Lecture 1

General Histology

Second Grade/ College of Dentistry/

University of Baghdad

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Cells:

The smallest living unit of organization in the body is the cell, because each cell is capable of performing any necessary functions without the aid of other cells **(Figures 1 and 2, Table 1)**. Each cell has a cell membrane, cytoplasm, organelles, and inclusions. Thus, every cell is a world unto itself (like a small gated city) surrounded by a boundary, having “factories” and other “industries” that make it almost self-sufficient.

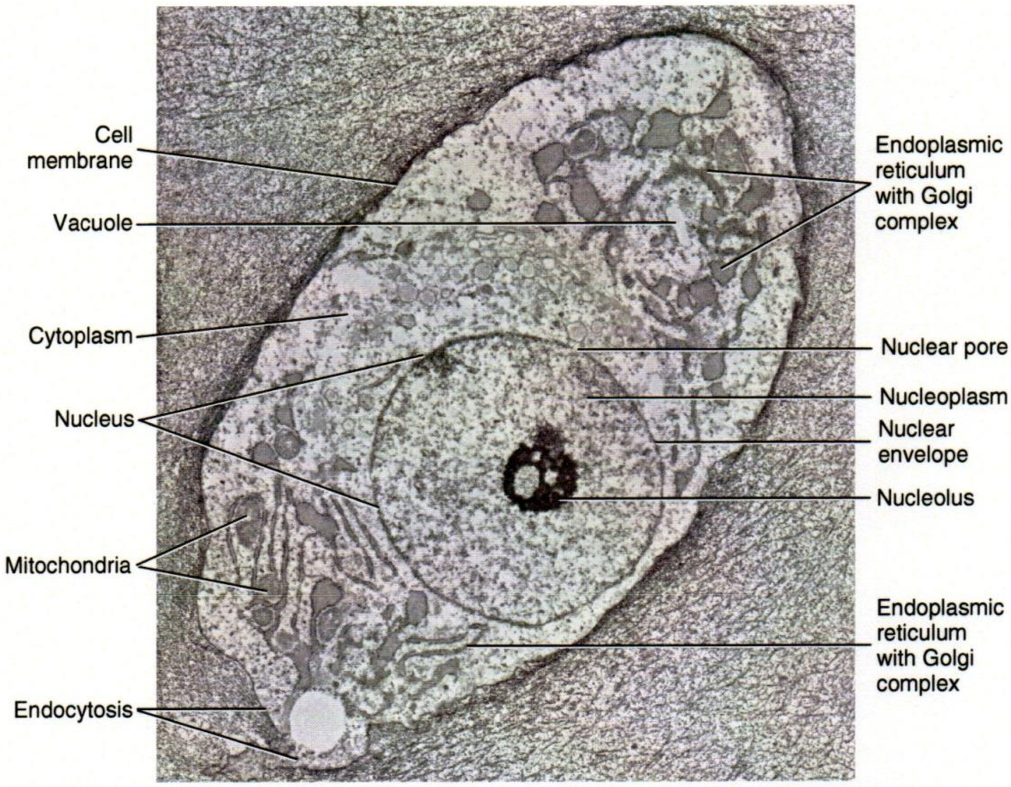


Figure 1. Electron micrograph of the cell and its most visible contents, such as its cell membrane and nucleus

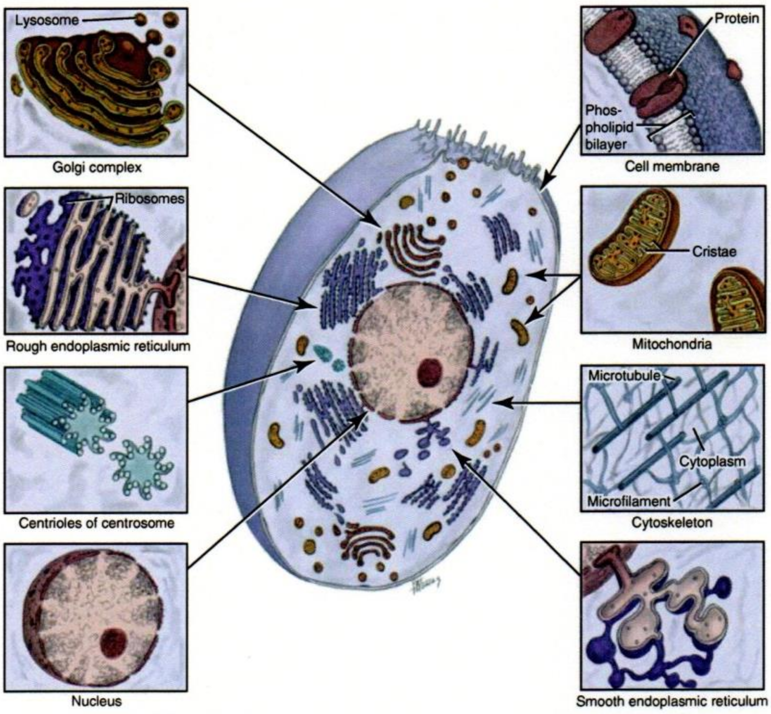


Figure 2. The cell with its organelles and cell membrane examined.

Table 1. Body Components

Body Components	**Features**
Cell	Smallest living unit of organization: epithelial cell, neuron, myofiber, chondrocyte, osteocyte, fibroblast, erythrocyte, macrophage, sperm
Tissue	Collection of similarly specialized cells: epithelium, nervous tissue, muscle, cartilage, bone, connective tissue, blood
Organ	Independent body part formed from tissue: skin, brain, heart, liver
System	Organs functioning together: central nervous system, respiratory system, immune system, cardiovascular system

Cells also interact with one another similar to how a city interacts with other cities. Cells with similar characteristics of form and function are grouped together to form a **tissue**, analagous to how states are then formed from cities having a common goal (see Table 1).

Thus, a tissue is a collection of similarly specialized cells, which are most often surrounded by extracellular materials. Various tissue types are then bonded together to form an **organ**, a somewhat independent body part that performs a specific function or functions, similar to countries formed from like-minded states. Organs can further function together globally as a **system**.

Cells in a tissue undergo cell division to reproduce and replace the dead tissue cells. As a result of the division process, two daughter cells that are identical to each other and to the original parent cell are formed. This process consists of different phases, in regard to the different components of the cell.

However, cells also interact with the extracellular environment in many ways. Cells can perform **exocytosis**, which is an active transport of material from a vesicle within the cell out into the extracellular environment. Exocytosis occurs when there is fusion of a vesicle membrane with the cell membrane and subsequent expulsion of the contained material.

The uptake of materials from the extracellular environment into the cell is **endocytosis**. Endocytosis can take place as an invagination of the cell membrane. Endocytosis can also take the form of **phagocytosis**, which is the engulfing and then digesting of solid waste and foreign material by the cell through enzymatic breakdown of the material.

Cell Anatomy

The **cell membrane** (or plasma membrane) surrounds the cell (see Figures 1 and 2). Despite its fragile microscopic structure, it is a tough and resourceful "gatekeeper" for the cell's interior. The cell membrane is associated with many of the mechanisms of intercellular junctions and other functions of the cell.

The **cytoplasm** includes the semifluid part contained within the cell membrane boundary, as well as the skeletal system of support or cytoskeleton. The cytoplasm contains not only a number of structures but also cavities or **vacuoles**.

Organelles

The **organelles** are metabolically active specialized structures within the cell (see Figures 1 and 2). The organelles allow each cell to function according to its genetic code. Organelles also subdivide the cell into compartments. The major organelles of the cell include the nucleus, mitochondria, ribosomes, endoplasmic reticulum, Golgi complex, lysosomes, and the cytoskeleton.

Inclusions

The cell also contains **inclusions**, which are metabolically inert substances that are also considered transient over time in the cell (see Figure 2). These include masses of organic chemicals and often are recognizable microscopically. These inclusions are released from storage by the cell and used as demand dictates. Lipids and glycogen can be decomposed for energy from inclusions in the cell. Melanin is stored as inclusions in certain cells of the skin and oral mucosa and is responsible for the pigmentation of these tissue types. Inclusions also include residual bodies, which are spent lysosomes and their digested material.

