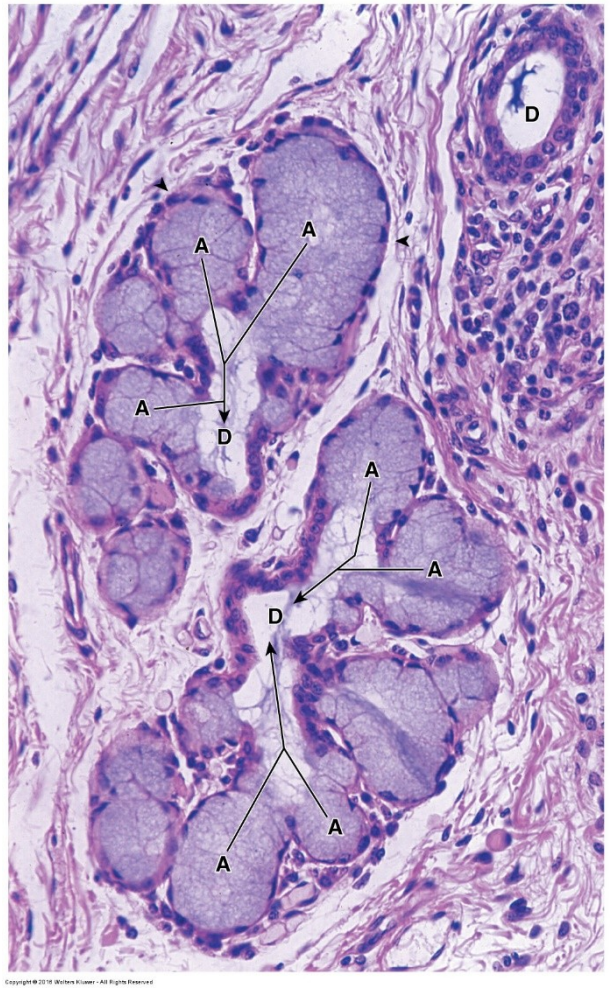
**Mucus-secreting surface cells of stomach.**
Photomicrograph of stomach surface. The epithelial cells lining the surface are all mucus-secreting cells, as are the cells lining the gastric pits (*P*). The cells of the gastric pit form simple tubular glands.

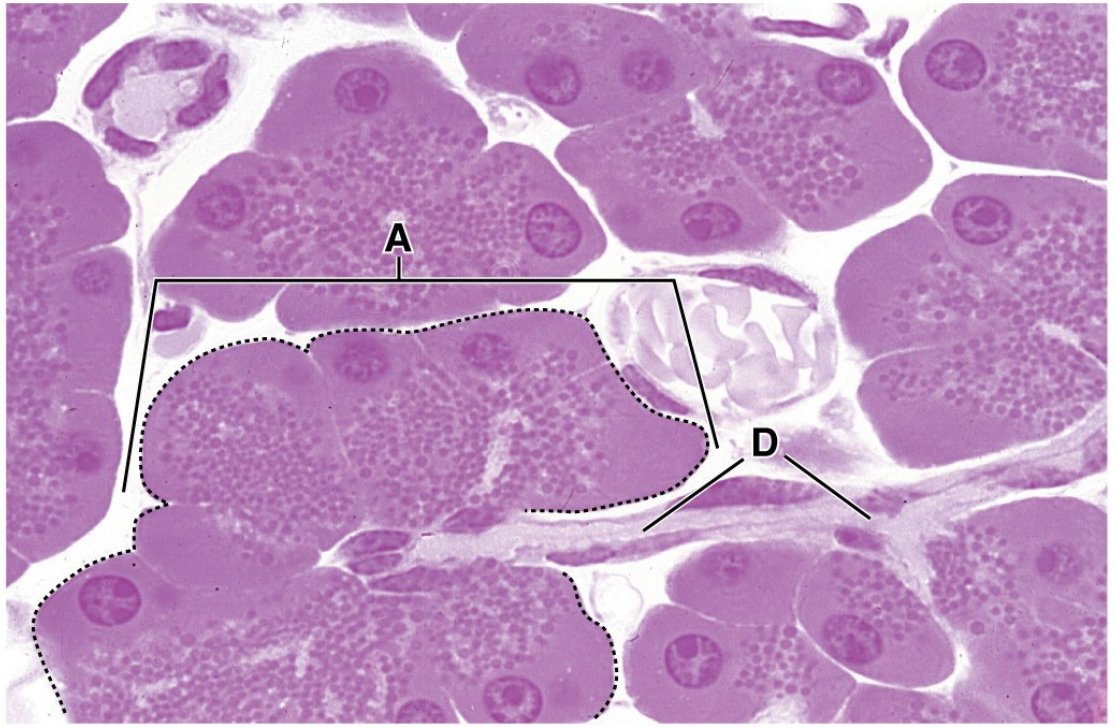
# Mucus-secreting compound gland




**Mucus-secreting compound gland.** Photomicro - graph showing two small lobes of a mucus-secreting gland associated with the larynx. Each displays the beginning of a duct (*D*) into which mucin is secreted (*arrows*). The individual secretory cells that form the acinus (*A*) are difficult to define. Their nuclei (*arrowheads*) are flattened and located in the very basal portion of the cell, a feature typical of mucus-secreting glands.

The cytoplasm is filled with mucin that has been retained during preparation of the tissue and appears stained

# Serous-secreting compound gland



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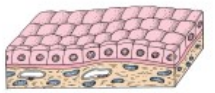
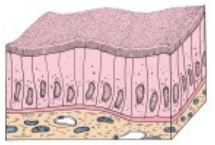
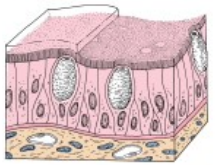
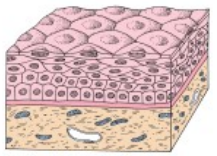
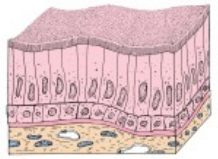
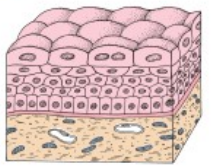
**Serous-secreting compound gland.** Photomicrograph of pancreatic acinus (*A;* outlined by the *dotted line*) with its duct (*D*). The small round objects within the acinar cells represent the zymogen granules, the stored secretory precursor material.

## Classification

The traditional classification of epithelium is descriptive and based on two factors: the number of cell layers and the shape of the surface cells. The terminology, therefore, reflects only structure, not function.

**TABLE 5.1 Types of Epithelium**

| | Classification | Some Typical Locations | Major Function |
|---|---|---|---|
|  | Simple squamous | Vascular system (endothelium)<br>Body cavities (mesothelium)<br>Bowman's capsule (kidney)<br>Respiratory spaces in lung | Exchange, barrier in central nervous system<br>Exchange and lubrication<br>Barrier<br>Exchange |
|  | Simple cuboidal | Small ducts of exocrine glands<br>Surface of ovary (germinal epithelium)<br>Kidney tubules<br>Thyroid follicles | Absorption, conduit<br>Barrier<br>Absorption and secretion |
|  | Simple columnar | Small intestine and colon<br>Stomach lining and gastric glands<br>Gallbladder | Absorption and secretion<br>Secretion<br>Absorption |
|  | Pseudostratified | Trachea and bronchial tree<br>Ductus deferens<br>Efferent ductules of epididymis | Secretion, conduit<br>Absorption, conduit |
|  | Stratified squamous | Epidermis<br>Oral cavity and esophagus<br>Vagina | Barrier, protection |
|  | Stratified cuboidal | Sweat gland ducts<br>Large ducts of exocrine glands<br>Anorectal junction | Barrier, conduit |
|  | Stratified columnar | Largest ducts of exocrine glands<br>Anorectal junction | Barrier, conduit |
|  | Transitional (urothelium) | Renal calyces<br>Ureters<br>Bladder<br>Urethra | Barrier, distensible property |

# Epithelial metaplasia is a reversible conversion of one mature epithelial cell type to another mature epithelial cell type.

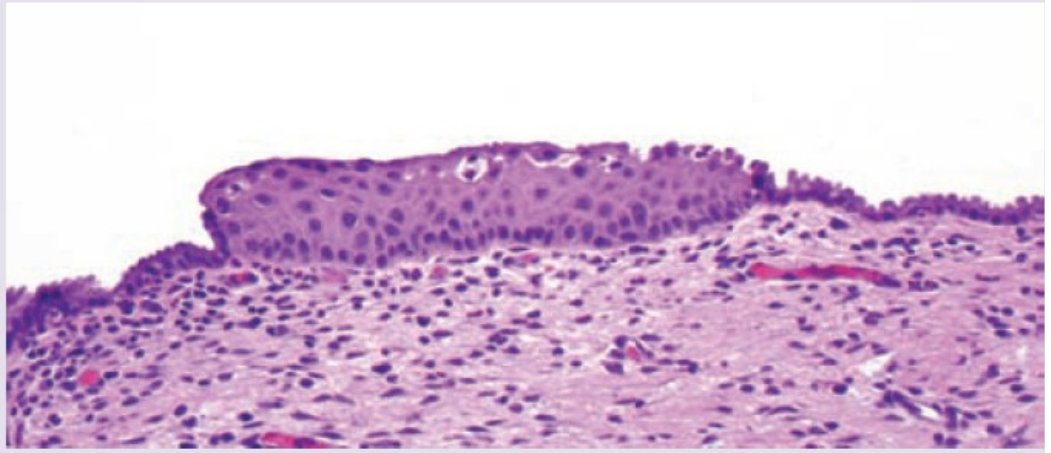


**FIGURE F5.1.1 • Squamous metaplasia of the uterine cervix.** Photomicrograph of a cervical canal lined by simple columnar epithelium. Note that the center of the image is occupied by an island containing squamous stratified epithelium. This metaplastic epithelium is surrounded on both sides by simple columnar epithelium. Since metaplasia is triggered by reprogramming of stem cells, metaplastic squamous cells have the same characteristics as normal stratified squamous epithelium. ×240. (Courtesy of Dr. Fabiola Medeiros.)

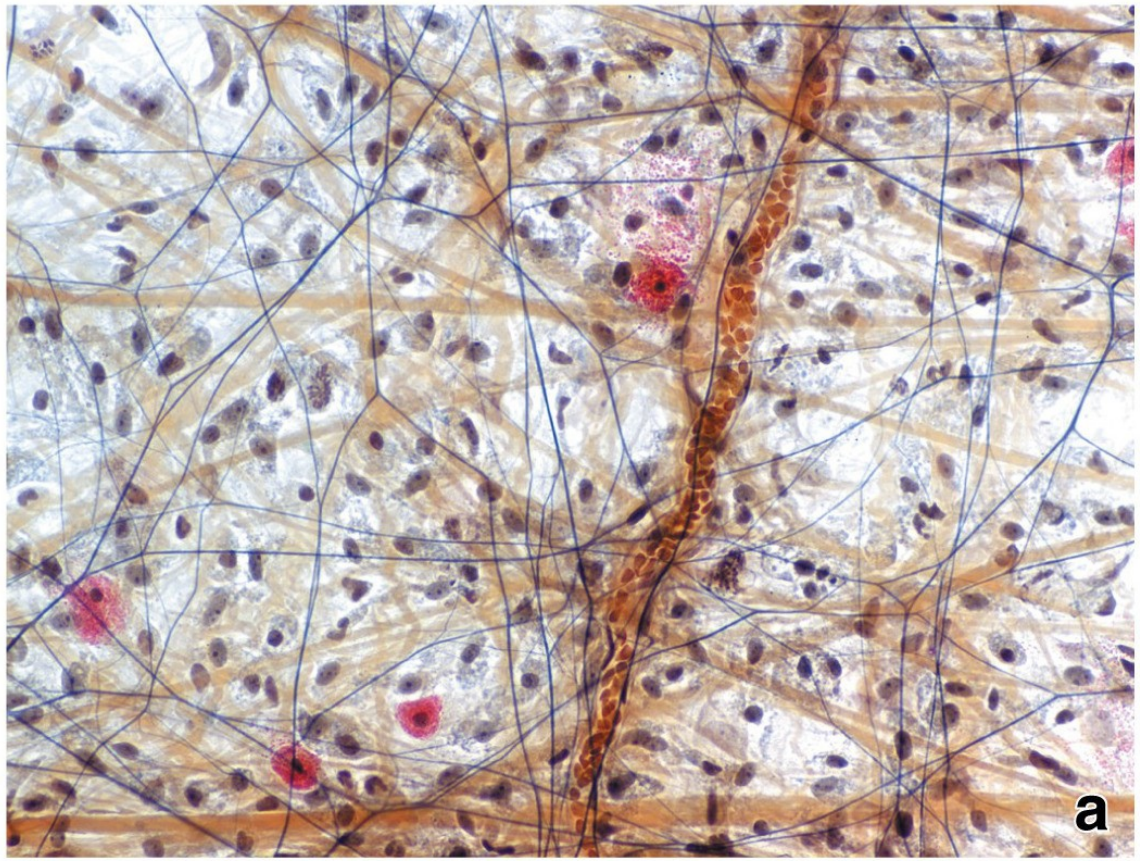
Cancers of the lung, cervix, and bladder often originate from squamous metaplastic epithelium. Squamous columnar epithelium may give rise to **glandular adenocarcinomas**.

