Lesson II: Tissue level of organization

As we learned in Lesson One, cells are arranged into tissues, groups of similar cells that have a similar function to carry out a specialized activity. There are four principal types of tissues in the body, epithelial, connective, muscle and nervous tissue. About 8 days after fertilization, the mass of developing cells differentiates into three primary germ layers, the **endoderm**, **mesoderm** and **ectoderm**. These three primary layers give rise to all succeeding tissues in the body. Whereas epithelial tissue arises from three primary germ layers, connective and muscle tissue arise from the mesoderm, and the nervous and integumentary system develops from the ectoderm.

To maintain the integrity and facilitate communication between the different cells of a particular tissue, most epithelial cells, as well as some muscle and a few nerve cells, form **cell junctions**. A cell junction is a point of contact between the plasma membrane of two or more cells, and there are three types of cell junctions: tight junctions, anchoring junctions and communicating junctions. **Tight junctions** are found among epithelial cells such as those that line the bladder, stomach and intestine to prevent fluid from leaking into the body cavities. **Anchoring junctions** (e.g. adherens junctions, desmosomes and hemidesmosomes) are found in tissues that are subject to stretching and friction, such as the outer layer of the skin, the muscle of the heart, the cervix and the epithelial lining of the digestive tract. **Communicating junctions** (e.g. gap junctions) allow for the rapid transmission of an electric impulse through minute fluid-filled tubules that connect two different cells, called an action potential.

I. Epithelial tissue

Epithelial tissue can be divided into two basic types of tissues: 1) covering and lining epithelium and 2) glandular epithelium. **Covering and lining epithelium** forms the external layer of the skin and lines the hollow portions of the digestive, respiratory, urinary and reproductive tracts, as well as the internal surfaces of blood vessels, ducts and

the body cavities. **Glandular epithelium** forms the secreting portion of glands, such as the sudoriferous (sweat) glands and the thyroid. In the formation of the special senses (i.e. sight, hearing, touch, smell and taste), epithelial tissue combines with nervous tissue to make up the special sense organs.

Epithelial tissue has distinguishing characteristics that differentiate from other kinds of tissue:

1. Epithelial tissue consists of densely packed cells with little extracellular fluid between them;
2. Epithelial cells is arranged in continuous sheets, in one or more layers, and has an apical surface that is exposed to a body cavity, and a basal surface which is attached to the basement membrane (discussed shortly);
3. Epithelial tissue has many cell junctions, ensuring that epithelial cells are firmly attached to one another;
4. Epithelial tissue is avascular, dependent upon the underlying connective tissue for the delivery of nutrients and the removal of wastes;
5. Epithelial tissue adheres firmly to the underlying connective tissue to prevent it from being ripped or torn off. The layer between the epithelial and connective tissue is a thin extracellular layer called the basement membrane, which attaches the epithelial tissue to the connective tissue and guides cell migration during development and tissue repair;
6. Epithelial tissue is supplied by nervous tissue;
7. Epithelial tissue has a high mitotic rate to compensate for the damage caused by wear and tear;
8. Epithelial tissue can have a wide range of functions, including protection, filtration, lubrication, secretion, digestion, absorption, transportation, excretion, sensory reception and reproduction.

The morphology of the cells that comprise covering and lining epithelium display a great diversity, dependent upon their unique functions. Epithelial tissues that function in absorption and filtration are comprised of a single layer of cells called **simple epithelium**, and are exposed to little in the way of wear and tear. If, on the other hand the epithelial tissue is exposed to a greater degree of wear and tear, it is comprised of several layers of cells, called **stratified epithelium**. A third type of epithelial arrangement, called **pseudostratified epithelium**, is much less common than the other two, and while it is comprised of a single layer of cells, has an uneven arrangement giving the tissue a stratified appearance.