Cell Division

Cell division or **mitosis** is a complex process involving many of the organelles of the cell. Mitosis functions during tissue growth or regeneration, and its activity is dependent on the length of the individual cell's lifespan.

Extracellular Materials

The cells in each tissue type are surrounded by extracellular materials, which include both tissue fluid and intercellular substance. **Tissue fluid** (or interstitial fluid) provides a medium or matrix for dissolving, mixing, and transporting substances and for carrying out chemical reactions. Similar to blood plasma in its content of ions and diffusible substances, tissue fluid contains a small amount of plasma proteins.

Tissue fluid enters the tissue to surround the cells by diffusing through the capillary walls as a filtrate from the plasma of the blood. Tissue fluid then drains back into the blood as lymph through osmosis, via the lymphatics. The amount of tissue fluid varies from tissue to tissue, with smaller variations occurring over time within any one tissue. An excess amount can accumulate when an injured tissue undergoes an inflammatory response, leading to edema with its tissue enlargement.

Intercellular substance (or ground substance) is shapeless, colorless, and transparent material in which the cells of a tissue are imbedded; it also fills the spaces between the cells in a tissue. The intercellular substance serves as a barrier to the penetration of foreign materials into the tissue as well as a medium for the exchange of gases and metabolic substances. The surrounding cells produce the intercellular substance, and one of its most common elements is hyaluronic acid.

Intercellular Junctions

Certain cells in varying tissue are joined by the mechanism of **intercellular junctions**. These are mechanical attachments formed between cells, and also between cells and adjacent noncellular surfaces. With the formation of these intercellular junctions, the cell membranes of different cells come close together but do not completely attach. Higher-power magnification is needed to visualize these attachments, which appear as dense bodies. All intercellular junctions involve some sort of intricate attachment device. The attachment device includes an attachment plaque that is located within the cell as well as adjacent tonofilaments.

An intercellular junction between cells is formed by a **desmosome**, such as that present in the superficial layers of the skin or oral mucosa (**Figure 3**).

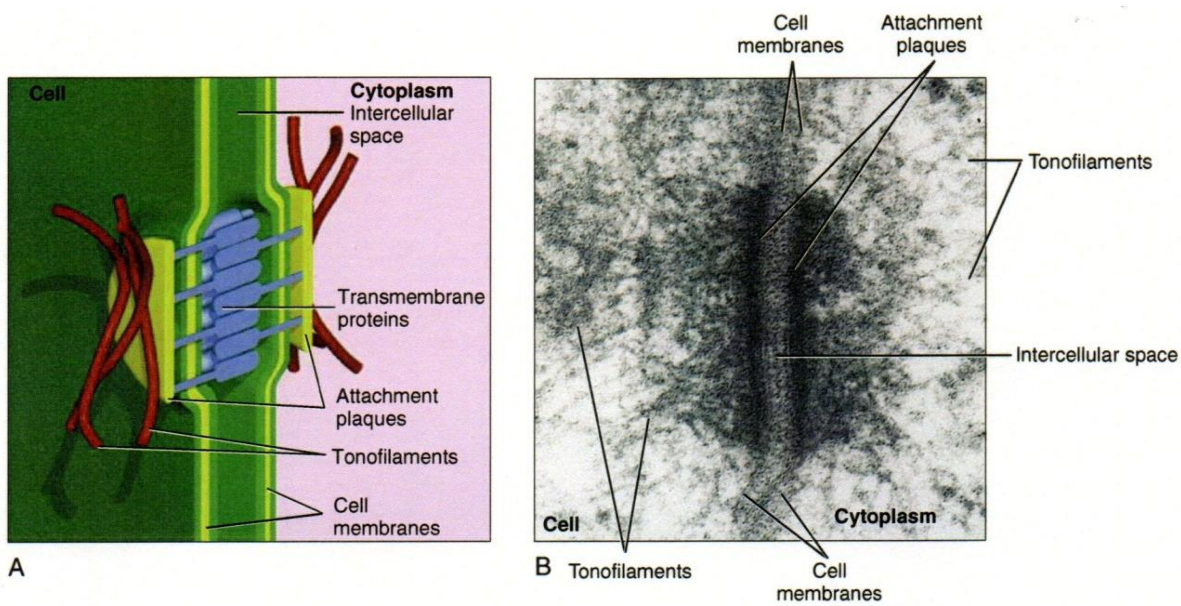


Figure 3. Intercellular junction between cells via a desmosome. A, Diagram. B, Electron micrograph. The cell adhesion between cell membranes is mediated by transmembrane proteins.

The desmosomal junctions are also released during tissue turnover and then become reattached in new locations as the cells migrate, such as during repair after an injury to the skin or oral mucosa (see Figure 3 in Lecture 3).

Another type of intercellular junction is formed by a **hemidesmosome**, which involves an attachment of a cell to an adjacent noncellular surface (**Figure 4**). This type of attachment is used for attaching the epithelium to connective tissue, such as with the basement membrane in the skin and oral mucosa (see Figure 4 in Lecture 3).

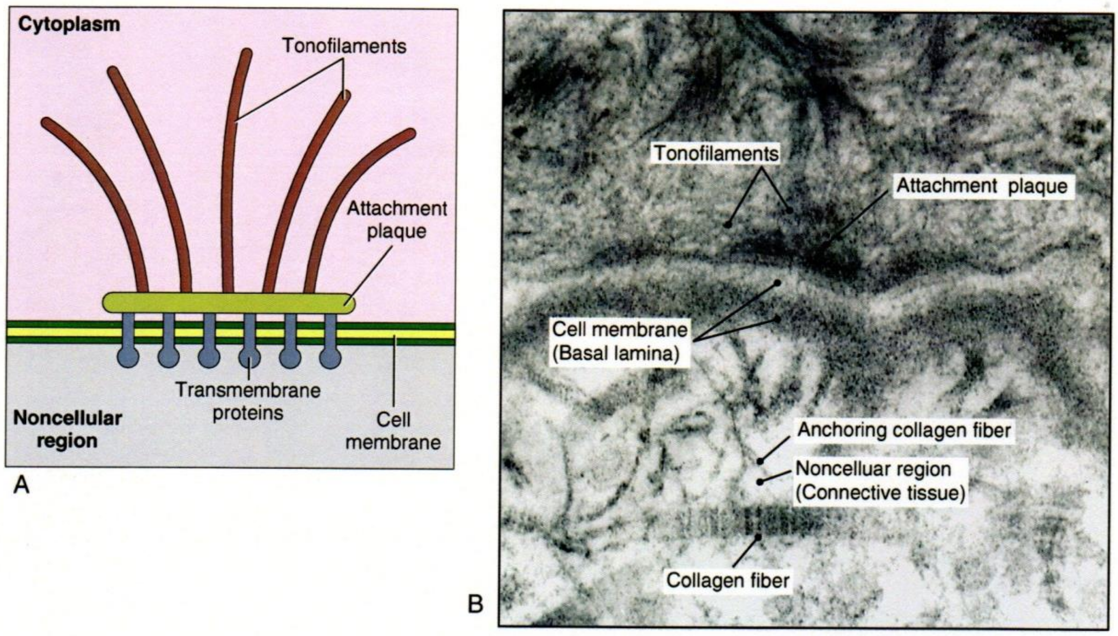


Figure 4. Intercellular junction between a cell with its cytoplasm and noncellular surface via a hemidesmosome. A, Diagram. B, Electron micrograph. The attachment of cells is to an adjacent noncellular surface is by the adhesion of the noncellular surface mediated by transmembrane protein.

The attachment device of a hemidesmosome represents half of a desmosome because it involves a smaller attachment plaque and has tonofilaments from only the cellular side. Thus, it appears as a thinner disc because the noncellular surface cannot produce the other half of the attachment mechanism. Hemidesmosomes are also involved as a mechanism allowing gingival tissue to be secured to the tooth surface by the epithelial attachment, which is similar to the attachment between the nails and adjoining nail beds.