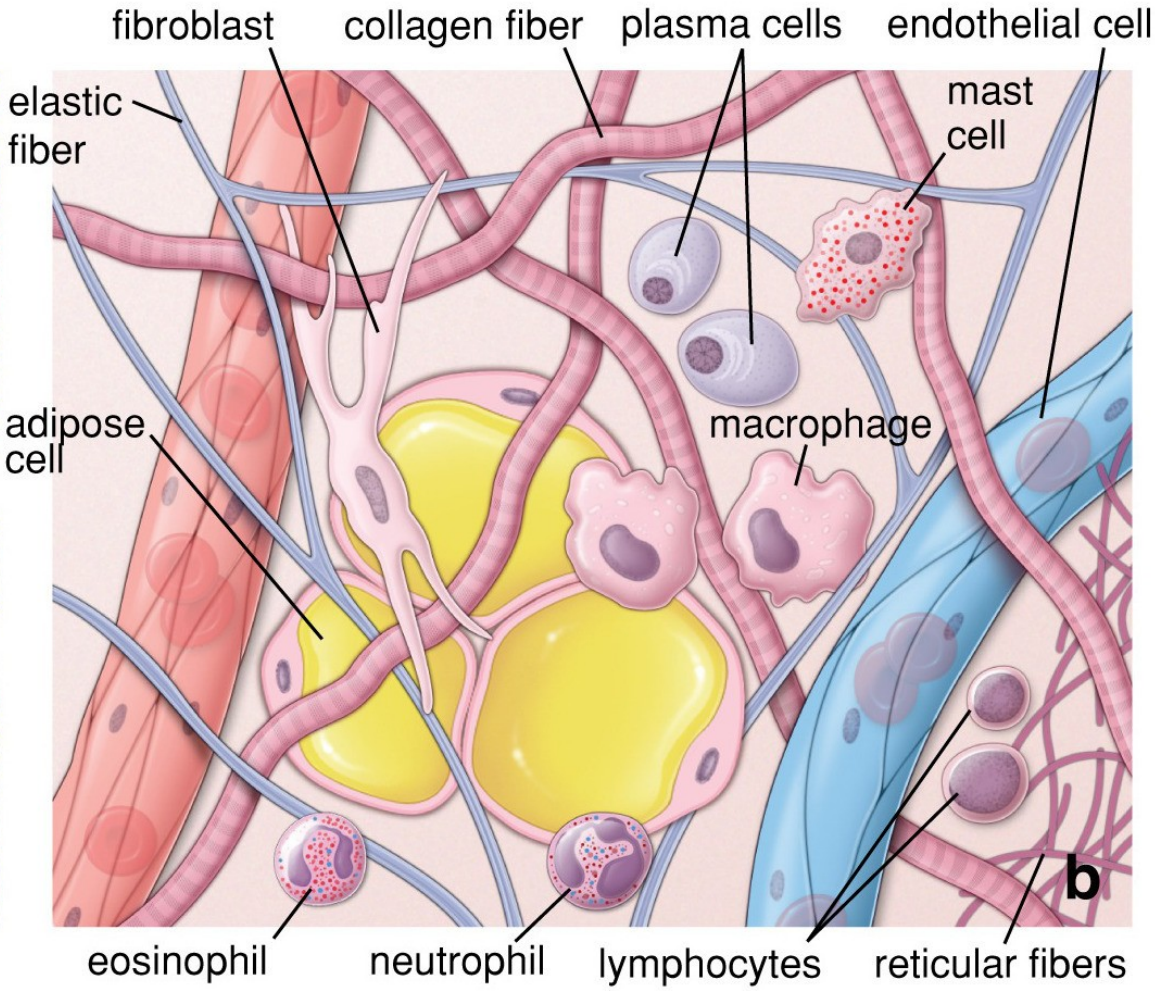
When metaplasia is diagnosed, all efforts should be directed toward removing the pathogenic stimulus (i.e., cessation of smoking, eradication of infectious agents, etc.) and monitoring the metaplastic site to ensure that cancerous changes do not begin to develop.

# Chapter 5 Connective Tissue Objectives

1. General properties of connective tissue: extracellular matrix, ground substance
2. Connective tissue cells: resident (fibroblasts, macrophages adipocytes, mast cells, stem cells) and wandering (lymphocytes, plasma cells, neutrophils, eosinophils, basophils, monocytes)
3. Connective tissue fibers: collagen, reticular, elastic
4. Extracellular matrix: proteoglycans, glycosaminoglycans, multiadhesive glycoproteins
5. Connective tissue proper: Loose, dense irregular, dense regular
6. Embryonic connective tissue: Mesenchyme, mucous connective tissue

# Loose Connective Tissue: A prototype of cells, fibers, and ECM

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# Cells of Fibrous Connective Tissue

- **Fibroblasts** produce fibers and ground substance
- **Macrophages** phagocytize foreign material and activate immune system when they sense foreign matter (antigen)
  - Arise from white blood cells called monocytes
- **Leukocytes**, or white blood cells
  - Neutrophils wander about attacking bacteria
  - Lymphocytes react against bacteria, toxins, and other foreign material
- **Plasma cells** synthesize disease-fighting antibodies
  - Arise from lymphocytes
- **Mast cells** are found alongside blood vessels
  - Secrete heparin to inhibit clotting
  - Secrete histamine to dilate blood vessels
- **Adipocytes** store triglycerides (fat molecules)

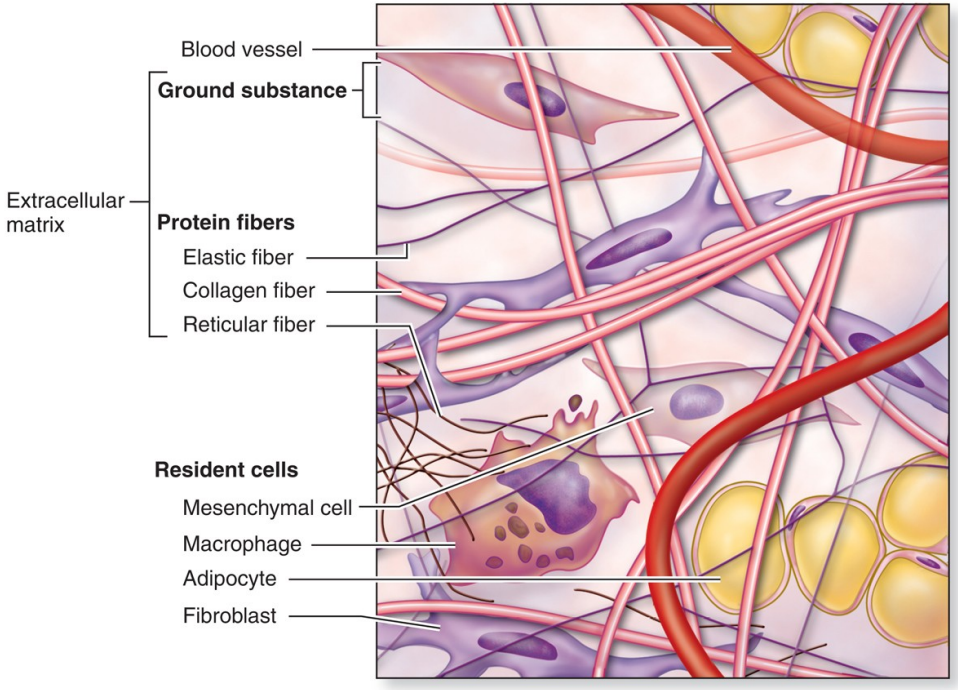
# Connective tissue cells can be resident or wandering.

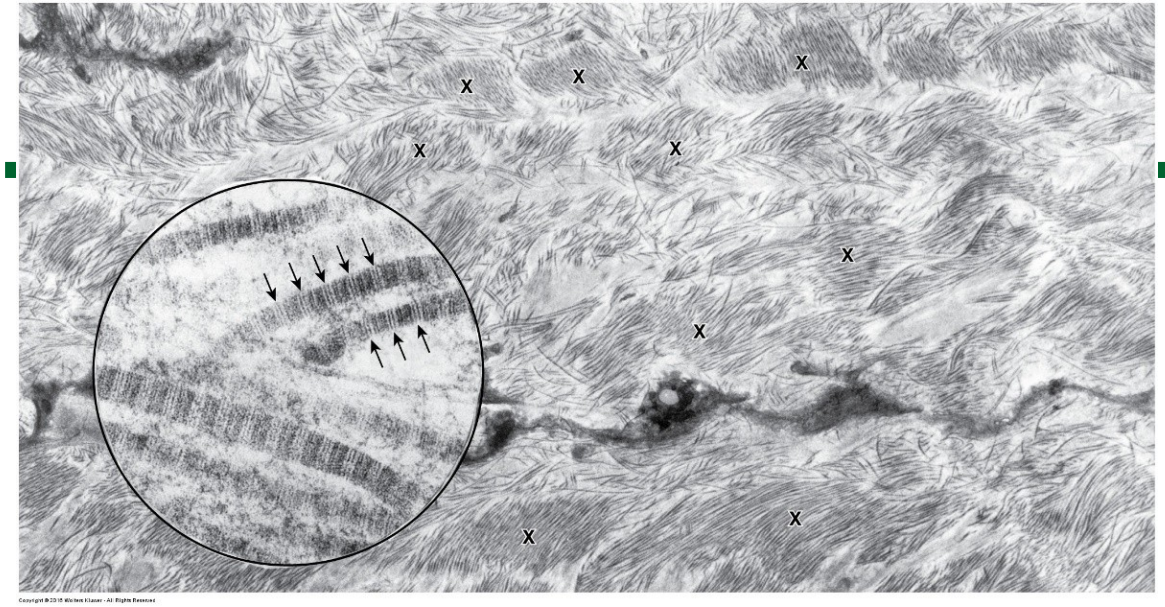
**Resident cell population** are relatively stable; they typically exhibit little movement and can be regarded as permanent residents of the tissue.

- **fibroblasts** and a closely related cell type, the **myofibroblast**
- **macrophages**
- **adipocytes**
- **mast cells**
- **adult stem cells**.

**Wandering cell population** or **transient cell population:** cells that have migrated into the tissue from the blood in response to specific stimuli.

- **lymphocytes**
- **plasma cells**
- **neutrophils**
- **eosinophils**
- **basophils**





**Electron micrograph of dense irregular connective tissue** from the capsule of the testis of a young male. The threadlike collagen fibrils are aggregated in some areas (*X* ) to form relatively thick bundles; in other areas, the fibrils are more dispersed

**Inset.** A longitudinal array of collagen fibrils from the same specimen seen at higher magnification. Note the banding pattern. The spacing of the arrows indicates the 68-nm repeat pattern.

# Connective Tissue Fibers

- Connective tissue fibers are present in varying amounts, depending on the structural needs or function of the connective tissue.
- Produced by fibroblasts
- Composed of protein consisting of long peptide chains.
  - **Collagen fibers**
  - **Reticular fibers**
  - **Elastic fibers**

# Fibers Fibrous Connective Tissue

- **Collagenous fibers**
  - Most abundant of the body's proteins—25%
  - Tough, flexible, and resist stretching
  - Tendons, ligaments, and deep layer of the skin are mostly collagen
  - Less visible in matrix of cartilage and bone

- **Reticular fibers**
  - Thin collagen fibers coated with glycoprotein
  - Form framework of such organs as spleen and lymph nodes

- **Elastic fibers**
  - Thinner than collagenous fibers
  - Branch and rejoin each other
  - Made of protein called elastin
  - Allows stretch and recoil
  - Yellow fibers—fresh elastic fibers

# Collagen Fibrils in Dense Irregular CT

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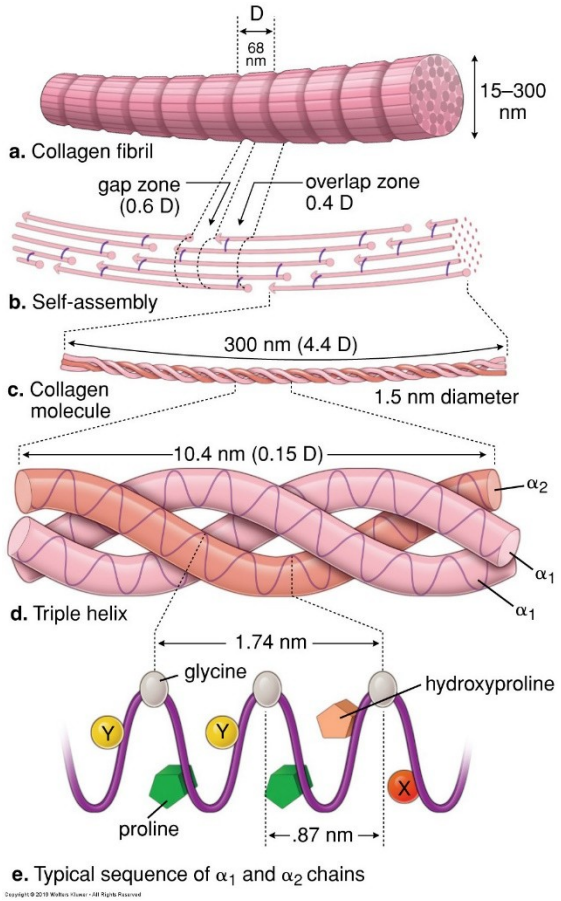