Besides the number and layers of cells that make up epithelial tissue, epithelial cells are classified according to

the individual shape of each cell. Epithelial cells that are flattened and scale-like are called **squamous**. **Cuboidal** cells look cube-shaped in cross-section. Epithelial cells that are tall and cylindrical, and often somewhat rectangular, are called **columnar**. **Transitional** cells are so-called because they change shape according to the amount of torsion, twisting and stretching that can occur, and range from being cuboidal to columnar. Simple epithelium can be squamous, cuboidal or columnar, and stratified epithelium can be all of these shapes, as well as transitional. A third classification of epithelial tissue is **pseudostratified columnar**.

Simple squamous epithelium

Simple squamous epithelium consists of a single layer of flat scale-like cells, highly adapted for diffusion, osmosis and filtration. When it lines the heart, blood and lymphatic vessels, as well as forms the walls of capillaries, it is called the **endothelium**. When it forms the epithelial layer of serous membranes it is called the **mesothelium**. It is also found in the air sacs (alveoli) of the lungs, the glomeruli of the kidneys and in the inner surface of the tympanic membrane of the ear.

Simple cuboidal epithelium

Simple cuboidal epithelium are only seen to be cuboidal when the tissues are sectioned at right angles. Its function is absorption of fluids and other substances by cells, and the secretion of substances like mucus, perspiration and enzymes. It is found on the internal surface of the ovaries, in portions of the eye, and in the kidney tubules and the ducts of small glands.

Simple columnar epithelium

Simple columnar epithelium are comprised of two types of cells: **non-ciliated simple columnar epithelium** and **ciliated simple columnar epithelium**. The non-ciliated variety may contain microscopic projections called **microvilli**, hair-like projections that serve to increase the surface area of the plasma membrane for the absorption of nutrients and fluids. The other type of non-ciliated simple columnar epithelium are **goblet cells**, cells which secrete the mucus that accumulates in the upper portion of the cell, giving a bulging shape resembling a goblet. Non-ciliated simple columnar epithelium line the gastrointestinal tract, from the stomach down to the anus, and are found in the

ducts of many types of glands, as well as in the gall bladder.

Ciliated simple columnar epithelial cells have larger hair like processes that move substances across the apical surface of the cell. In the respiratory tract ciliated cells are interspersed with goblet cells, and function to move foreign particles trapped in the mucus up and out of the air passages to be expectorated. Other areas that contain ciliated simple columnar epithelium include the fallopian tubes, uterus, paranasal sinuses and the central canal of the spinal cord.

Stratified squamous epithelium

Stratified squamous epithelium are comprised of several layers of cells, the superficial layers flat, and the cells in the deeper layers ranging from cuboidal to columnar. As the dead cells in the most superficial layer are sloughed off, they are replaced by cells that migrate upwards, becoming progressively smaller, harder and more dehydrated as they move away from the basement membrane. Stratified squamous epithelium exist in two forms, as either keratinized or non-keratinized. **Keratin** is a waterproof protein that is resistant to friction and bacteria, and keratinized stratified squamous epithelium is present on the outer layer of the skin. Non-keratinized stratified squamous epithelium is lines the buccal mucosa, tongue, esophagus, portions of the epiglottis, and vagina.

Stratified cuboidal epithelium

Stratified cuboidal epithelium is an uncommon form of stratified epithelium comprised of more than two layers of cells, and functions in protection. It is found in the ducts of the sudoriferous glands and portions of the male urethra.

Stratified columnar epithelium

Similar to stratified cuboidal epithelium, stratified columnar epithelium is an uncommon epithelial tissue functioning in protection and secretion. It can be found in the lining in portions of the male urethra, in large excretory ducts of certain glands, in some areas of the anal mucous membrane and in portions of the conjunctiva.

Stratified transitional epithelium

The main characteristic of stratified transitional epithelium is that it maintains a variable appearance. In a relaxed state it appears to be similar to stratified cuboidal epithelium,

except for the cells in the superficial layers that are large and rounded. When the tissue is distended the cells in this superficial layer can stretch without breaking the cell junctions which them together, and appear to be similar to stratified squamous epithelium. Stratified transitional epithelium is found lining the urinary bladder and portions of the ureters and urethra.