Lecture 2

General Histology/ **Dr.Ayat A. Sabeeh.**

Basic Tissue:

Basic Tissue Properties:

Dental professionals must have a clear understanding of the histology of the basic tissue types before studying the distinct tissue types present in the oral cavity and associated regions of the face and neck. This information will help dental professionals fully understand the processes involving tissue renewal and repair and the process of aging during clinical care to promote orofacial health, as well as the underlying pathologic processes that can occur.

As was discussed in **Lecture 1**, the smallest living unit of organization in the body is the cell because each cell is capable of performing any necessary functions without the aid of other cells (see Figures 1 and 2 in Lecture 1). It was also noted that a group of cells with similar characteristics of form and function together form a tissue (see Table 1 in Lecture 1). A tissue is a collection of similarly specialized cells that will then form into organs.

Tissue types are categorized according to four basic histologic types. These basic histologic tissue types include epithelial, connective, muscle, and nerve tissue **(Table 1)**. In addition, these basic tissue types have subcategories that serve specialized functions.

Table 1. Basic Tissue Classification

Tissue	**Types**
Epithelium	Simple: Squamous, cuboidal, columnar, pseudostratified
	Stratified: Squamous (keratinized, nonkeratinized), cuboidal, columnar, transitional
Connective tissue	Solid soft: Connective tissue proper, specialized (adipose, fibrous, elastic, reticular) Solid firm: Cartilage Solidrigid:Bone Fluid: Blood, lymph
Muscle	Involuntary: Smooth, cardiac Voluntary: Skeletal
Nerve	Afferent: Sensory Efferent: Motor

It is during prenatal development that embryonic cell layers differentiate into the various basic embryologic tissue types, including ectoderm, mesoderm, and endoderm, that will later form in some manner into these basic histologic tissue types of the body.

Most tissue of the body undergoes **regeneration** as the individual cells die and are removed from the tissue and new ones take their place. Regeneration is the natural renewal of a tissue and thus an organ; it is produced by growth and differentiation of new cells and intercellular substances. Regeneration occurs through growth from the same type of tissue that has been destroyed or from its precursor. Regeneration is a continuous physiologic process that occurs with most tissue types and in most organs; it even occurs with injury and disease. However, tooth enamel is an example of a tissue type that sadly does not undergo regeneration.

The **turnover time** is the time it takes for the newly divided cells to be completely replaced throughout the tissue. The turnover time differs for each of the basic tissue types in the orofacial region, as well as for specific regions of the oral cavity. A more complete understanding of turnover time may be the future basis for how the aging process as well as disease processes in the body are delayed or prevented, including those occurring in the oral cavity.

Lecture 3

General Histology Dr.Ayat A. Sabeeh

Basic Tissue

Epithelium Properties

Epithelium (plural, epithelia) is the tissue that covers and lines both the external and internal body surfaces, including vessels and small cavities. Epithelium not only serves as a protective covering or lining but is also involved in tissue absorption, secretion, sensory, and other specialized functions. It serves to protect the more complex inner structures from physical, chemical, and pathogenic attack, as well as dehydration and heat loss by its formation as an epithelial barrier.

Depending on individual classification, epithelial tissue can be derived from any of the three embryonic cell layers based on the location when developing. Importantly, for dental professionals, both the epithelium of the skin and oral mucosa are of similar ectodermal origin. In comparison, those lining the respiratory and digestive tract are of endodermal origin, and those lining the urinary tract are derived from mesoderm.

Epithelium Histology

Epithelium generally consists of closely grouped polyhedral cells surrounded by very little or no intercellular substance or tissue fluid **(Figure 1)**.

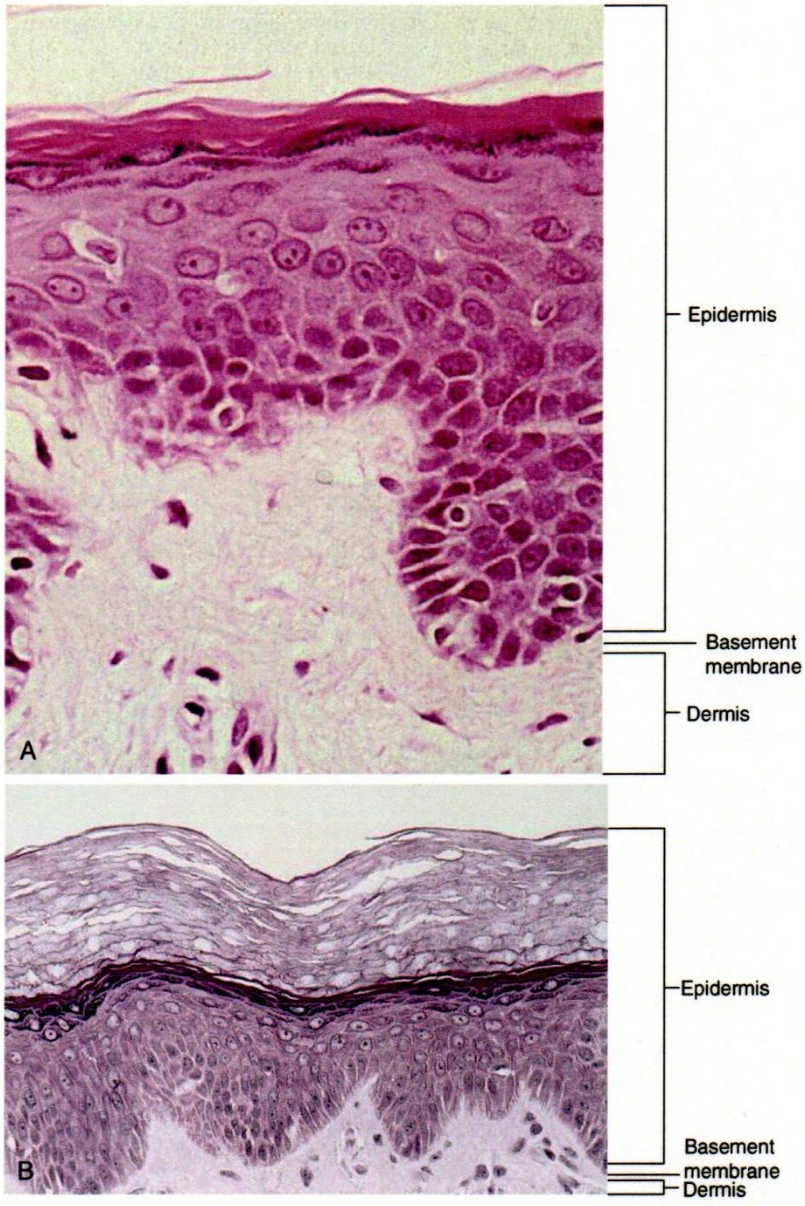


Figure 1. Microscopic sections of the skin (A and B), which demonstrates the epidermis and dermis or epithelium and connective tissue, respectively. A basement membrane is located between these two tissue types.

Epithelium is avascular, having no blood supply of its own. Cellular nutrition consisting of oxygen and metabolites is obtained by diffusion from the adjoining connective tissue, which is usually highly vascularized, sharing its source of nutrition.

This tissue is capable of rapid cellular turnover. In fact, epithelium is highly regenerative because its deeper germinal cells are capable of reproduction by mitosis. Epithelial cells usually undergo cellular differentiation as they move from the deeper germinal layers to the surface of the tissue to be shed or lost. An exception to the process of cellular maturation is the junctional epithelium of the gingival sulcular region that is attached to the tooth surface.