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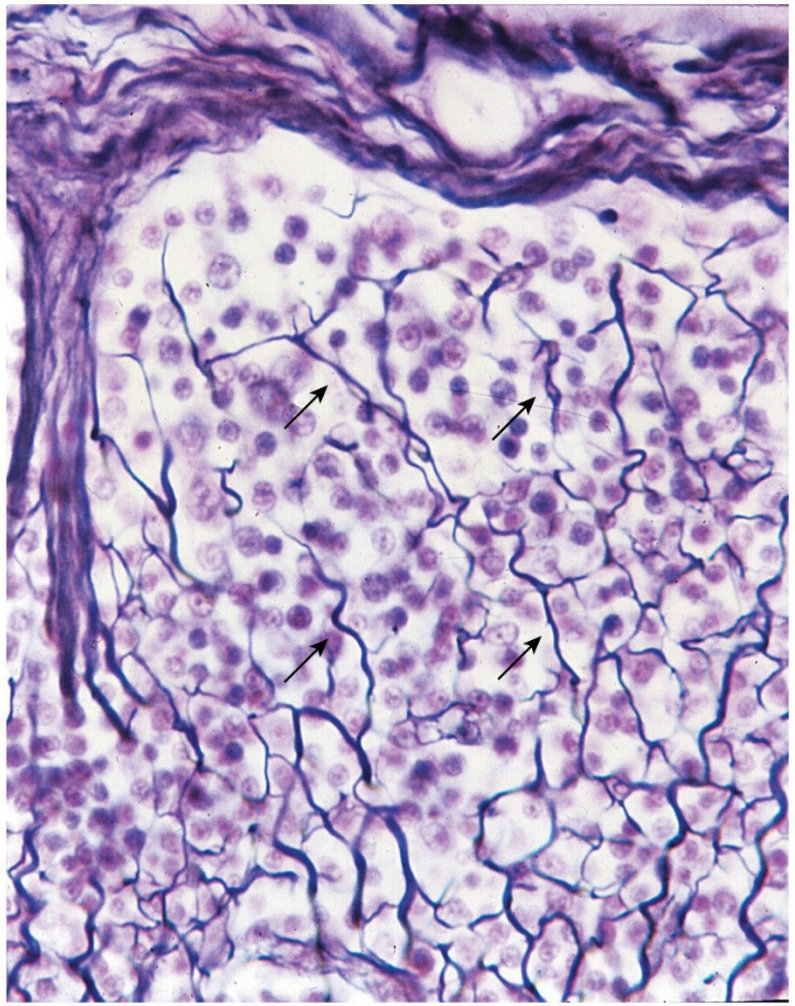
**MEDICAL APPLICATION**
A keloid is a local swelling caused by abnormally large amounts of collagen that form in scars of the skin.
**Stretch marks**

**MEDICAL APPLICATION**
Scurvy Lack of vitamin C, a required cofactor for collagen synthesis results in ulceration of gums, hemorrhages

# Reticular Fibers in the Lymph Node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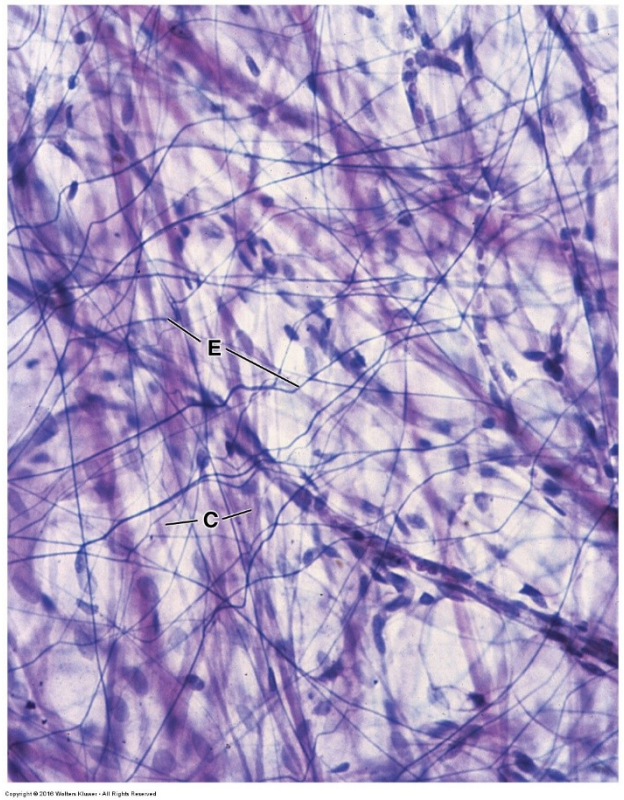
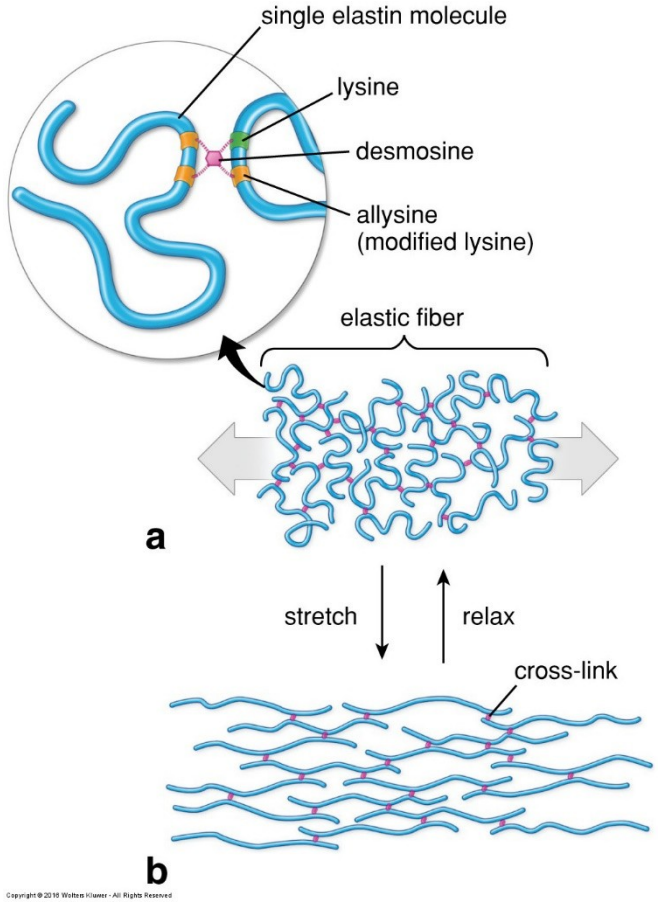
**Reticular fibers** exhibit a branching pattern, and typically do not bundle to form thick fibers

Photomicrograph of a lymph node silver preparation showing the connective tissue capsule at the top and a trabecula extending from it at the left. The reticular fibers (*arrows*) form an irregular anastomosing (connection of branching structures) network.

# Elastic Fibers




**Elastic fibers** are typically thinner than collagen fibers, branching pattern. The fibers are interwoven with collagen fibers to limit the distensibility of the tissue and prevent tearing from excessive stretching

**MEDICAL APPLICATION:**
Mutations in the fibrillin genes result in **Marfan syndrome**, a disease characterized by a lack of resistance in tissues rich in elastic fibers. Because the walls of large arteries are rich in elastic components and because the blood pressure is high in the aorta, patients with this disease often experience aortic swellings called aneurysms, which are life-threatening conditions.

**What Lincoln had:** http://www.nature.com/news/2007/071130/full/news.2007.226.html

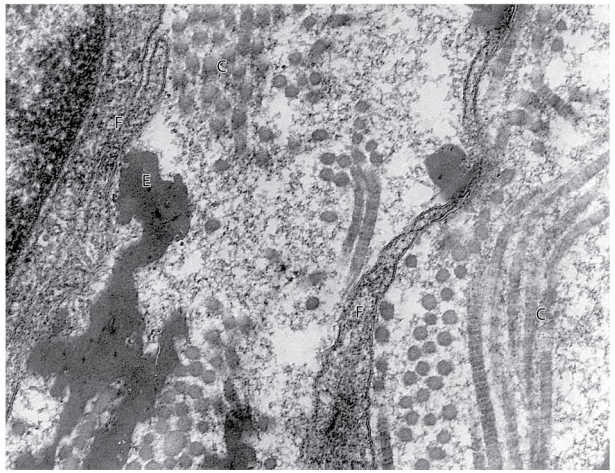
# Clinical Correlation: Sun Exposure and Molecular Changes in Photoaged Skin

**Chronological aging:** changes in stratified squamous epithelium (epidermis) and connective tissue of the dermis.

**Photoaging:** Chronic sun exposure leads to decreased production of type I and type III collagen fibers

- Altered crosslinking that occurs between collagen molecules resulting in abnormal stability and decreased resistance to enzymatic degradation.
- number of abnormally thick and nonfunctional elastic fibers increases

# Extracellular Matrix (ECM)




**Ultrastructure of the extracellular matrix (ECM).** TEM of the connective tissue ECM reveals ground substance as either empty or containing fine granular material that fills spaces between the collagen (**C**) and elastic (**E**) fibers and surrounds fibroblast cells and processes (**F**).

The **extracellular matrix (ECM)** structural network that surrounds and supports cells within the connective tissue.

**ground substance:**

- **proteoglycans** (e.g., aggrecan, syndecan)
- **multiadhesive glycoproteins** (such as fibronectin and laminin)
- **glycosaminoglycans** (e.g., dermatan sulfate, keratan sulfate, hyaluronan).

**MEDICAL APPLICATION** Edema is the excessive accumulation of water in the extracellular spaces of connective tissue. This water comes from the blood, passing through the capillary walls that become more permeable during inflammation