Pseudostratified columnar epithelium

Like all of the previously mentioned epithelial tissues, the basal surface of pseudostratified columnar epithelium is continuous with the basement membrane, but some cells may not reach the apical surface, giving the tissue a stratified appearance. Cells that reach the apical surface are either mucus secreting glands or are ciliated, and both can be found in portions of the respiratory and genitourinary tracts, as well as in the Eustachian tubes.

Glandular epithelium

Like the name implies, the function of glandular epithelium is secretion, performed by cells that often lay below the covering and lining epithelium. One or more of these cells form a gland, a specialized form of epithelium that secrete the substances it produces into ducts, onto a surface or in the blood. All glands found in the body are one of two types: exocrine and endocrine.

Exocrine glands secretes substances through one or more ducts that either discharge on the surface of covering and lining epithelium, such as on the skin, or directly onto a free surface, as in digestive secretions into the lumen of the small intestine. They can be unicellular, comprised of just one cell, or multicellular, comprised of two or more cells. Example of exocrine glands are sudoriferous glands that release perspiration to regulate body temperature, and salivary glands that secrete salivary amylase in the preliminary digestion of carbohydrates in the mouth. In performing the task of glandular secretion, an exocrine gland can either secrete a substance that it produces, or release portions of its own cells. The cells that comprise **holocrine** glands manufacture a secretory product in their cells, and when mature, the cell dies and is released by the gland. An example of a holocrine gland is the sebaceous glands of the skin that secrete oil. **Merocrine** glands produce a substance that is secreted by exocytosis, and include most exocrine glands, such as the salivary glands and the pancreas. **Apocrine** glands accumulate their

secretory substance on the apical surface of the glandular cells, which then pinches off from the rest of the cells to be secreted by the gland.

Different from exocrine glands, **endocrine** glands are ductless. The secretions of these glands are hormones, discharged directly into the blood stream to bind with specific receptors to regulate a wide variety of physiological processes. Examples of exocrine glands include the thyroid and pituitary gland. The pancreas is both an exocrine and an endocrine gland.

II. Connective tissue

The most abundant tissue in the body is connective tissue, binding, supporting, insulating, protecting and strengthening all other body tissues. It is comprised of three basic elements: **cells**, **ground substances** and **fiber**. Both the ground substance and fiber form the **matrix**, and unlike epithelial tissue, connective tissue cells are separated from each other by large quantities of matrix. The matrix ranges from a semifluid to completely calcified substance, secreted by connective tissue cells that lie adjacent to it. In the blood however, the matrix is not secreted by blood cells, and occurs as a fluid (plasma). Another difference between connective tissue and epithelial tissue is that connective tissue never occurs on the external surfaces of the body, and for the most part is highly vascularized and innervated. The exception is cartilage, such as tendons, which is poorly supplied by blood and is devoid of nervous tissue.

Connective tissue cells

Connective tissue cells are derived from the embryonic mesoderm, and are called **mesenchymal** cells. All the major types of connective tissue cells are derived from immature cells, designated with the suffix *-blast*. These immature have the capacity to divide as needed and secrete the matrix. When mature, these cells mature into cells that for the most part lose the capacity for cell division and function to maintain the matrix. These mature cells are identified with the suffix *-cyte.* An example is the osteoblasts that form bone, which then mature into the osteocytes that reside in bone tissue.

The following is a brief description of some of the major connective tissue cells:

1. Fibroblasts- large, flat, spindle-shaped cells that secrete the matrix.
2. Macrophages- derived from monocytes, they are a type of white blood cell that engulfs foreign substances and cellular debris by phagocytosis.
3. Plasma cells- derived from B lymphocytes (another type of white blood cell), they secrete antibodies that assist in immune function
4. Mast cells- found lining blood vessels, these cells contain histamine, a chemical that promotes inflammation, and heparin, which inhibits blood clotting
5. Adipocytes- cells which function to store fat
6. Leukocytes- also known as white blood cells, these are key components of the immune system.