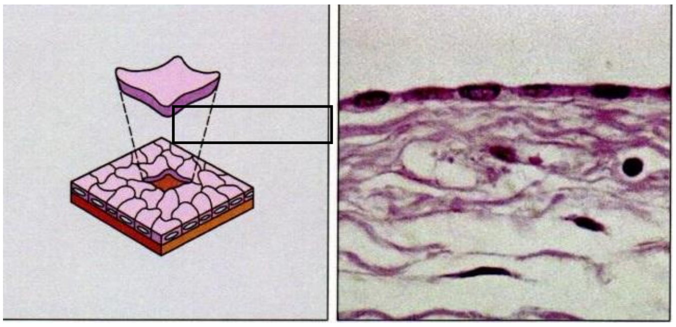
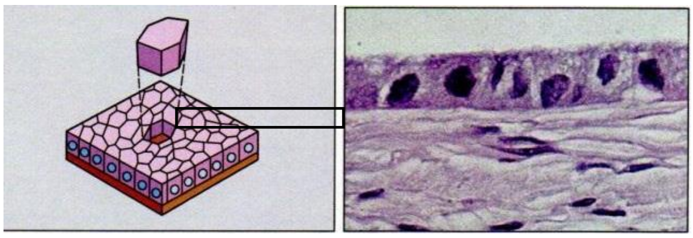
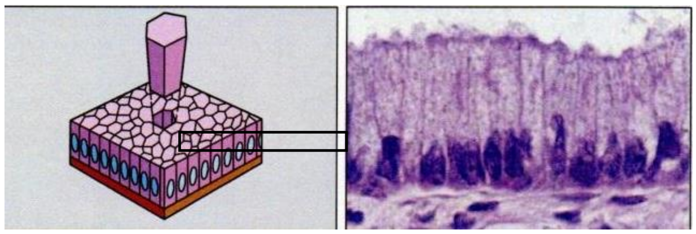
Epithelial cells are usually tightly joined to each another by intercellular junctions provided for by the desmosomes except in the more superficial layers (see Figure 3 in Lecture 1). The epithelial cells are also tightly joined in some cases to adjacent noncellular surfaces by hemidesmosomes, as is the case with its relationship to the basement membrane (see Figure 4 in Lecture 1) as well as the junctional epithelium of the gingival sulcular region that is attached to the tooth surface.

A basement membrane is located between most epithelium and deeper connective tissue, such as with both the skin and oral mucosa. Components of basement membrane are produced by both the overlying epithelium as well as the adjoining connective tissue.

Epithelium Classification

Epithelium can be classified into two main categories based on the arrangement into layers of cells: simple and stratified (see Table 1 in Lecture 2). **Simple epithelium** consists of a single layer of epithelial cells. The further classification of the tissue involves different types of epithelial cells according to cellular structure; they can be classified as either simple squamous, simple cuboidal, or simple columnar (**Table 2**).

Table 2. Epithelial Cell Types

Cell Types and Features	**Microscopic Structure***
Squamous cells Flattened cells with cell height much less than cell width (i.e., endothelium)	
Cuboidal cells Cube-shaped cells with approximately equal cell height and cell width (i.e., salivary gland duct lining)	
Columnar cells Rectangular cells in which cell height exceeds cell width (i.e., salivary gland duct lining)	

*Note that these epithelial cells are shown only within simple epithelium.

Simple squamous epithelium consists of flattened platelike epithelial cells, or **squames**, lining blood and lymphatic vessels, heart, and serous cavities, as well as interfaces in the lungs and kidneys. The term **endothelium** is used to refer to the simple squamous epithelium lining of these vessels and serous cavities.

Simple cuboidal epithelium consists of cube-shaped cells that line the ducts of various glands, such as certain ducts of the salivary glands. Simple columnar epithelium consists of rectangular cells, such as in the lining of other salivary gland ducts, as well as the inner enamel epithelium of a maturing tooth germ, whose cells become enamel-forming ameloblasts.

Epithelium can also be considered **pseudostratified columnar epithelium**, which is named as such since it falsely appears as multiple cell layers when viewed with lower power magnification due to the cells' nuclei appearing at different levels (**Figure 2**).

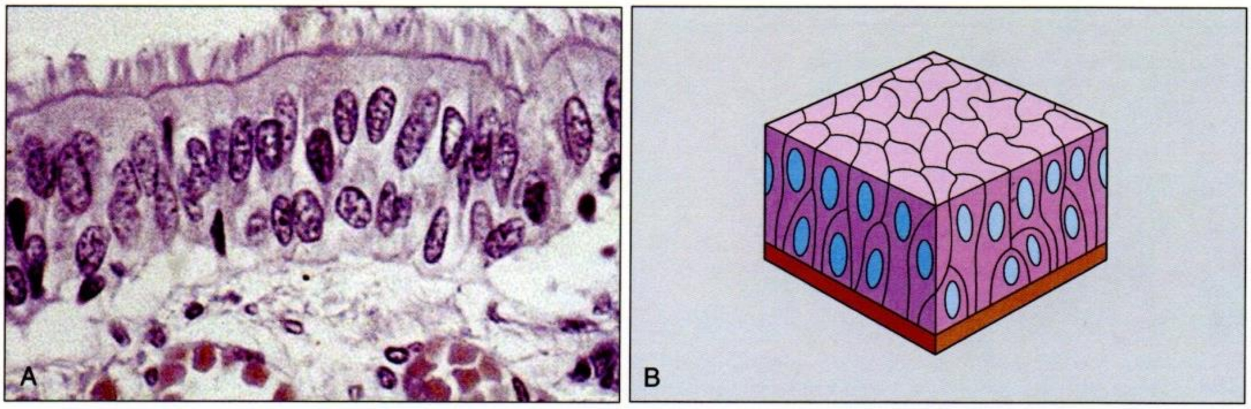


Figure 2. Pseudostratified columnar epithelium. A, Photomicrograph. B, Diagram. This type of epithelium can line the respiratory system.

However, in reality, as viewed with higher power magnification, only cells of different heights are seen. Thus, this is a type of simple epithelium because all the cells line up to contact the inner surface of the basement membrane even if not all the cells reach the outer surface of the tissue. Pseudostratified columnar epithelium lines the upper respiratory tract, including the nasal cavity and paranasal sinuses. This type of epithelium may have cilia or be nonciliated at the tissue surface.

In contrast to simple epithelium, **stratified epithelium** consists of two or more layers of cells, with only the deepest layer lining up to contact the basement membrane (see Table 1 in Lecture 2). It is important to note that only the cellular shape of the surface layer is used to determine the classification of stratified epithelium. Thus, stratified epithelium can consist of cuboidal, columnar, or squamous epithelial cells, or a combination of cell types, as seen in a transitional epithelium.

Most epithelium in the body consists of **stratified squamous epithelium**, which includes the superficial layer of both the skin and oral mucosa (see Figure 1) and (see Figure 8 in Lecture 4). Only the most superficial layers of this tissue are flat cells, or squames; the deeper cells vary from the deeper cuboidal to the more superficial polyhedral. Interdigitation of the outer epithelium with the deeper connective tissue occurs with the epithelial tissue forming **rete ridges** (or rete pegs) (see Figure 8 in Lecture 4); however, there is always a basement membrane located between these two tissue types.

Stratified squamous epithelium can be nonkeratinized or keratinized. Nonkeratinized tissue can be found in certain regions of the oral mucosa as well as keratinized tissue. The keratin found within the keratinized tissue is a tough, fibrous, opaque, waterproof protein that is impervious to pathogenic invasion and resistant to friction. Keratin is produced during the maturation of the keratinocyte epithelial cells as they migrate from near the basement membrane to the surface of the keratinized tissue.

Another example of keratinized stratified squamous epithelium is **epidermis**, which is the superficial layer of the skin (see Figure 1) and (see Figure 8 in Lecture 4). The epidermis overlies a basement membrane and the adjoining deeper layers of connective tissue (dermis and hypodermis, respectively). The skin has varying degrees of keratinization depending on the region of the body. Areas such as the palms of the hands and bottom of the feet have thicker layers of keratin, which form calluses. However, the keratin is less densely packed in both the skin and oral cavity, as compared with the densely packed hard keratin of the nails and hair.

Epithelium Regeneration, Turnover, and Repair

Turnover of both the epithelium in skin or oral mucosa occurs as a result of the cell division during the regeneration process. Cellular turnover of epithelium occurs as the newly formed deepest cells migrate superficially from their formation near the basement membrane. Thus, the turnover time is the time needed for a cell to divide during mitosis and pass through the entire thickness of tissue. In order to migrate, the cells release and then regain their desmosomal connections at the intercellular junctions in the more superficial location.