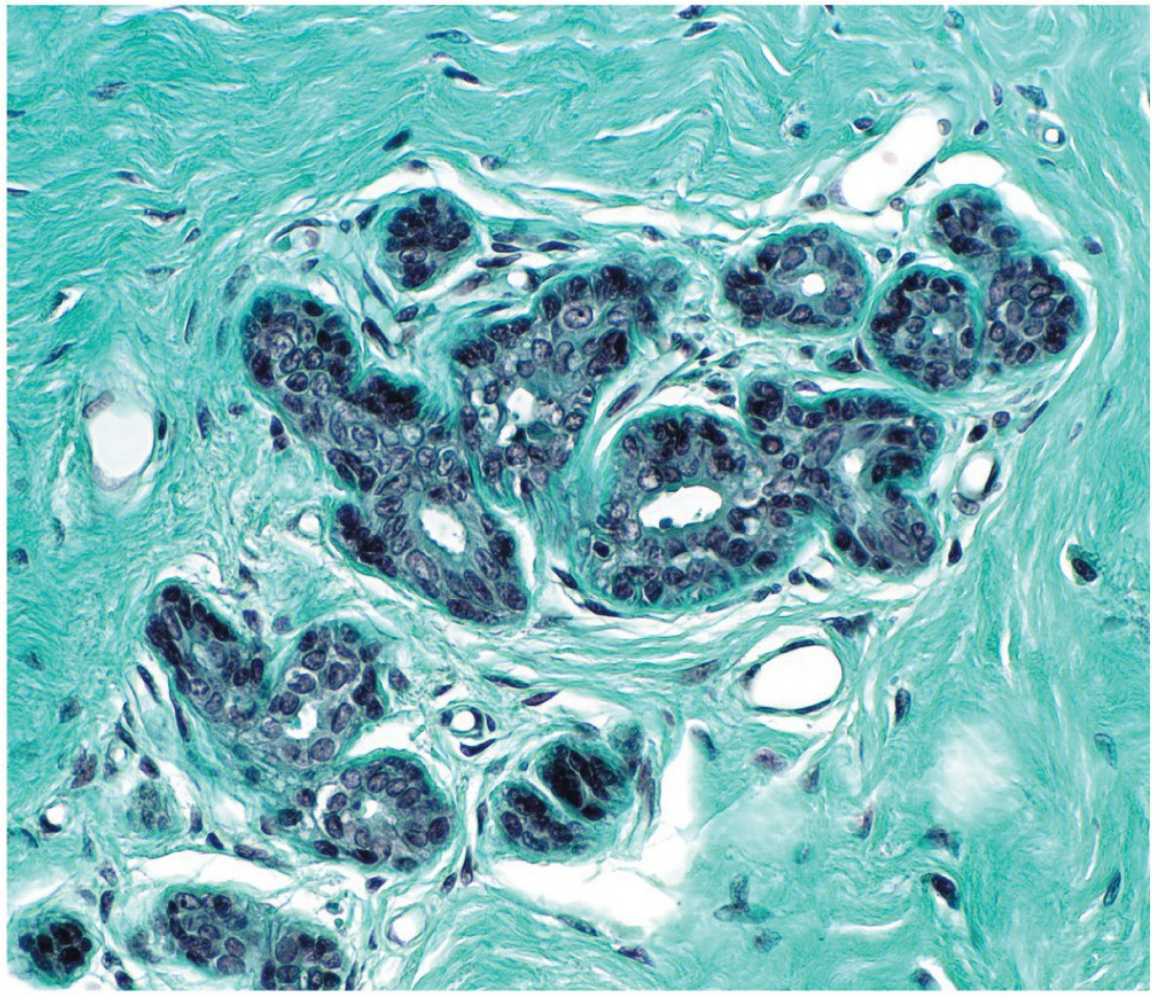
# Classification of Connective Tissue

**TABLE 5–6** Classification of connective or supporting tissues.

| | General Organization | Major Functions | Examples |
|---|---|---|---|
| **Connective Tissue Proper** | | | |
| Loose (areolar) connective tissue | Much ground substance; many cells and little collagen, randomly distributed | Supports microvasculature, nerves, and immune defense cells | Lamina propria beneath epithelial lining of digestive tract |
| Dense irregular connective tissue | Little ground substance; few cells (mostly fibroblasts); much collagen in randomly arranged fibers | Protects and supports organs; resists tearing | Dermis of skin, organ capsules, submucosa layer of digestive tract |
| Dense regular connective tissue | Almost completely filled with parallel bundles of collagen; few fibroblasts, aligned with collagen | Provide strong connections within musculoskeletal system; strong resistance to force | Ligaments, tendons, aponeuroses, corneal stroma |
| **Embryonic Connective Tissues** | | | |
| Mesenchyme | Sparse, undifferentiated cells, uniformly distributed in matrix with sparse collagen fibers | Contains stem/progenitor cells for all adult connective tissue cells | Mesodermal layer of early embryo |
| Mucoid (mucous) connective tissue | Random fibroblasts and collagen fibers in viscous matrix | Supports and cushions large blood vessels | Matrix of the fetal umbilical cord |
| **Specialized Connective Tissues** | | | |
| Reticular connective tissue (see Chapter 14) | Delicate network of reticulin/ collagen III with attached fibroblasts (reticular cells) | Supports blood-forming cells, many secretory cells, and lymphocytes in most lymphoid organs | Bone marrow, liver, pancreas, adrenal glands, all lymphoid organs except the thymus |
| Adipose Tissue (Chapter 6) | | | |
| Cartilage (Chapter 7) | | | |
| Bone (Chapter 8) | | | |
| Blood (Chapter 12) | | | |

Connective Tissue: Types, Functions & Disorders: https://www.youtube.com/watch?v=eJ7snAlCaCg

# Loose and Dense Irregular CT



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**Dense irregular connective tissue**

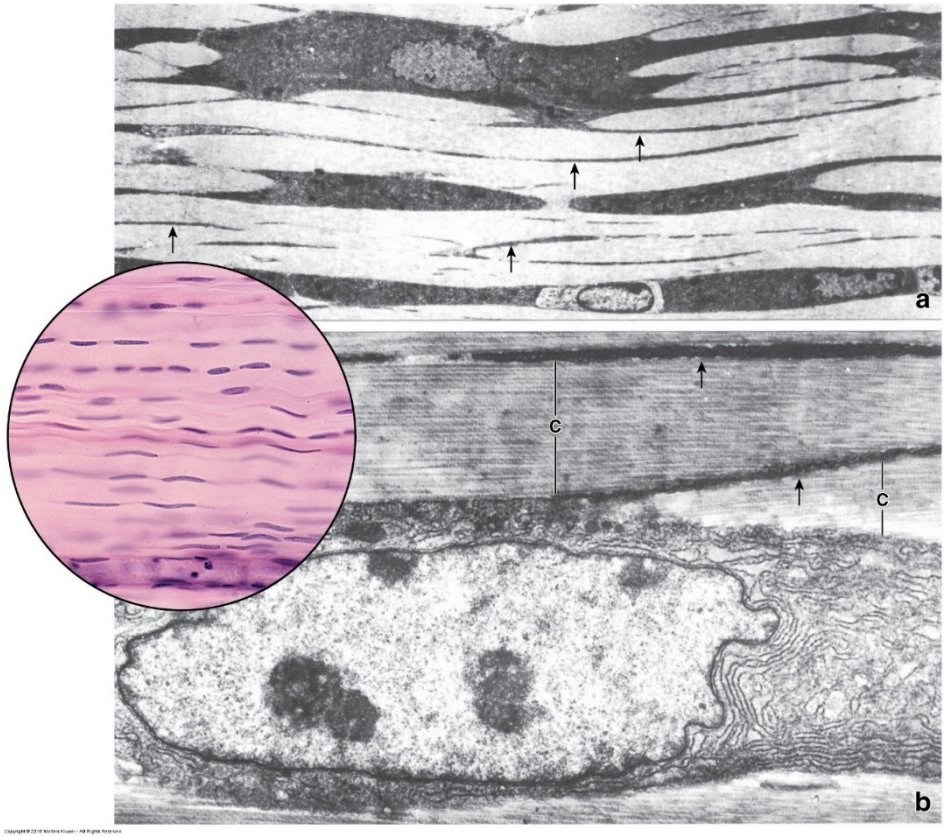
- contains mostly collagen fibers.
- Cells are sparse fibroblasts.
- contains relatively little ground substance

**Mammary gland** stained with Masson's trichrome:

- Center: loose connective tissue surrounds the glandular epithelium. Note wispy arrangement of collagen fibers with many cells.
- upper left: dense irregular connective tissue. few nuclei, collagen is considerably more abundant and is composed of very thick fibers

Skin contains dense irregular connective tissue called the **reticular layer** of the dermis, which provides resistance to tearing from stretching forces from different directions

# Dense Regular CT




**Dense regular connective tissue**

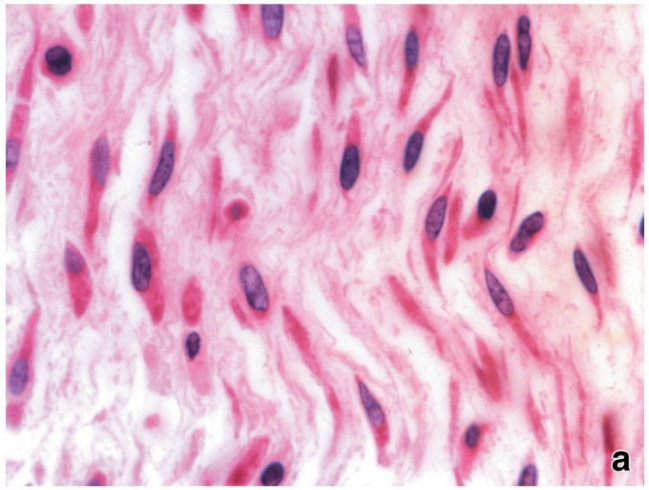
- tendons, ligaments, and aponeuroses.
- fibers are the prominent feature
- little ECM

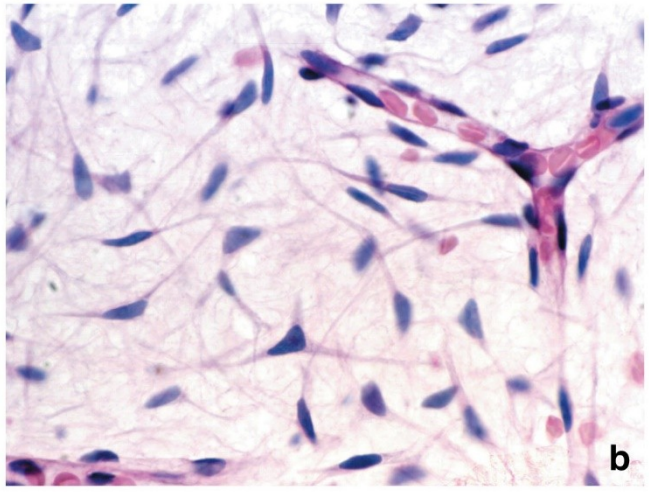
a) Electron micrograph of a tendinocytes (fibroblasts) and their thin processes (*arrows*) lying between the collagen bundles.
b) higher magnification. The collagen fibers (*C*). Orderly and regular alignment of the bundles of collagen fibers.

**❯❯ MEDICAL APPLICATION**

Overuse of tendon-muscle units can result in **tendonitis,** characterized by inflammation of the tendons and their attachments to muscle. Common locations are the elbow, the Achilles tendon of the heel, and the shoulder rotator cuff. The swelling and pain produced by the localized inflammation restricts the affected area's normal range of motion and can be relieved by injections of anti-inflammatory agents such as cortisone. Fibroblasts eventually repair damaged collagen bundles of the area.

# Embryonic Connective Tissue




a) Although morphologically the mesenchymal cells appear as a homogeneous population, they give rise to cells that will differentiate into various cell types.
b) Wharton's jelly consists of a specialized, almost gelatin like ground substance that occupies large intercellular spaces located between the spindle-shaped mesenchymal cells

**MEDICAL APPLICATION**

Some cells in mesenchyme are multipotent stem cells potentially useful in regenerative medicine after grafting to replace damaged tissue in certain patients.

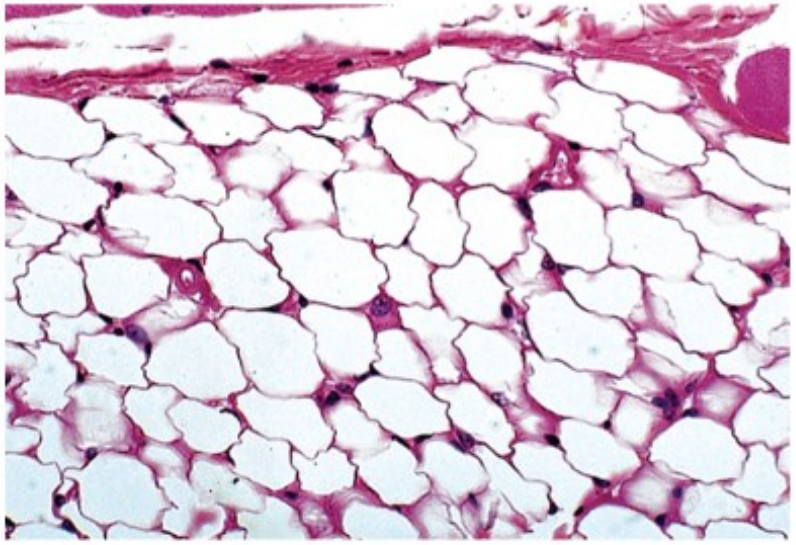
Stem cells to allow growing new teeth: https://www.youtube.com/watch?v=_Gyv-BVniAw

# Chapter 6 Adipose Objectives

1. Adipose tissue is a specialized connective tissue that plays an important role in energy homeostasis (stores energy in lipid droplets in the form of triglycerides) and hormone production (adipokines).
2. White adipose tissue with supporting collagen and reticular fibers forms the subcutaneous fascia, is concentrated in the mammary fat pads, and surrounds several internal organs.
3. White adipocytes differentiate from mesenchymal stem cells
4. Brown adipose tissue is abundant in newborns (5% of total body mass) but is markedly reduced in adults.
5. Adipocytes are able to undergo white-to-brown and brown-to-white transformation (transdiferentiation) in response to the thermogenic needs of the body.