Connective tissue matrix

As mentioned previously, the matrix is composed of ground substance and fibers. The ground substance is a gel-like ground substance that has many important constituents, such as **proteoglycans** and **glycosaminoglycans**, which are complexes of protein and polysaccharides. **Hyaluronic acid** is a viscous, slippery substance that functions to bind cells together, lubricate joints, and assisting in the migration of phagocytes to damaged tissue. Some bacteria secrete an enzyme called hyaluronidase, also found in other body tissues, to break down the ground substance to a watery consistency during infection, easing their passage through the tissues. **Chondroitin sulfate** is a jelly-like substance that provides adhesiveness and support in cartilaginous tissues, as well as bone, skin and blood vessels. Other types of molecules found in the ground substance include **dermatan sulfate**, in skin, the heart, blood vessels and tendons, and **keratan sulfate**, found in bone, cartilage and the cornea of the eye. **Glucosamine sulfate** is a supplement that has used increasingly in the last few years in the treatment of osteoarthritis to support the matrix, providing the building blocks needed in its repair.

Embedded between connective tissue cells are protein fibers that help to maintain the structure of connective tissue. There are three types of fibers: collagen, elastic and reticular. **Collagen fibers** are made up of collagen, the most abundant protein in the body, and are composed of bundles of tiny collagen fibrils that lie parallel to one another, affording great strength. Collagen fibers are present in most types of connective tissue, including bone, cartilage, tendons and ligaments. The repair of damaged

collagen fibers is dependent upon many nutrients, including vitamin C. **Elastic fibers** are smaller than collagen fibers and consist of a protein called elastin. Similar to collagen fibers, elastic fibers provide strength, but have the additional property of being able to stretch by up to 150% of their state. Elastic fibers are found in tissues that undergo dilation and contraction, such as the skin, blood vessels and lungs. **Reticular fibers** are a combination of collagen and a glycoprotein that are produced by fibroblasts, providing a framework around many soft tissues, such as the spleen and lymph nodes. Reticular fibers also help to form the basement membrane.

Connective tissue types

Connective tissue is a diverse range of tissue types, and the following is an overview of them:

A. Loose Connective tissue
    1. Areolar
    2. Adipose
    3. Reticular
B. Dense Connective tissue
    1. Dense Regular
    2. Dense Irregular
    3. Elastic
C. Cartilage
    1. Hyaline
    2. Fibrocartilage
    3. Elastic
D. Bone
E. Blood

Loose connective tissue

Loose connective tissue is comprised of protein fibers that are loosely woven, and is made up of areolar, adipose and reticular connective tissues.

Areolar connective tissue is one of the most common and widely distributed connective tissues in the body, and contains many different kinds of cells, including fibroblasts, macrophages, plasma cells, mast cells, adipocytes and some white blood cells. The ground substance is fluid to gelatinous, contain hyaluronic acid, chondroitin sulfate, dermatan sulfate and keratan sulfate. It is located in the subcutaneous layer of the skin, in the superficial regions of the dermis, in mucous membranes, and in blood vessels, nerves and around body organs. Areolar connective tissue supports and helps to maintain the strength and elasticity of body tissues.

Adipose tissue consists of adipocytes, cells whose nuclei are located in the periphery of the cell, and specialize in the storage of triglycerides. Adipocytes are found in the subcutaneous layer of the skin, in the yellow marrow of long bones, in the padding around joints and behind the eyeball.

Reticular connective tissue consists of a framework of interlocking reticular fibers and cells. It is the stroma (supporting tissue) of the liver, spleen and lymph nodes, and is also found in the portions of the red bone marrow, basement membrane, muscle and blood vessels. Reticular connective tissue also binds together smooth muscle cells.

Dense connective tissue

Unlike loose connective tissue, dense connective tissue consists of fewer cells, but has more numerous, thicker protein fibers.

Dense regular connective tissue has a shiny appearance and is comprised of regularly arranged bundles of collagen fibers with fibroblasts interspersed between them. It forms the **tendons** (attaching muscle to bone), **ligaments** (attaching bone to bone) and **aponeuroses** (attaching muscle to muscle, or muscle to bone). Its function is to maintain the integrity of the musculoskeletal system.