The turnover time is faster for all types of epithelium, as compared to connective tissue. This faster turnover time is a result of the higher level of mitosis in those deepest dividing cells near the basement membrane. Thus, the older, superficial epithelial cells are being shed or lost at the same rate as the deeper germinal cells are dividing into more cells during turnover time.

These overall faster turnover times vary only slightly but sometimes importantly for the different types of epithelium. The epithelium of the oral mucosa generally has a faster turnover time than the epidermis of the skin (**Table 3**).

Table 3. Oral Tissue Mean Turnover Time

Oral Tissue	**Mean Turnover Time**
Hard palate	24 days
Floor of mouth	20 days
Buccal and labial mucosa	14 days
Attached gingiva	10 days
Taste buds	10 days
Junctional epithelium (attached to tooth)	4 to 6 days

*Note that for comparison, the turnover time for the skin is 27 days.

More specifically within the oral cavity, the epithelium of the buccal mucosa that lines the cheek tissue has a faster turnover time (14 days) than the epithelium that covers the skin (27 days).

The differences of turnover time are especially noted during repair or healing of the tissue after injury. Immediately after an injury to either the skin or oral mucosa, a clot from blood products forms in the area, and the inflammatory response is triggered by the white blood cells from the blood supply as they migrate into the tissue (**Figure 3**).

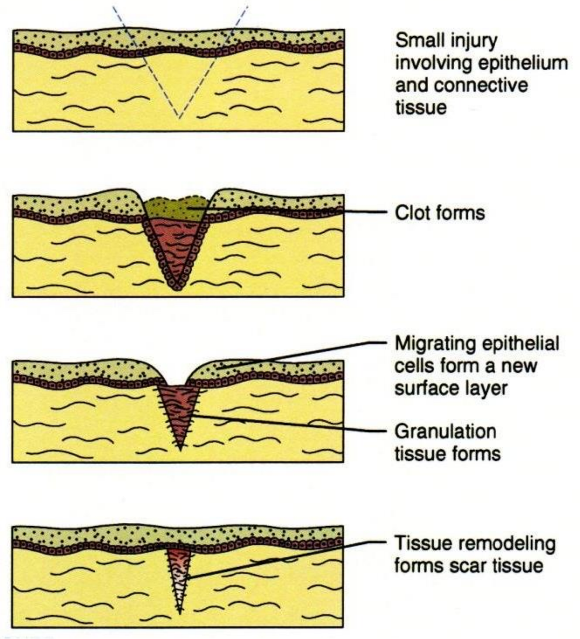


Figure 3. Repair process of the skin or oral mucosa after an injury. Note the initial formation of the clot and migrating epithelial cells from the surrounding intact tissue and formation of granulation tissue in the later days of repair. Later, the tissue will remodel and form scar tissue.

If the source of injury is removed, tissue repair can begin within the next few days. The epithelial cells at the periphery of the injury lose their desmosomal intercellular junctions and then are able to migrate to form a new epithelial surface layer beneath the clot.

Thus, a clot is very important in repair of the epithelium and must be retained in the first days of repair because it acts as a guide to form a new surface. A clot stays moist in the oral cavity but dries out on the skin (called a *scab* when on the skin). Later, after the epithelial surface is repaired, the clot is then broken down by enzymes because it is no longer needed for healing. Repair of the epithelium is a process that is also tied to repair in the deeper connective tissue.

Basement Membrane Properties

The **basement membrane** is a thin, acellular structure always located between any form of epithelium and the underlying connective tissue, as noted in both the skin and oral mucosa (**Figure 4**) and (see Figure 4 in Lecture 1) and (see Figure 8 in Lecture 4). This type of structure is even present between the components of the tooth germ during tooth development.

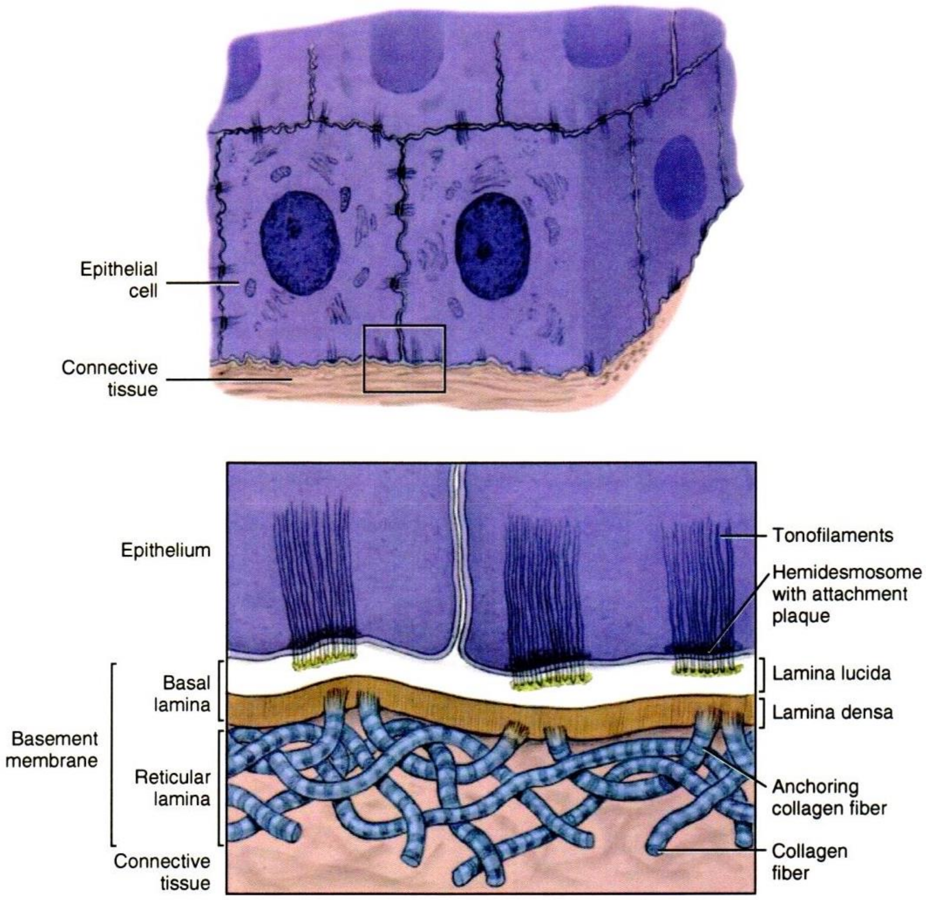


Figure 4. Basement membrane with its basal lamina and reticular lamina. Close-up view shows the attachment devices from an epithelial cell by way of hemidesmosomes and tonofilaments with attachment plaques connecting to the connective tissue by way of anchoring collagen fibers.

Basement Membrane Histology

The details of the basement membrane are not seen when it is viewed by scanning or lower-power magnification; only its location can be indicated. A higher-power magnification, such as that afforded by an electron microscope, is needed to see the intricacies of the basement membrane. The basement membrane consists of two layers: basal lamina and reticular lamina. The terms *basement membrane* and *basal lamina* are sometimes used interchangeably, but the basal lamina is, in fact, only a part of the basement membrane. The term “basal lamina” is usually used with electron microscopy, whereas the term “basement membrane” is usually used with lower-power light microscopy.

The superficial layer of the basement membrane is the **basal lamina**, which is produced by the epithelium, and it is about 40 to 50 nm thick. Microscopically, the basal lamina consists of two sublayers: The *lamina lucida* is a clear layer that is closer to the epithelium, and the *lamina densa* is a dense layer that is closer to the connective tissue. The deeper layer of the basement membrane is usually the **reticular lamina** (the exception is lung alveoli and kidney, with fusion of basal laminae). The reticular lamina consists of collagen fibers and reticular fibers produced and secreted by the underlying connective tissue.