# Adipose Tissue

- Description
  - Closely packed adipocytes, nucleus pushed to one side by fat droplet Function
  - Provides reserve food fuel
  - Insulates against heat loss
  - Supports and protects organs
  - Most adult fat is called white fat
  - Brown fat: in fetuses, infants, children. a heat-generating tissue
  - Empty-looking cells with thin margins; nucleus pressed against cell membrane
  - Space between adipocytes is occupied by areolar tissue, reticular tissue, and blood capillaries
- Location: Under skin, around kidneys, Behind eyeballs, within abdomen and in breasts



(a)

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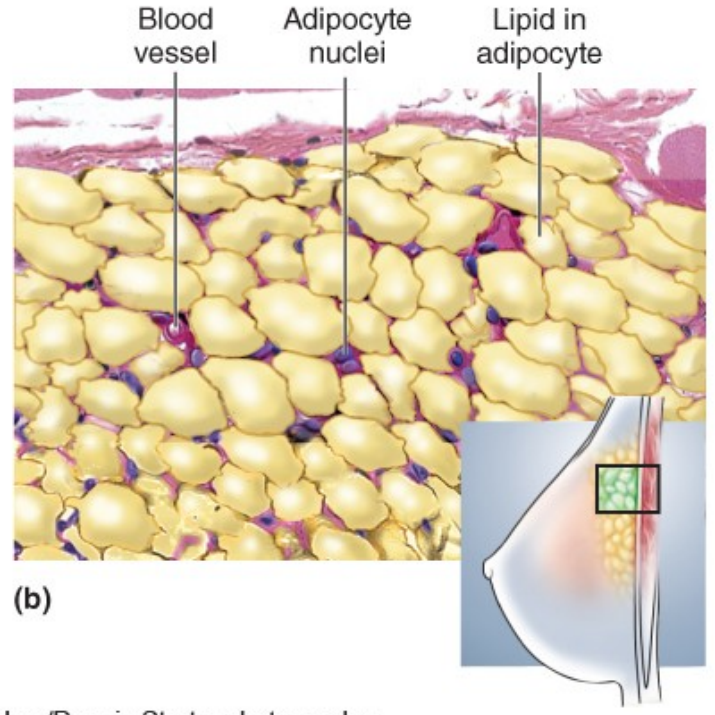
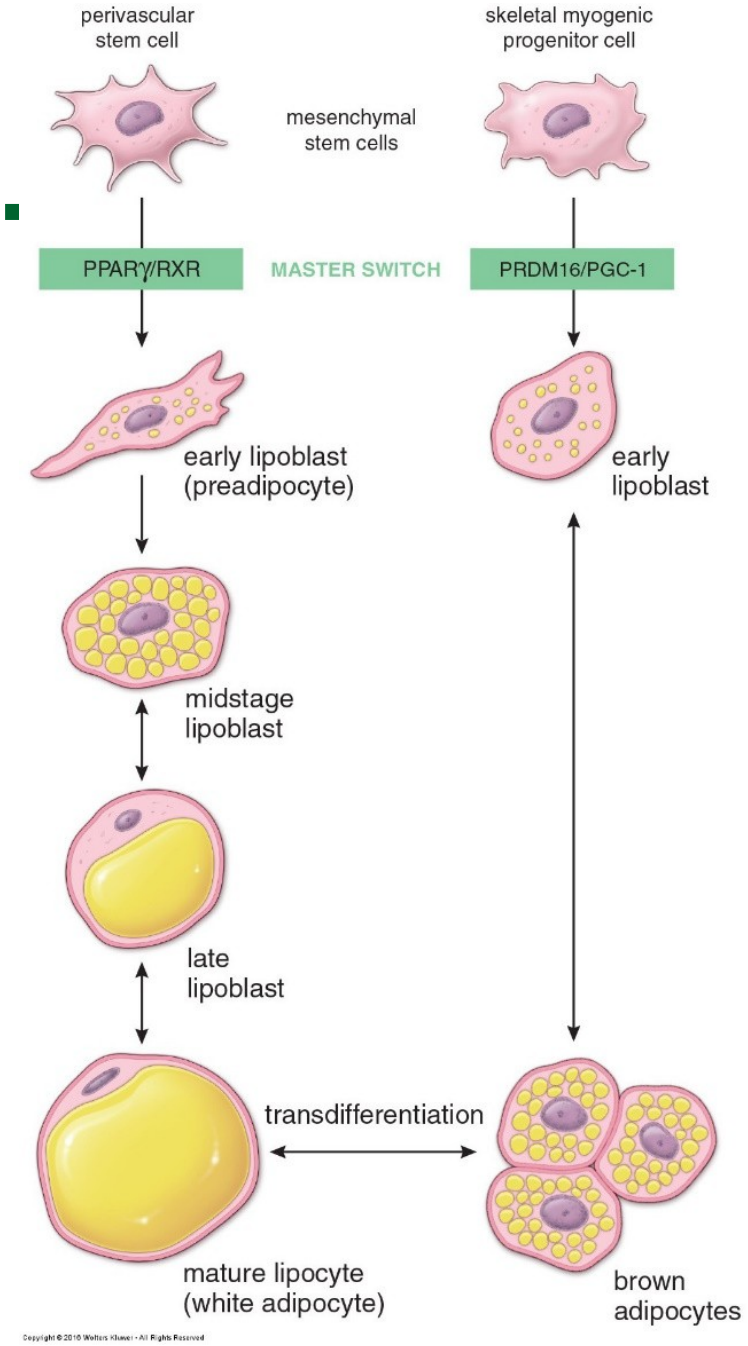



Inc./Dennis Strete, photographer



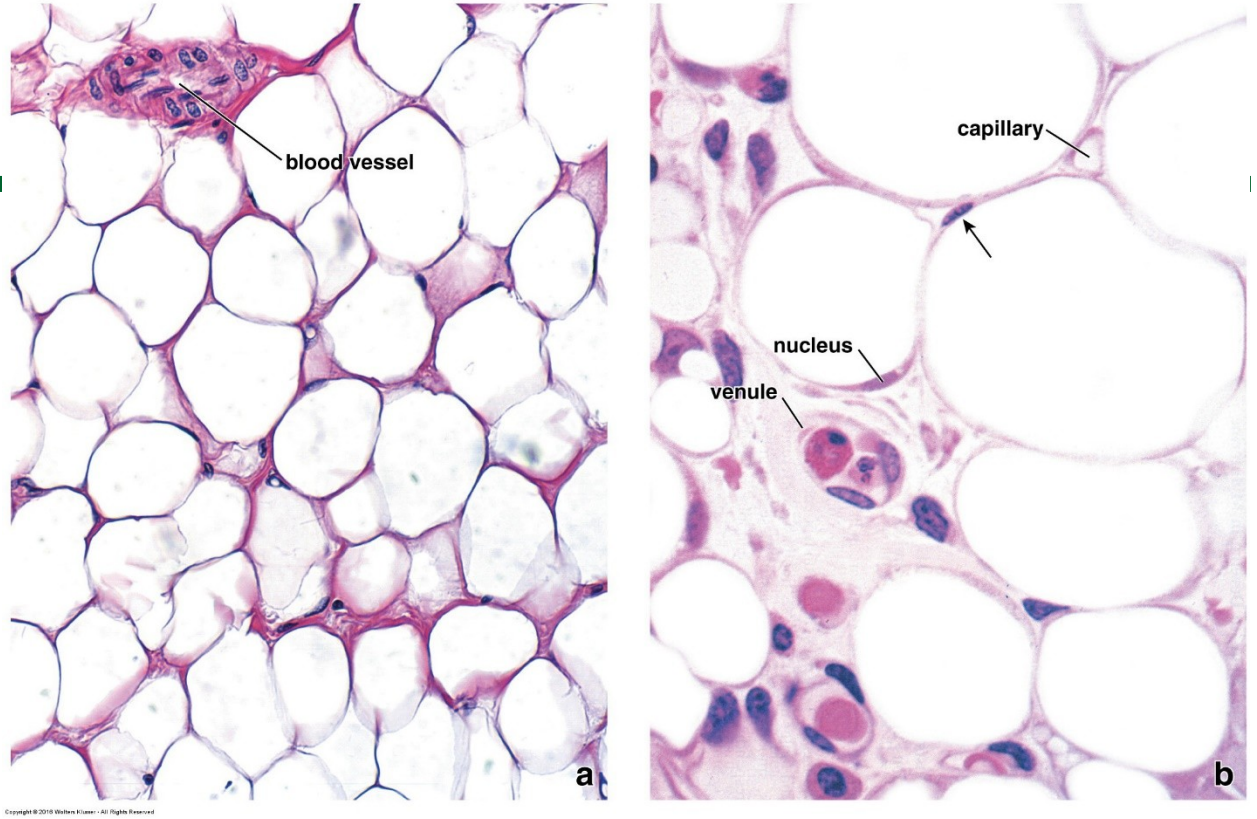

# White adipose tissue begins to form midway through fetal development.

- White adipocytes differentiate from mesenchymal stem cells under the control of **PPARγ/RXR** transcription factors ("master switch" for white adipocyte differentiation).
- Brown adipocytes differentiate from mesenchymal stem cells under the control of **PRDM16/PGC-1** transcription factors ("master switch" for brown adipocyte differentiation).
- **Transdifferentiation**: white to brown conversion is induced by cold or physical activity
- **Research application:** Mice with abundant natural or induced brown adipose tissue are resistant to obesity, Genetically modified mice without functional brown adipocytes are prone to obesity and type 2 diabetes.

# White Adipose Tissue

White adipose tissue represents at least 10% of body weight in a normal healthy adult.

- Forms subcutaneous fascia, is concentrated in the mammary fat pads, and surrounds several internal organs.



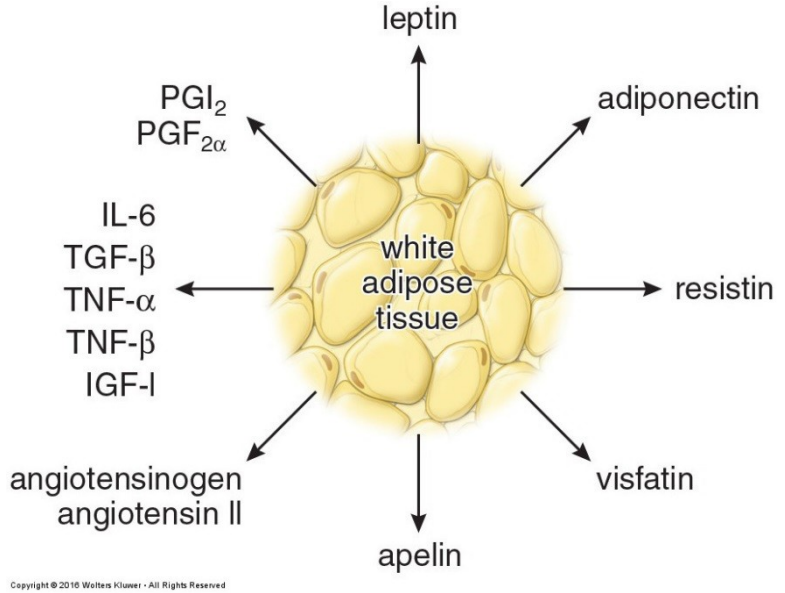

White adipocytes are very large cells (100 μm or more in diameter) with a single, large lipid droplet (unilocular), a thin rim of cytoplasm, and a flattened, peripherally displaced nucleus.
A single large lipid droplet within the white adipocyte represents cytoplasmic inclusion and is not membrane bound.

White adipose tissue secretes a variety of adipokines, which include hormones (e.g., leptin), growth factors, and cytokines.

# White adipose tissue produces a variety of hormones, growth factors, and cytokines.

Leptin: **circulating satiety factor** that controls food intake when the body's store of energy is sufficient.

**❯❯ MEDICAL APPLICATION**: In most obese humans adipocytes produce adequate or excess quantities of leptin, but target cells are not responsive due to mechanisms downstream of leptin receptors.

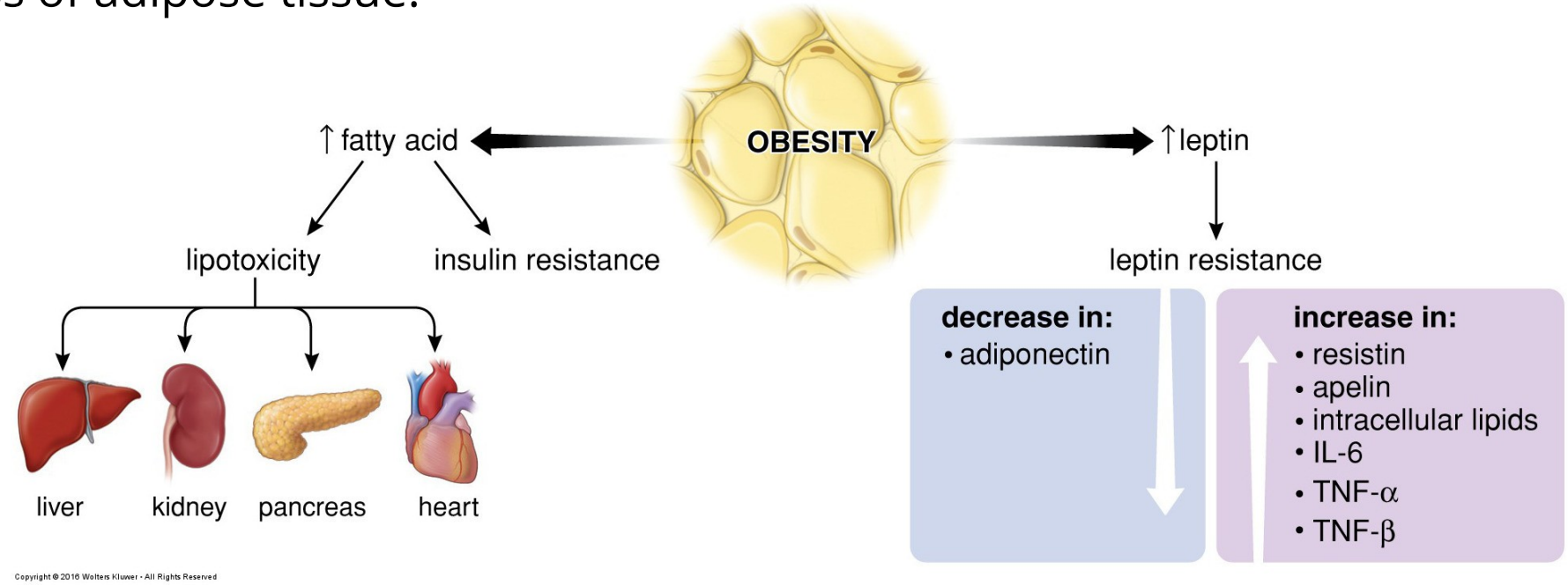



**❯❯ MEDICAL APPLICATION**

In addition to leptin, white adipose tissue secretes numerous other cytokines. It is not clear whether these are produced by adipocytes or other cells of the tissue such as macrophages or fibroblasts. With its increased amounts of white adipose tissue, obesity is characterized by a state of chronic mild inflammation and inflammation-related disorders associated with obesity, such as diabetes and heart disease.