Dense irregular connective tissue consists primarily of collagen fibers and fibroblasts in a random arrangement. It makes up the fascia, the deep regions of the dermis, the periosteum of bone, joint capsules and membrane capsules around various organs (e.g. kidneys, liver, testes), as well as the valves of the heart. Its main function is to provide strength.

Elastic connective tissue consists of freely branching elastic fibers, with fibroblasts located between them. It is found in most tissues that undergo contraction and expansion, such as in the lung tissue, arterial walls, the trachea and bronchial tubes, in the suspensory ligament of the penis, and in the ligaments that connect the vertebrae.

Cartilage

Cartilage is a form of dense connective tissue that has a greater capacity for stress than the other kinds of dense connective tissues. It is a dense network of chondrocytes (mature cartilage cells), collagen and elastic fibers

embedded in the jelly-like chondroitin sulfate. The strength of cartilage is attributable to the collagen and elastic fibers, and its ability to retain its shape after torsion and twisting is the property of the chondroitin sulfate ground substance. There are three types of cartilage: hyaline cartilage, fibrocartilage and elastic cartilage.

Hyaline cartilage is also called gristle, consisting of collagen fibers and chondrocytes. It is a glossy bluish-white substance located on the end of long bones, the anterior ends of the ribs, the nose, as well as portions of the larynx, trachea, bronchi and bronchial tubes. It provides for joint movement and strength.

Fibrocartilage consists of chondrocytes scattered throughout bundles of collagen fibers. It is located in the pubic symphysis (where the hip bones join anteriorly), the intervertebral disks and the menisci of the knee. It helps to maintain the strength of the joint by fusing them together.

Elastic cartilage consists of chondrocytes held inside of a thread-like network of elastic fibers. It is located in the epiglottis of the larynx, as well as in the external ear and Eustachian tubes.

B o n e

Along with cartilage and the other tissues that forms joints, bone is the primary component of the skeletal system. Bone is of two primary types, compact or spongy, dependent upon the presence of matrix in the bone.

The primary unit of **compact bone** is the **osteon**, consisting of concentric rings of matrix called a **lamella**, filled with **mineral salts** (tricalcium phosphate and calcium carbonate) that give the bone its hardness, and collagen fibers that give the bone its strength. The osteon surrounds the central canal that contains blood vessels and nerves. Scattered throughout the lamella, and in adjacent areas of bone tissue are lacuni of mature bone cells called **osteocytes**, supplied with tiny channels called **canaliculi** that supply the osteocytes with nutrients and remove wastes.

Unlike compact bone, spongy bone has no osteons, but instead consists of a lattice-work of thin plates of bone called a **trabeculae**, the spaces between the lattice, in some bones, filled with the red marrow that generates red blood cells.

Blood

Blood is a connective tissue with a liquid matrix called plasma. Suspended within the watery plasma are the various formed element of the blood. These include cells such as **erythrocytes**, **leukocytes** and **platelets**. Other dissolved substances such as nutrients, gases, ions, hormones and wastes are also found in the plasma matrix.

Membranes

There are three major types of membranes found in the human body: mucous, serous and synovial. Both serous and mucous membranes are composed of an epithelial layer and an underlying connective tissue layer. Synovial membranes, on the other hand, are composed entirely of connective tissue.

Mucous membranes are an important defense mechanism in the body, secreting mucus that protects and lubricates the underlying tissues, and traps foreign substances for removal.

Serous membranes line a cavity that does not open directly to the exterior, and covers the organs that sit within that cavity. They consist of two, thin layers of areolar connective tissue covered by a layer of **mesothelium**, the outer layer called the **parietal layer**, and the inner layer called the **visceral layer**. In between these layers, the epithelium secretes a lubricating fluid called **serous fluid** that allows the organs to glide against one another or against the walls of the body cavity. Two important examples of a serous membrane include the membrane that protects the lungs, called the pleura, and the membrane that protects the heart, called the pericardium.