Attachment mechanisms are also part of the basement membrane. These involve hemidesmosomes with the attachment plaque as well as tonofilaments from the epithelium and the **anchoring collagen fibers** from the connective tissue (see Figure 4 in Lecture 1). The tonofilaments from the epithelium loop through the attachment plaque, whereas the collagen fibers of the reticular lamina loop into the lamina densa of the basal lamina, forming a flexible attachment between the two tissue types.

It is important to note that the interface between the epithelium and connective tissue of both the skin and oral mucosa where the basement membrane is located is not two-dimensional, as seen in microscopic cross sections of the tissue with its epithelial rete ridges and connective tissue papillae. Instead, in reality, the interface consists of three-dimensional interdigitation of the two tissue types. This complex arrangement increases the amount of surface area for the interface, thus increasing the mechanical strength of the interface, as well as the nutrition potential for the avascular epithelium from the vascularized connective tissue.

General Histology Lec/4

Dr.Ayat A. Sabeeh

Connective Tissue Properties

All of the **connective tissue** of the body when taken together represents, by weight, the most abundant type of basic tissue in the body— even if it is epithelium that is mainly seen when clinically examining the body. Connective tissue is derived from the somites during prenatal development. The functions of connective tissue are as varied as its types; connective tissue is involved in support, attachment, packing, insulation, storage, transport, repair, and defense.

Connective Tissue Histology

Compared with epithelium, connective tissue is usually composed of fewer cells spaced farther apart and containing larger amounts of matrix between the cells (except for adipose connective tissue) (see Figure 1 in Lecture 3). Within connective tissue, the matrix is composed of intercellular substance and fibers.

Most connective tissue is renewable because its cells are capable of mitosis, and because most of its cells can even produce their own matrix of intercellular substance and fibers. In most cases, connective tissue is vascularized (except cartilage), each having its own blood supply.

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Differing cells are found within the various types of connective tissue. The most common cell in all types of connective tissue is the **fibroblast** (**Figure 5**).

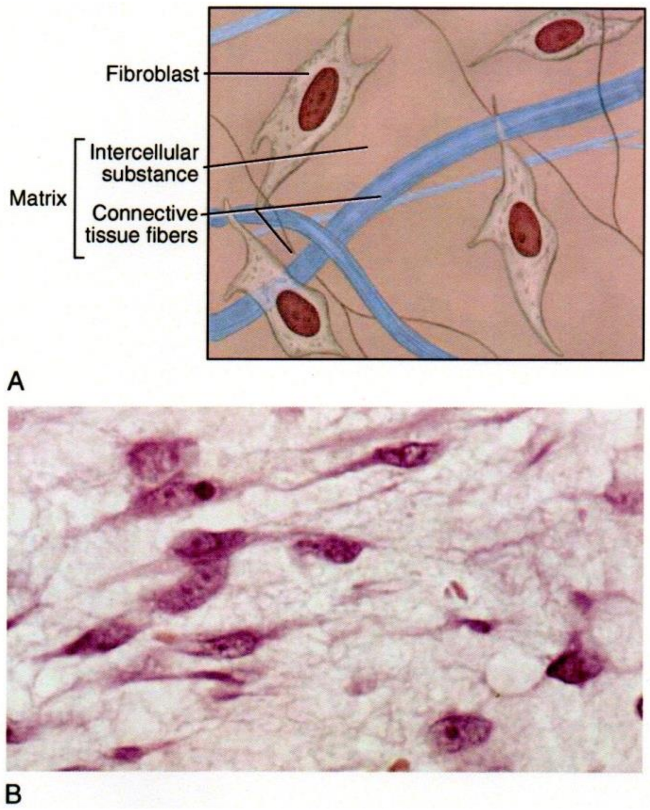


Figure 5. Fibroblasts. A, Diagram. B, Photomicrograph. The fibroblasts are within loose connective tissue, showing their spindle or fusiform shape. The cell forms the fibers of the connective tissue, as well as the intercellular substance between the tissue components.

Fibroblasts synthesize certain types of protein fibers and intercellular substances needed to sustain the connective tissue. They are flat, elongated spindle-shaped cells with cytoplasmic processes at each end. Subpopulations of fibroblasts may be possible within connective tissue. Fibroblasts are considered fixed cells in connective tissue because they do not leave the tissue to enter the blood as compared to cells with mobility, such as white blood cells.

Young fibroblasts that are actively engaged in the production of fibers and intercellular substance appear to have large amounts of cytoplasm, mitochondria, and rough endoplasmic reticulum. Fibroblasts can show aging and inactivity, with a reduction in cytoplasm, mitochondria, and rough endoplasmic reticulum, which is evident in the later stages of chronic advanced periodontal disease. If adequately stimulated during repair, however, fibroblasts may revert to a more active state.

Other cells found in connective tissue include migrated white blood cells from the blood supply, such as monocytes (macrophages), basophils (mast cells), lymphocytes (including plasma cells), and neutrophils.

Differing types of protein fibers are found in various types of connective tissue. The main connective tissue fiber type found in the body is the **collagen fibers** (**Figure 6**).

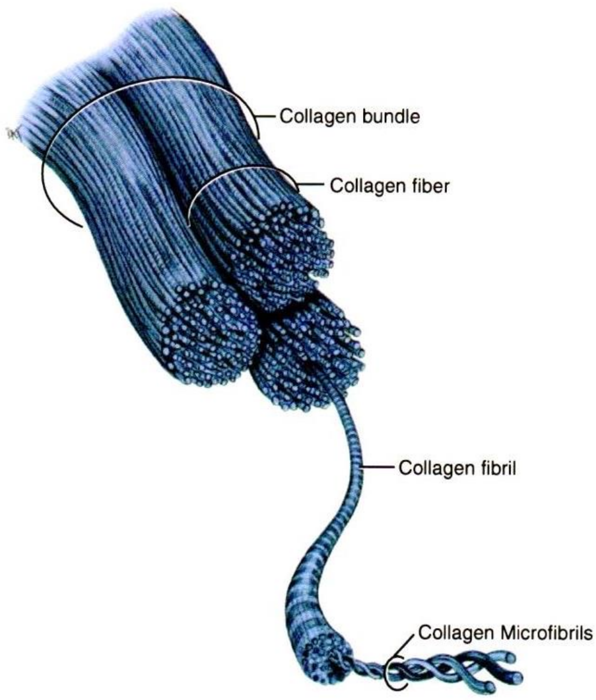


Figure 6. Collagen bundle that is composed of fibers, and smaller subunits—fibrils and microfibrils.

Tissue containing a large amount of collagen fibers is considered a *collagenous connective tissue*, but all connective tissue (except blood) contain some collagen fibers. Collagen fibers are composed of the protein collagen, including distinct types that have been shown by immunologic study to have great tensile strength. All collagen fibers are composed of smaller subunits, or *fibrils*, which are composed of *microfibrils*— similar to a strong, intact rope that is composed of smaller entwined strands of roping material.

Over 29 types of collagen have been identified and described; however, over 90% of the collagen in the body or in fetal tissue is composed of only Types I-IV collagen (**Table 3**).

Table 3. Collagen Types

Main Types of Collagen	**Features**
Type I	Most common type in dermis of skin, skeletal bone, tendons, and virtually all connective tissue of the body as well as lamina propria of oral mucosa, dentin, pulp, periodontium, and the jawbones
Type II	In hyaline and elastic cartilage
Type III	In granulation tissue, produced quickly by young fibroblasts before tougher Type I synthesized, thus commonly found alongside Type I; main component of reticular fibers but also found in artery walls, skin, intestines, and uterus
Type IV	In basal laminae of basement membrane, eye lens, and filtration system of capillaries and kidney’s nephron glomeruli

The most common type of collagen protein is Type I collagen, which is found in the teeth, lamina propria of the oral mucosa, dermis of the skin, bone, tendons, and virtually all other types of connective tissue. Cells responsible for the synthesis of Type I collagen include fibroblasts and osteoblasts, which produce fibers and intercellular substance as well as bone, respectively, and odontoblasts, which produce dentin.