# Clinical Correlation: Obesity

Adult-onset obesity is very often associated with age related metabolic changes and may involve reduced activity of the hormone-sensitive lipases of adipocytes, causing less effective fat mobilization out of the cells. The increased number of adipocytes produced during childhood obesity predisposes an individual to obesity in later life. Despite claims of various fad diets, there is no evidence that any particular type of caloric restriction is more effective than others; rather, any intake of calories that is lower than the energy expenditure will result in loss of adipose tissue.



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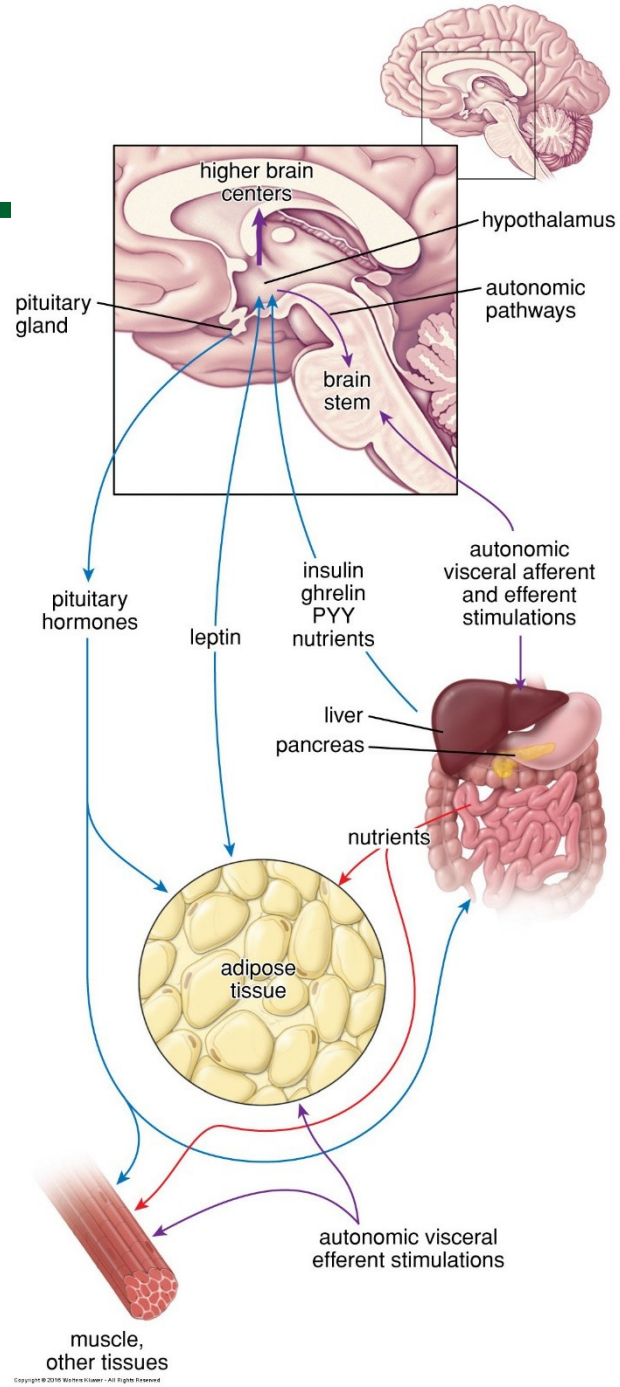
# Regulation of Adipose Tissue: brain-gut-adipose axis

Short-term weight regulation: controls appetite via GI tract hormones **ghrelin** (appetite stimulant) and **peptide YY** (PYY, appetite suppressant)

Long term weight regulation:

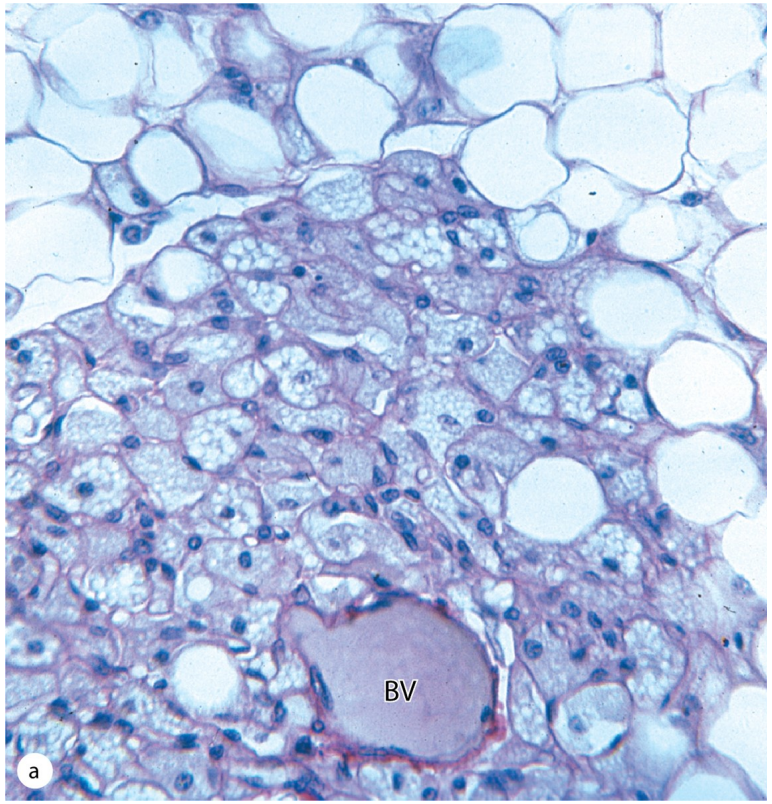
**Leptin:** controls food intake. Mice lacking leptin are obese, however obese humans overexpress leptin. The effect of leptin in satiety may be downstream of the receptor.

**Insulin:** regulates blood glucose levels by encouraging conversion of glucose to triglyceride. It also acts on the hypothalamus.




http://www.hhmi.org/biointeractive/leptin-feedback-control-system

# Brown adipose tissue, abundant in newborns, is markedly reduced in adults.




In newborns, brown adipose tissue makes up about 5% of the total body mass which helps to offset the extensive heat loss that results from the newborn's high surface-to-mass ratio and to avoid lethal hypothermia (a major risk of death for premature babies).

Brown (multilocular, multiple fat droplets) adipose tissue cells are smaller than those of white adipose tissue.

Brown adipose tissue can expand in response to increased blood levels of norepinephrine

**Nonshivering themogenesis**: Metabolism of lipid in brown adipose for heat, common in hibernating animals. UCP-1 (uncoupling protein 1 in mitochondria) uncouples oxidation of fatty acids from ATP production in favor of heat production.

**TABLE 9.2 Summary of Adipose Tissue Features**

| Features | White Adipose Tissue | Brown Adipose Tissue |
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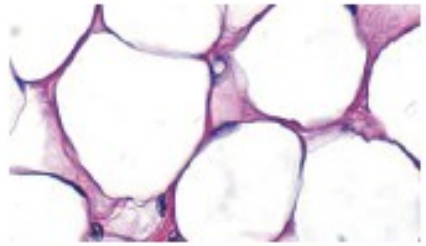
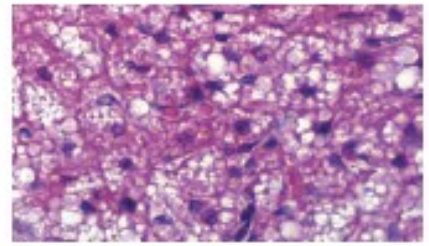
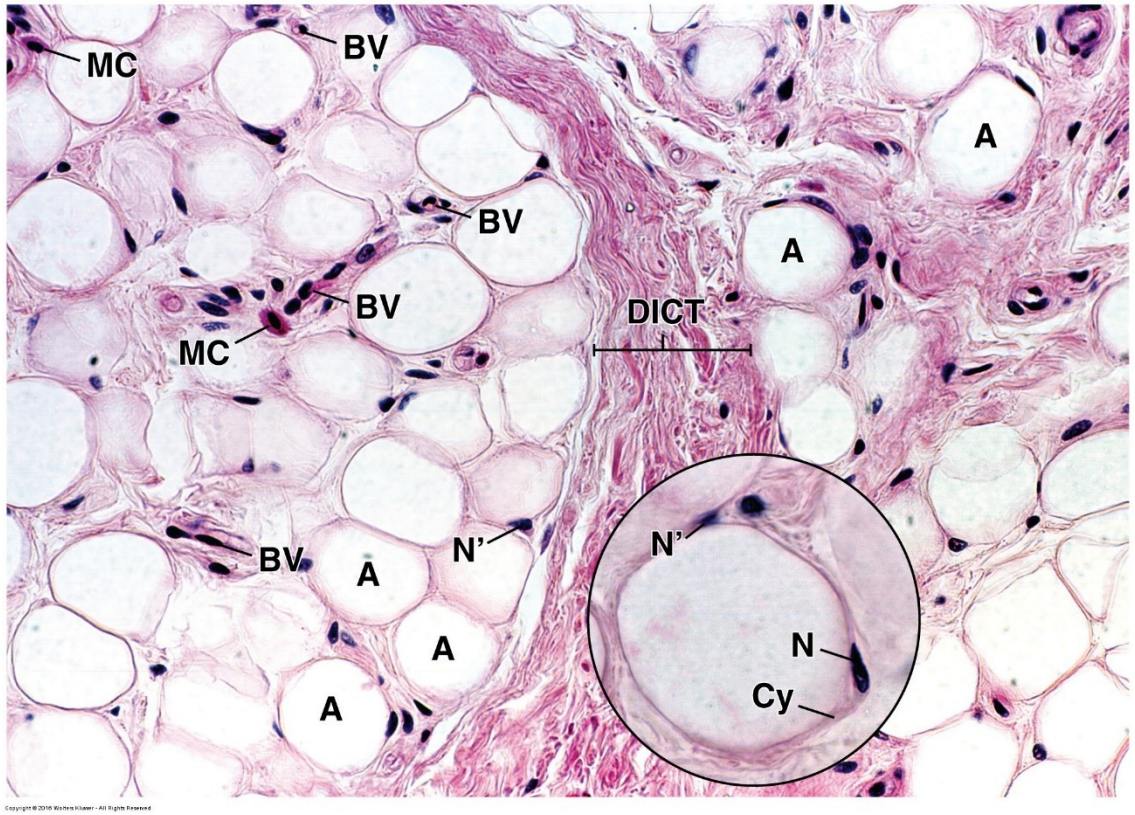
| |  |  |
| Location | Subcutaneous layer, mammary gland, greater omentum, mesenteries, retroperitoneal space, visceral pericardium, orbits (eye sockets), bone marrow cavity | Large amounts in newborn<br>Remnants in adults at the retroperitoneal space, deep cervical and supraclavicular regions of the neck, interscapular, paravertebral regions of the back, mediastinum |
| Function | Metabolic energy storage, insulation, cushioning, hormone production, source of metabolic water | Heat production (thermogenesis) |
| Adipocyte morphology | Unilocular, spherical, flatten nucleus, rim of cytoplasm<br>Large diameter (15–150 μm) | Multilocular, spherical, round eccentric nucleus<br>Smaller diameter (10–25 μm) |
| Transcription factors "master switch" in differentiation | PPAR-γ/RXR | PRDM16/PGC-1 |
| UCP-1 genes expression | No | Yes (unique to brown fat) |
| Mitochondria | Few, poorly developed | Many, well developed |
| Innervation | Few sympathetic nerve fibers | High density of sympathetic nerve fibers |
| Vascularization | Few blood vessels | Highly vascularized tissue |
| Response to environmental stress (cold exposure) | Decreased lipogenesis<br>Increased lipoprotein lipase activity | Increased lipogenesis<br>Decreased lipoprotein lipase activity |
| Growth and differentiation | Throughout entire life from stromal-vascular cells | Only during fetal period<br>Decreases in adult life (exception: individuals with pheochromocytoma and hibernoma) |

# White adipose tissue, human, H&E




Dense irregular connective tissue (DICT) separates the lobules from surrounding structures.

adipocytes (A) with very thin rim of cytoplasm surrounding a single, large fat-containing vacuole fat is lost during tissue preparation