Synovial membranes line the cavities between diarthroses, or freely-movable joints. They are wholly composed of connective tissue and secrete synovial fluid, a highly viscous and slippery substance that prevents the degeneration of the articular surfaces of the bones, as well as nourishes the cartilage.

III. Muscle tissue

Among the connective tissues, muscular has a characteristic arrangement of cells that exist for the singular purpose of

generating the force necessary for contraction. There are three principle types of muscle tissue: skeletal, cardiac and smooth muscle.

Skeletal muscle is so named because it is attached to bones. It maintains a striated appearance, which refers to alternating dark and light bands that are perpendicular to the long axes of muscle fibers. Skeletal muscle is for the most part **voluntary**, meaning that that it can be made to contract or relax through conscious control.

Cardiac muscle refers to the muscle that is responsible for the pumping action of the heart, and like skeletal muscle, it is striated. Unlike the latter however, cardiac muscle is largely **involuntary**.

Smooth muscle is neither striated nor voluntary; it is located in the hollows of internal organs such as the blood vessels, the respiratory passages, and in the digestive and genitourinary tracts. Its contraction, called peristalsis, is a wave-like motion that propels substances through the lumen of the organ.

IV. Nervous tissue

The nervous system is a highly complex network of two principle kinds of cell: neurons and neuroglia. **Neurons**, or nerve cells, are the functional units of the nervous system. They convert the information they receive from various stimuli into nerve impulses (called action potentials). These impulses are then analyzed and reorganized into an appropriate response to the stimuli. Neurons have three basic components, a **cell body** (which contains the nucleus), a **dendrite** (which receives an action potential) and an **axon** (which transmits the nerve impulse).

Neuroglia, unlike nerve cells, do not transmit action potentials at all, but function to nourish and support the nerve cells

V. Tissue repair

As the fetus develops in the womb, and each kind of tissue is generated, some tissues lose their ability to divide and others retain it. Muscle and nervous tissue both lose their

capacity for mitosis, whereas epithelial and connective tissues generally have the ability for continuous renewal. The body however also manufactures immature, undifferentiated stem cells that can divide to replace lost or damaged cells.

When damage or injury occurs in a tissue, the repair originates in the stroma, the supporting connective tissue, or in the parenchyma, the functional tissue of an organ. When the parenchymal cells repair the tissue there is a complete restoration of function, called regeneration. When stromal cells repair the tissue however, fibroblasts synthesize collagen and other matrix materials in a process called **fibrosis** that is used to form scar tissue. Organs with a lot of scar tissue never retain the functional capacity they had prior to damage or injury.

When damage has occurred to a tissue, such as in large wounds, both parenchymal and stromal cells are active in the repair. Fibroblasts divide rapidly and synthesize new matrix components and blood capillaries regrow to provide nutrients and oxygen to the developing tissues. All of these components working together are collectively called granulation tissue, which in addition to repairing the tissue, secretes a fluid which has an antimicrobial activity.

There are many nutrients that are crucial to tissue repair, and their availability will determine how quickly and how well a tissue will regenerate. Many of these nutrients are an important strategy in wound-healing, and under proper supervision, can be used in large doses to facilitate healing:

1. Vitamin A- essential to the repair of epithelial tissue
2. Vitamin B complex- needed by enzyme systems in many cells, necessary to assist in the metabolism of other vitamins and nutrients
3. Vitamin C- ensures the healthy production of matrix materials, promotes new blood vessel growth, ensures blood vessel integrity
4. Vitamin D- assists in calcium absorption, necessary in the healing of fractures
5. Vitamin E- promotes tissue healing and prevents scarring
6. Vitamin K- needed for blood clotting

In addition to these vitamins, additional nutrients are also required, such as the protein needed to build new tissue, and oxygen and glucose. Many micronutrients, such as zinc, or accessory nutrients such as bioflavonoids are also important, and may be considered to part of an overall treatment strategy. Many medicinal plants also seem to

have an affinity in the repair of tissues, including *Crataegus oxycanthoides, Calendula officinalis, Astragalus membranaceous* and *Prunella vulgaris*, some of which act by enhancing the cross-linking of collagen fibers.