The **elastic fibers** are another type of fiber, composed of microfilaments embedded in the protein elastin, which results in a very elastic type of tissue. Thus, this tissue has the ability to stretch and then to return to its original shape after contraction or extension. Certain regions in the oral cavity, such as the soft palate, contain elastic fibers in the connective tissue of lamina propria to allow this type of tissue movement (**Figure 7**).

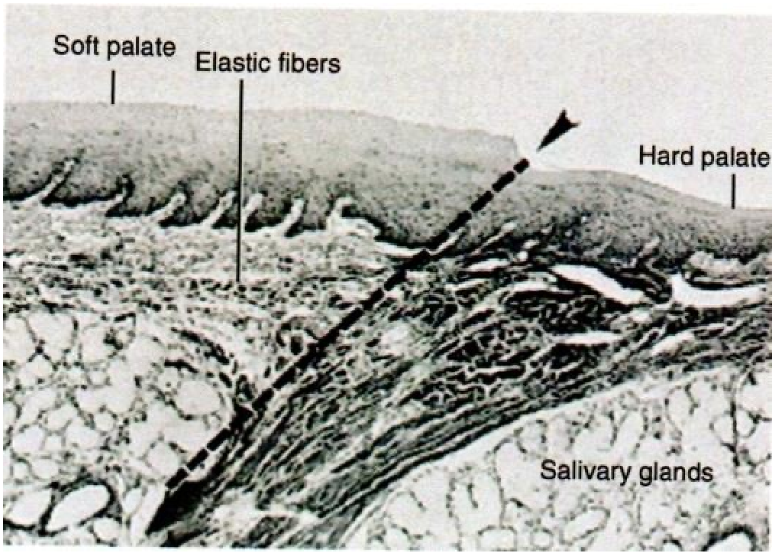


Figure 7. Photomicrograph of the junction of the soft palate and hard palate (arrow with dotted line), which is also a junction between a lining mucosa and a masticatory mucosa, as well as a junction between nonkeratinized epithelium and keratinized epithelium.

The **reticular fibers** can be found in relationship to an evolving embryonic tissue and thus are found more rarely in the adult body. Reticular fibers are composed of the protein reticulin and are very fine, hairlike fibers that branch, forming a network in the tissue that contains them. However, reticular connective tissue still predominates in the lymph nodes and spleen in an adult.

Connective Tissue Classification

One method of classifying connective tissue is according to texture, which can be soft, firm, rigid, or fluid in nature (see Table 1 in Lecture 2). Soft connective tissue includes the tissue found in the deeper layers of both the skin and oral mucosa, such as a connective tissue proper. Firm connective tissue consists of different types of cartilage. Rigid, hard form of connective tissue consists of bone. Fluid connective tissue consists of blood with all its components and lymph.

Connective Tissue Proper

Soft connective tissue can be classified as loose, dense, or specialized. Both loose and dense types of connective tissue are found together in two adjoining layers as the **connective tissue proper**. The connective tissue proper is found deep to the epithelium and basement membrane, in the deeper layers of both the skin and oral mucosa.

The connective tissue proper in the skin is the **dermis** and is found deep to the epidermis (see Figure 1 in Lecture 3) and (**Figure 8**).

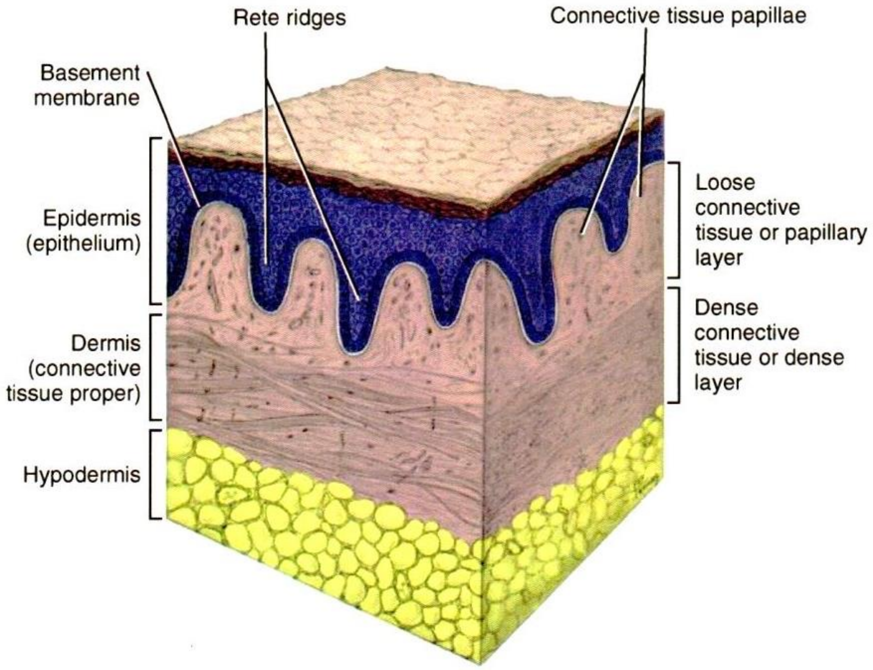
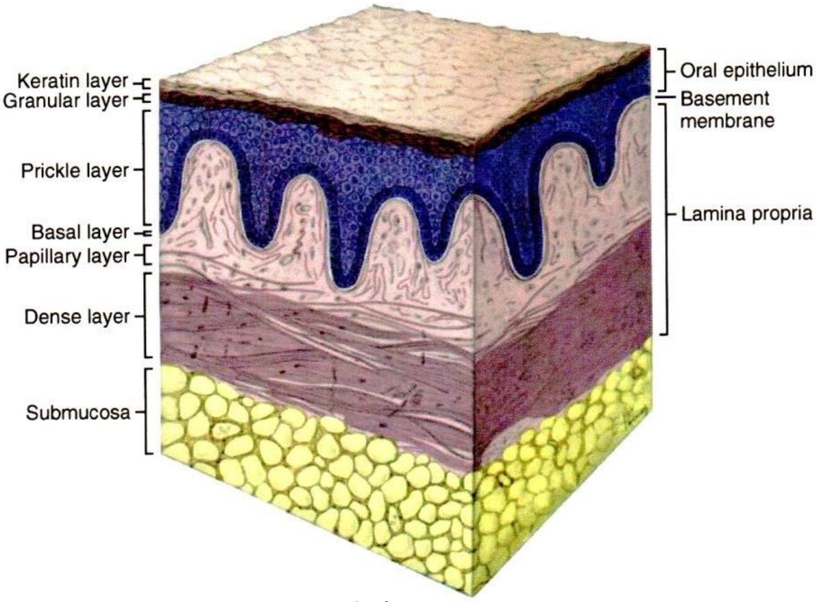


Figure 8. Skin with its epidermis and dermis layers. The hypodermis is present deep to the dermis. Note the interdigitating rete ridges of the epidermis with the connective tissue papillae of the dermis.

Even deeper to the dermis is the **hypodermis**, a subcutaneous tissue that is composed of loose connective tissue and adipose connective tissue, which is a specialized connective tissue, as well as glandular tissue, large blood vessels, and nerves. Cartilage, bone, and muscle can be present deep to the hypodermis of the skin, depending on the region of the body. In oral mucosa, the connective tissue proper is considered the lamina propria, and the deeper connective tissue sometimes present is the submucosa, similar to the hypodermis in the skin (**Figure 9**).



Oral Mucosa
(and underlying tissue)

Figure 9. General histologic features of an oral mucosa composed of stratified squamous epithelium overlying lamina propria with a deeper submucosa present.

Loose Connective Tissue: The superficial layer of both the dermis of the skin and lamina propria of the oral mucosa is composed of **loose connective tissue** (see Figure 8). In both the dermis or lamina propria of oral mucosa, this layer of loose connective tissue is also considered the **papillary layer**. The papillary layer forms **connective tissue papillae**, which is interdigitated with the epithelial rete ridges (see Figure 8). This papillary layer has no overly prominent connective tissue element; all of the components of the papillary layer are present in equal amounts. Thus, equal amounts of cells, intercellular substance, fibers, and tissue fluid are in an irregular and loose arrangement. This loose layer of the connective tissue proper serves as protective padding for the deeper structures of the body.