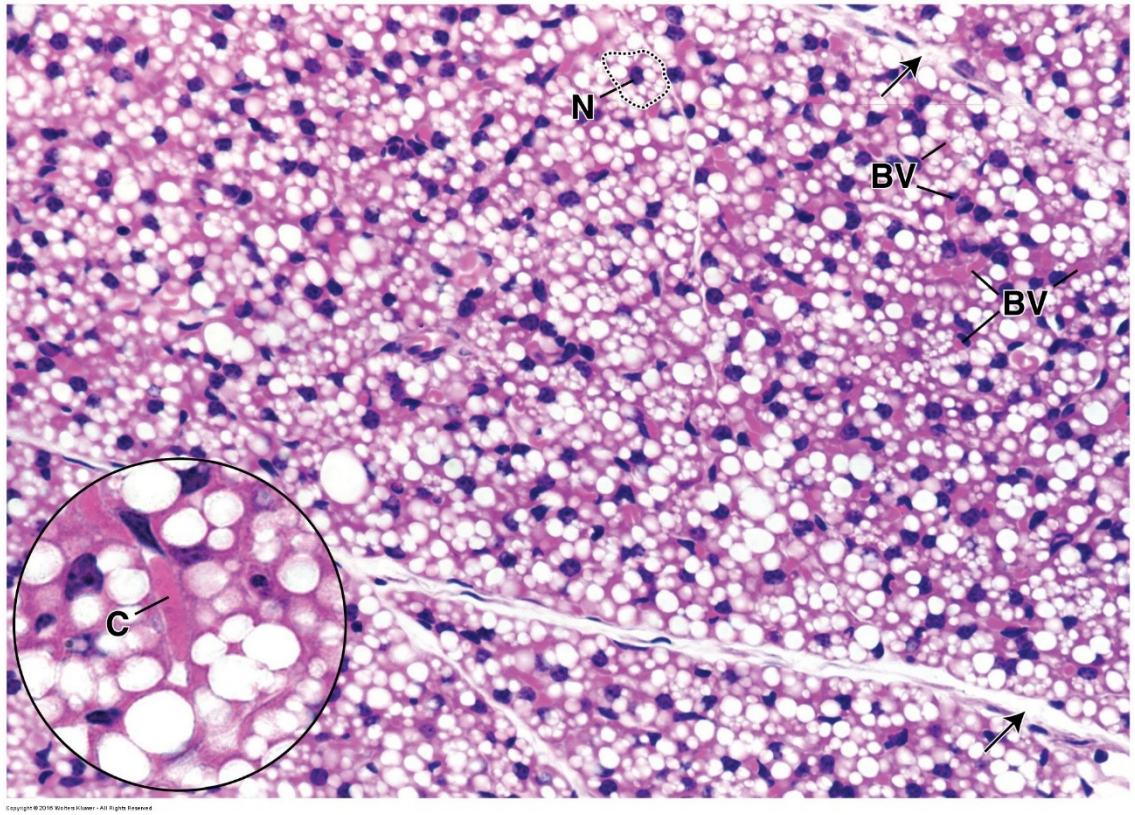
blood vessels (BV), mostly capillaries and venules.

inset shows an adipocyte whose nucleus (N) is relatively easy to identify. It appears to reside within the rim of cytoplasm (Cy), giving the adipocyte the classic “ signet ring”  appearance.

Because of the  relatively large size of the adipocyte, it is very infrequent that the nucleus of the cell is included in the plane of section of a given cell.

Other cells that may be seen within the delicate connective tissue stroma are mast cells (MC) and Nuclei of Fibroblasts (N’)

# Brown adipose tissue, human, H&E




Small fat cells that are very closely packed with minimal intercellular space.

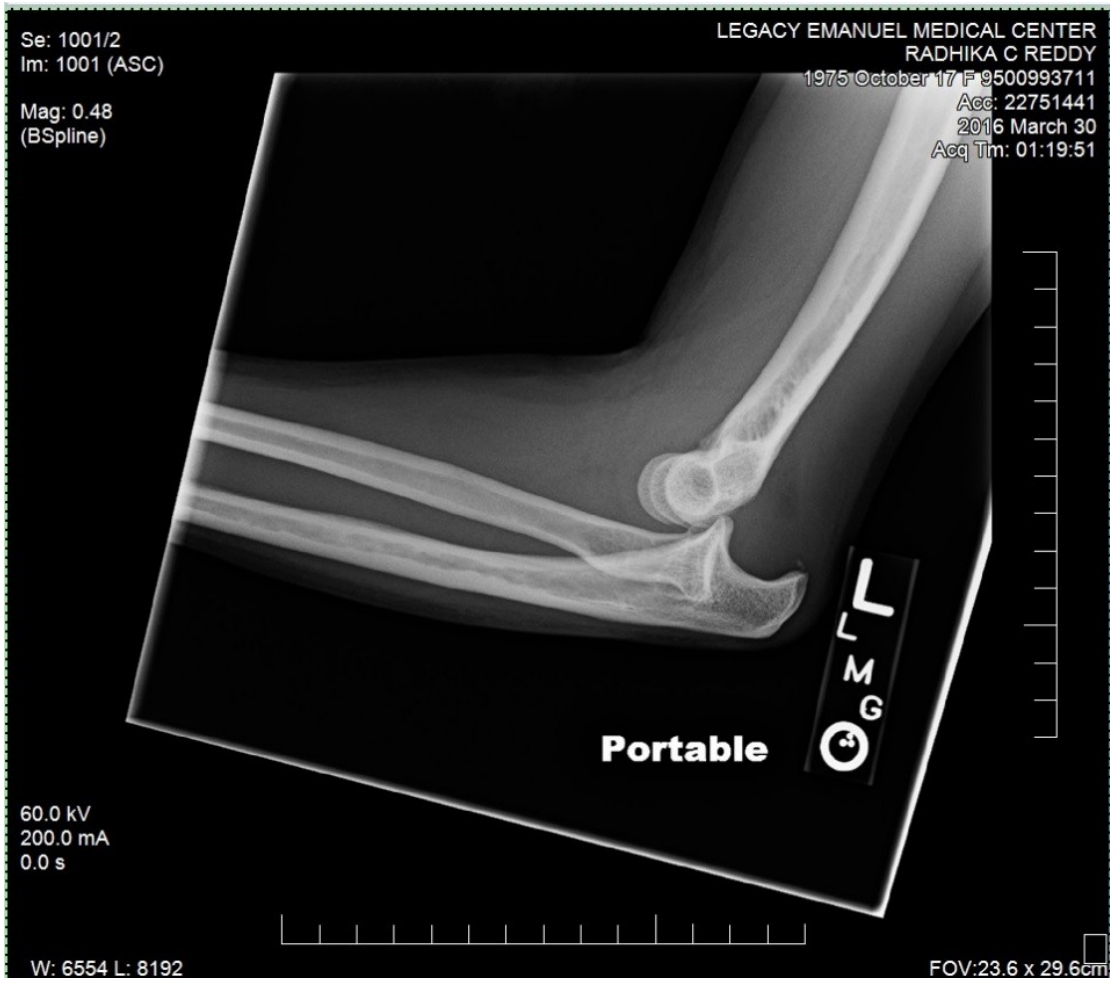
Each cell contains many small, fat-containing vacuoles surrounded by cytoplasm. Included in this cell is its nucleus (N).

Brown adipose tissue is highly vascularized

A capillary (C) can be identified in the inset

# Chapter 7 Cartilage Objectives

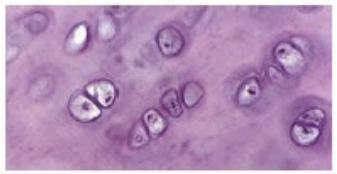
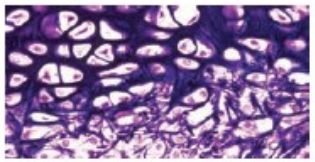
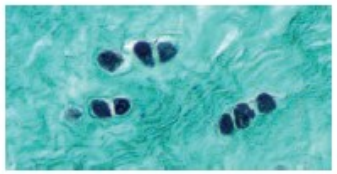
1. General properties of cartilage: Chondrocytes, lacunae, ECM, avascularity
2. Hyaline cartilage
3. Fibrocartilage
4. Elastic cartilage
5. Formation, growth and repair



# Cartilage is a form of connective tissue composed of cells called chondrocytes and a highly specialized extracellular matrix.

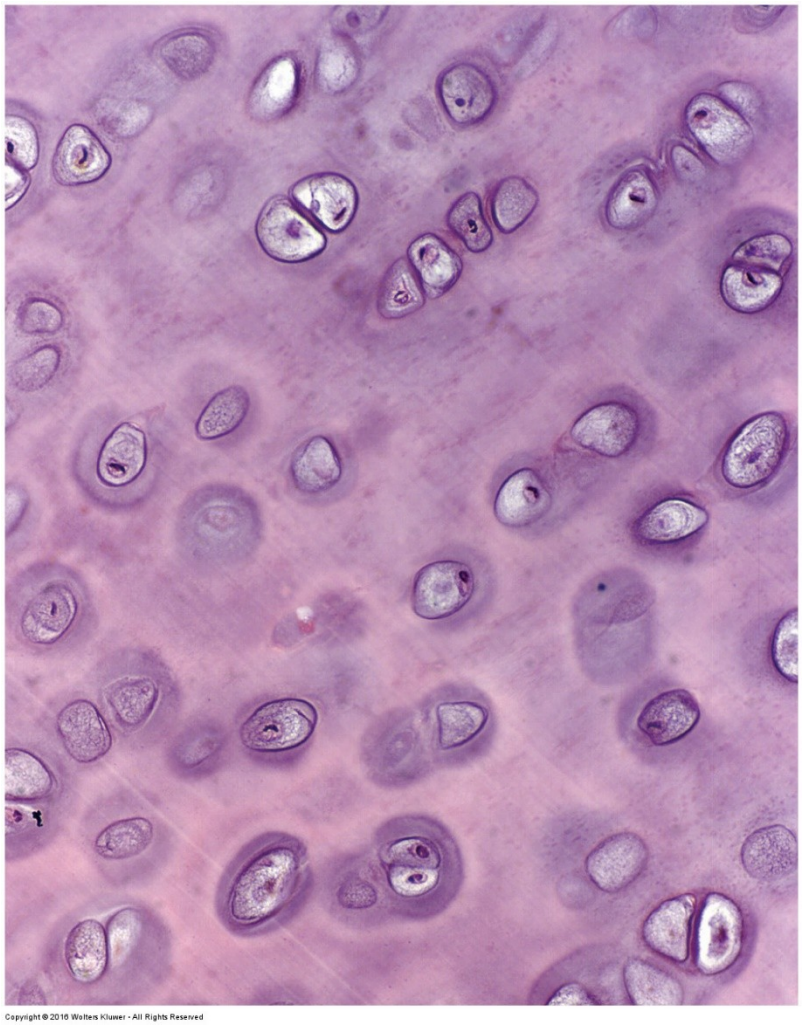
- Supportive connective tissue with flexible, rubbery matrix that gives shape to ear, tip of nose, and larynx
- **Chondroblasts** produce matrix and surround themselves until they become trapped in little cavities (lacunae)
- **Chondrocytes**: cartilage cells in lacunae
- **Perichondrium**: sheath of dense irregular connective tissue that surrounds elastic and most hyaline cartilage (not articular cartilage)
  - Contains a reserve population of chondroblasts that contribute to cartilage growth throughout life
- **No blood vessels**: Diffusion brings nutrients and removes wastes, heals slowly
- Matrix rich in chondroitin sulfate and contains collagen fibers

**TABLE 7.1 Summary of Cartilage Features**

| Features | Hyaline Cartilage | Elastic Cartilage | Fibrocartilage |
|---|---|---|---|
| |  |  |  |
| Location | Fetal skeletal tissue, epiphyseal plates, articular surface of synovial joints, costal cartilages of rib cage, cartilages of nasal cavity, larynx (thyroid, cricoid, and arytenoids), rings of trachea and plates in bronchi | Pinna of external ear, external acoustic meatus, auditory (Eustachian) tube, cartilages of larynx (epiglottis, corniculate, and cuneiform cartilages) | Intervertebral discs, symphysis publis, articular discs (sternoclavicular and temporomandibular joints), menisci (knee joint), triangular fibrocartilage complex (wrist joint), insertion of tendons |
| Function | Resists compression<br>Provides cushioning, smooth, and low-friction surface for joints<br>Provides structural support in respiratory system (larynx, trachea, and bronchi)<br>Forms foundation for development of fetal skeleton and further endochondral bone formation and bone growth | Provides flexible support | Resists deformation under stress |
| Presence of perichondrium | Yes (except articular cartilage and epiphyseal plates) | Yes | No |
| Undergoes calcification | Yes (i.e., during endochondral bone formation, during aging process) | No | Yes (i.e., calcification of fibrocartilaginous callus during bone repair) |
| Main cell types present | Chondroblasts and chondrocytes | Chondroblasts and chondrocytes | Chondrocytes and fibroblasts |
| Characteristic features of extracellular matrix | Type II collagen fibrils and aggrecan (the most important proteoglycan) | Type II collagen fibrils, elastic fibers, and aggrecan | Types I and II collagen fibers and versican (a proteoglycan secreted by fibroblasts) |
| Growth | Interstitially and appositionally, very limited in adults | | |
| Repair | Very limited capability, commonly forms scar, resulting in fibrocartilage formation | | |