Dense Connective Tissue: Deep to the loose connective tissue is **dense connective tissue**, such as that found in the deepest layers of both the dermis or lamina propria (see Figure 8). Similar to loose connective tissue, all of the same components of connective tissue are still present. However in contrast to loose connective tissue, dense connective tissue is tightly packed with a regular arrangement, and it also consists mainly of protein fibers, which give this tissue its strength.

The dense connective tissue in both the dermis and lamina propria is also considered the **dense layer** (or reticular layer). Thus, the dense layer is deep to the papillary layer in the connective tissue proper. In contrast, tendons, aponeuroses, and ligaments are a type of dense connective tissue that has a regular arrangement of strong, parallel collagen fibers with few fibroblasts or cells.

Connective Tissue Proper Regeneration, Turnover, and Repair

Turnover of both the connective tissue proper in skin or oral mucosa occurs as a result of the production of fibers and intercellular substance by the fibroblasts during regeneration (see Figure 5). Other types of cells can also undergo mitosis and create additional cells, such as certain white blood cells and endothelial cells. The overall turnover time for a connective tissue proper is slower than its adjoining epithelium; it also demonstrates individual variance from region to region.

When injured, the connective tissue proper in both the skin or oral mucosa goes through stages of repair that are related to the events in the more superficial epithelium (see Figure 3 in Lecture 3). After a clot forms and an inflammatory response is triggered with white blood cells, fibroblasts migrate to produce an immature connective tissue deep to the clot and newly forming epithelial surface.

This immature connective tissue is considered **granulation tissue** and has few fibers and an increased amount of blood vessels. Granulation tissue can clinically appear as a redder, soft tissue that bleeds easily after injury or surgery, such as in the oral cavity after a tooth extraction. In addition, this tissue may become abundant, interfering with the repair process. Surgical removal of excess granulation tissue may be necessary to allow for optimum repair; this sometimes occurs after chronic advanced periodontal disease.

Later, during the repair process, this temporary granulation tissue is replaced by paler and firmer scar tissue in the area. It is paler because scar tissue contains an increased amount of fibers and fewer blood vessels. The amount of scar tissue varies, depending on the type and size of the injury, amount of granulation tissue, and movement of tissue after injury. Interestingly, the skin shows more scar tissue production both clinically and microscopically after repair than does the oral mucosa. This difference may be based on differing developmental origins of the tissue producing differing types of fibroblasts and thus different types of fibers.

The repair process can also be affected by hormones such as noted with systemic glucocorticoids (for example, cortisone) hinder repair by depressing the inflammatory reaction or by inhibiting the growth of fibroblasts, the production of collagen, and the formation of endothelial cells. Systemic stress, thyroidectomy, testosterone, adrenocorticotropic hormone, and large doses of estrogen suppress the formation of granulation tissue and impair healing. Progesterone increases and accelerates the vascularization of granulation tissue and appears to increase the susceptibility of the gingival tissue to mechanical injury by causing dilation of the marginal vessels.

Clinical Considerations with Skin Aging

At birth, the skin has not developed a sufficient protective layer or facilitated the synthesis of immune cells. It often looks to be transparent and therefore is sensitive to damage, and it must be protected by extra clothing and kept away from environmental stress. At puberty, glandular and hair development, as well as the immune system, begins to function at an increased rate, giving extra protection to the skin against the coming adult world. During this time, the skin is in a very active metabolic state but still vulnerable to sensitization by allergens.

By age 20, however, the skin begins to deteriorate, and by the age of 50 is in a rapid state of degradation due to the aging process. Collagen fibers begin to fall apart; elastic fibers stiffen and thicken, wrinkling the skin. Oil glands in skin cease production, and melanin production decreases, leading to more pallid color and grey hairs. Keratin cells cease production and already produced keratin becomes thin and stiff.

Most importantly to dental professionals, the skin with aging begins to heal poorly after injury with fibroblasts now having less replication activity (considered replicative senescence). The skin also becomes susceptible to disease states that include inflammation (such as with dermatitis), infection (such as with herpes zoster), and cancer (such as with basal cell carcinoma and melanoma). Solar damage will accelerate the aging process in skin, as does increased environmental toxicity (chronic alcohol and tobacco use).

Specialized Connective Tissue Properties

Specialized connective tissue includes adipose, elastic, or reticular. **Adipose connective tissue** is a fatty tissue that is found beneath the skin, around organs and various joints, and in regions of the oral cavity. Unlike most connective tissue, this type of connective tissue has cells packed tightly together with little or no matrix. After fibroblasts, the predominant type of cell found in this tissue is the adipocyte, which stores fat intracellularly.

Elastic connective tissue has a large number of elastic fibers in its matrix, which combine strength with elasticity, such as in the tissue of the vocal cords. **Reticular connective tissue** is a delicate network of interwoven reticular fibers forming a supportive framework for blood vessels and internal organs.

Muscle Properties

The muscle in the body is part of the muscular system, and similar to connective tissue, most muscles are derived from somites. Each muscle shortens under neural control, causing soft tissue and bony structures of the body to move. The three types of muscle are classified according to structure, function, and innervation: skeletal, smooth, and cardiac (see Table 1 in Lecture 2).

Muscle Classification

Each type of **muscle** has its own type of action, which is the movement accomplished when the muscle cells contract. Smooth muscle and cardiac muscle are considered involuntary muscles because they are under autonomic nervous system control (discussed next). Smooth muscles are located in organs, glands, and the linings of blood vessels. Cardiac muscle is in the wall of the heart (myocardium).

Skeletal muscles are considered voluntary muscles because they are under voluntary control, involving the somatic nervous system (**Figure 10**).

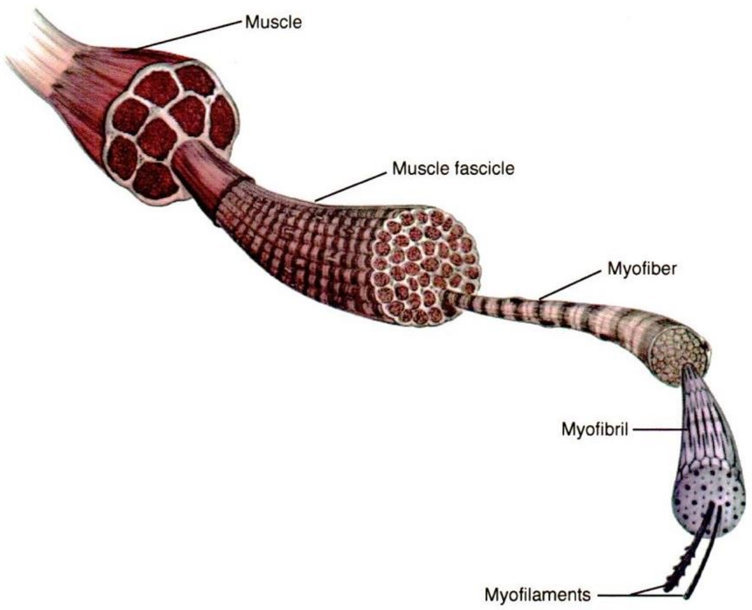


Figure 10. Skeletal muscle with its striations and which is composed of smaller muscle bundles, fascicles, myofibers, myofibrils, and myofilaments.

All the major muscles of the body's appendages and trunk are skeletal muscles. Thus, skeletal muscles are usually attached to bones of the skeleton. Skeletal muscles also include the muscles of the facial expression, tongue, pharynx, and upper esophagus, as well as the muscles of mastication that assist the temporomandibular joint in the actions involved in mastication.

Skeletal Muscle Histology

Skeletal muscles are also called *striated muscles* because the muscle cells appear striped microscopically. Each muscle is composed of numerous muscle bundles, or fascicles, which then are composed of numerous muscle cells, or myofibers. Each *myofiber* extends the entire length of the muscle and is composed of smaller myofibrils surrounded by the other organelles of the cell. Each myofibril is composed of even smaller myofilaments.