# Hyaline cartilage is distinguished by a homogeneous, amorphous matrix.

- extensive extracellular matrix
- sparse population of chondrocytes
- Throughout the **cartilage matrix** are spaces called **lacunae**.
- **Chondrocytes** within these lacunae provides a low-friction surface, participates in lubricating synovial joints, and distributes applied forces to the underlying bone.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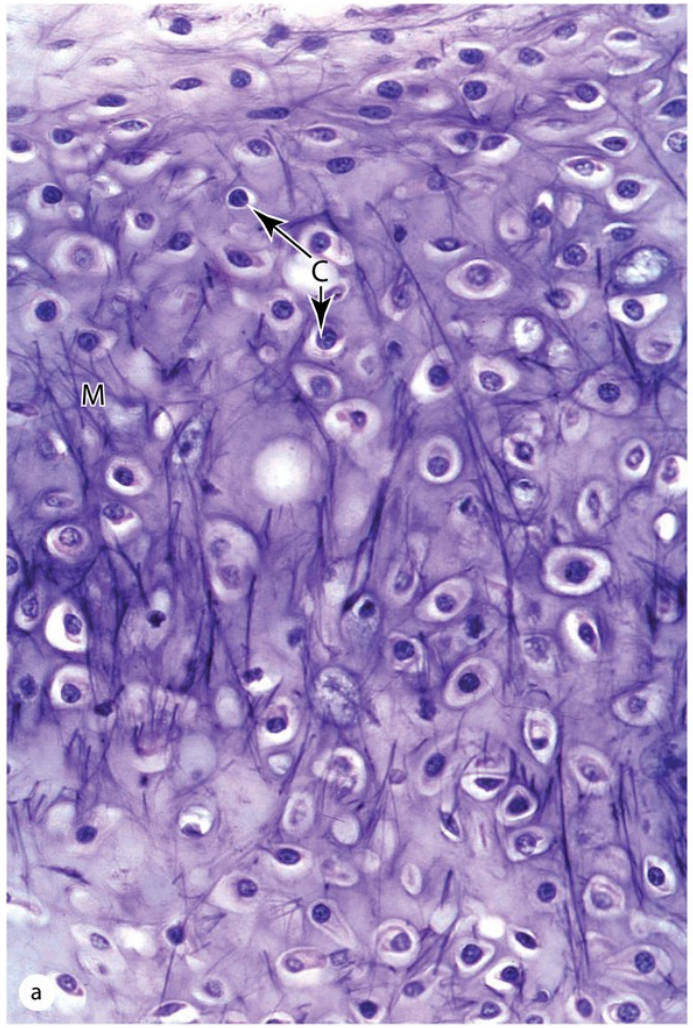
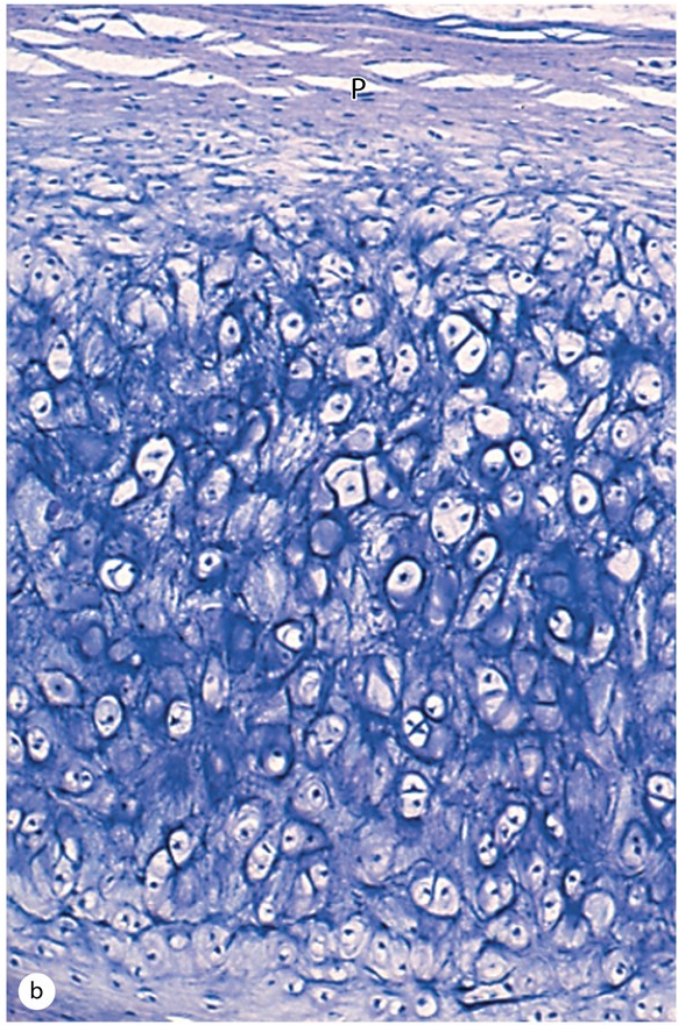
**MEDICAL APPLICATION**
Many genetic conditions in humans or mice that cause defective cartilage, joint deformities, or short limbs are due to recessive mutations in genes for collagen type

**MEDICAL APPLICATION**
Osteoarthritis, a chronic condition that commonly occurs during aging, occurs most in joints that are weightbearing (knees, hips) or heavily used (wrist, fingers) are most prone to cartilage degeneration

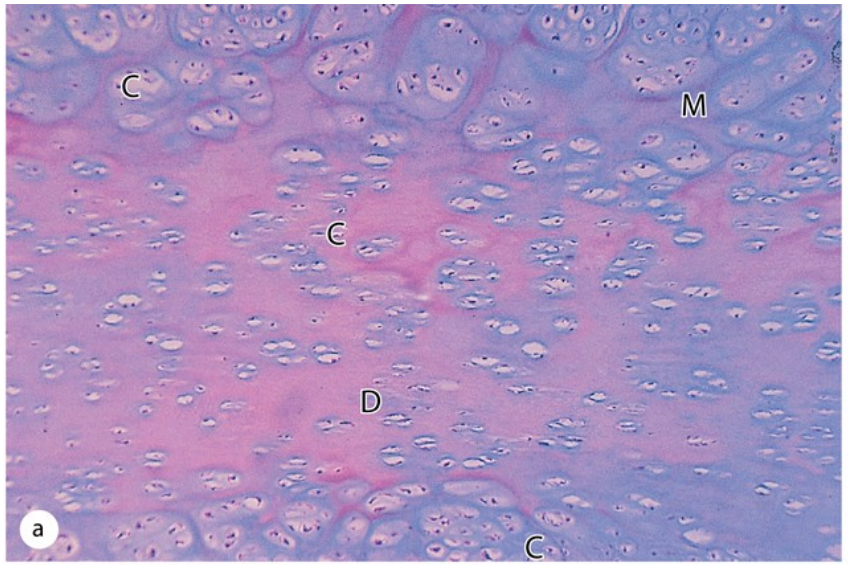
# The chondrocytes (C) and overall organization of elastic cartilage are similar to those of hyaline cartilage.

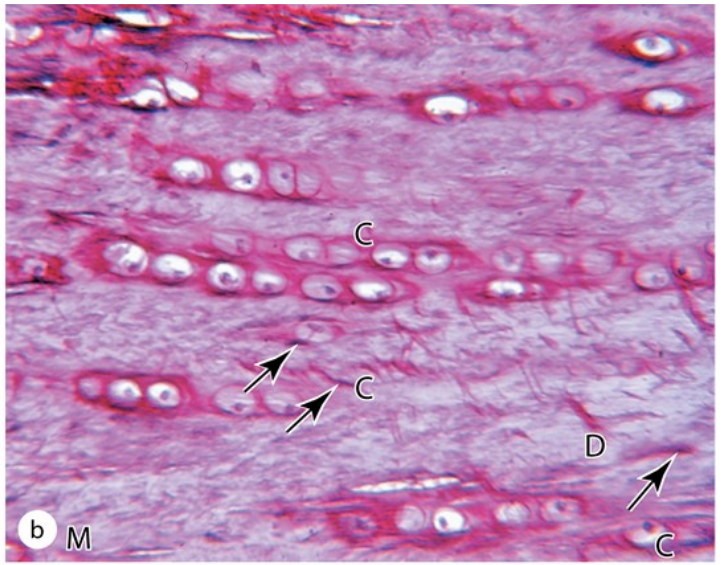



Stains for elastin, however, reveal many dark-staining elastic fibers in the matrix (**M**), in addition to the major components found in hyaline matrix. Elastic fibers provide greater flexibility to this form of cartilage. The section in part **b** includes perichondrium (**P**) that is also similar to that of hyaline cartilage. **(a)** X160. Hematoxylin and orcein. **(b)** X100. Weigert resorcin-fuchsin.

# Fibrocartilage varies in different organs, but is essentially a mixture of hyaline cartilage and dense connective tissue.

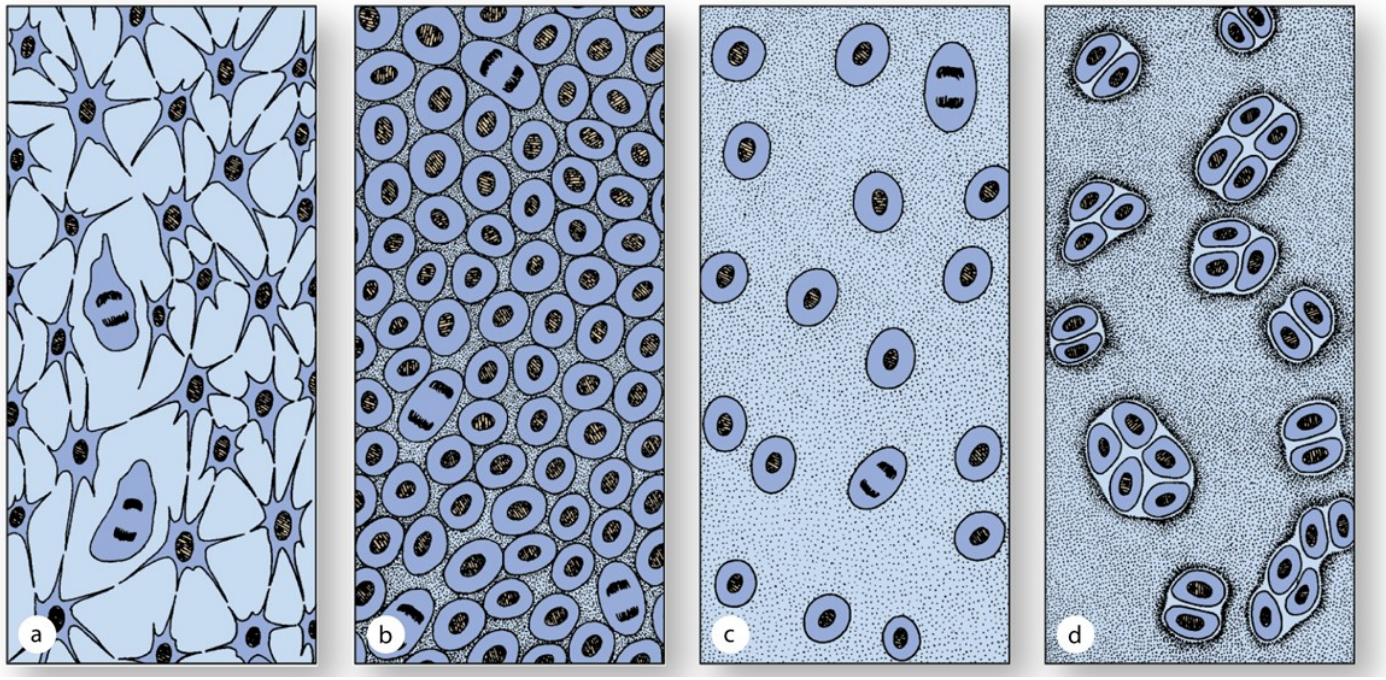



Shotgun Histology Fibro-Cartilage: https://www.youtube.com/watch?v=imDyTwvgNaQ

**(a)** A section of pubic symphysis shows lacunae with isolated and grouped chondrocytes (**C**) surrounded by matrix (**M**) and separated in some areas by dense regions (**D**) containing more concentrated acidophilic type I collagen. No separate perichondrium is present on fibrocartilage. X100. H&E.
**(b)** At higher magnification in a small region of intervertebral disc, the axially arranged aggregates of chondrocytes (**C**) are seen to be surrounded by small amounts of matrix and separated by larger regions with dense collagen (**D**) and a small number of fibroblasts with elongated nuclei (arrows). X250. Picrosirius-hematoxylin.

# Major stages by which embryonic cartilage is formed




(a) Mesenchyme is the precursor for all types of cartilage.
(b) Mitosis and early differentiation produces a tissue with **chondroblasts**.
(c) Chondroblasts are then separated from one another again by their production of ECM.
(d) Multiplication of chondroblasts within the matrix gives rise to **isogenous cell aggregates** surrounded by a condensation of territorial matrix.