

CHAPTER 1 INTRODUCTION

A. ATOMS AND MOLECULES:

Matter is composed of **elements** which are substances that cannot be broken down into smaller component parts by typical chemical methods. Examples would be **carbon, hydrogen, oxygen, and nitrogen**. Each element is composed of its respective building blocks which are the **atoms**. All the atoms for any element are identical. While there are 108 known elements, only 9 will be listed here along with their symbol. **These nine are carbon (C), hydrogen (H), oxygen (O), nitrogen (N), sodium (Na), potassium (K), calcium (Ca), phosphorus (P) and chlorine (Cl)**. An atom is made up of **electrons** (negative charge) in orbits around a **nucleus** with **protons** (positive charge) and **neutrons** (neutral).

B. IONS , ATOMS AND MOLECULES:

Ions are charged atoms (Fig. 1). Normally an atom has a balance of charges. These charges are determined by the number of **electrons** (negative charge) in the **orbit** compared with the number of **protons** (positive charge) in the nucleus. If an atom has more electrons than protons it is negatively charged. If it has more protons than electrons than it is positively charged. Thus, sodium forms a positively charged ion because it gives off an electron, while chlorine forms a negatively charged ion because it takes on an electron. Both of these events happen in the presence of atoms that can either take up or lose an electron. Once the atom becomes an ion, its reactivity with other atoms is enhanced. Thus, the sodium ion is much more reactive than is the sodium atom.

Molecules are groups of atoms bound together by atomic forces. They may be simple combinations of two atoms, such as molecular oxygen, or very complex as in the case of proteins or nucleic acids.

C. IMPORTANT BIOLOGICAL MOLECULES

1. PROTEINS. Proteins are large molecules (Fig. 2) that comprise some 10% to 30% of the cell. They are made up of building blocks called **amino acids**. They contain **carbon, hydrogen, oxygen and nitrogen** and may contain **sulfur and phosphorus** as well. You construct your own proteins by using amino acids as their building blocks. There are 20 common amino acids that are assembled into long chains (sometimes hundreds of amino acid units long) to form each protein.

Amino acids are **assembled into proteins on the ribosomes of the cell**. The information for assembling amino acids into proteins is stored in your **chromosomes**, thus is part of your inheritance. You get your supply of amino acids for protein manufacture from the foods you eat.

Proteins are major components of **structures** of the cell. They contribute to membranes and organelles in their structural role. Some proteins are **contractile**, thus are able to move things within the cell. They are also very important in that they make up **enzymes** which are critical in regulating the rate of chemical reactions in the body. Without enzymes the body would not be able to function.

2. CARBOHYDRATES (Fig. 3). These are molecules composed of various combinations of **carbon and water** (thus carbo- hydrate). Approximately 1% to 2% of the cell is composed of these molecules. Carbohydrates include **sugars and starches**. These molecules are used as **energy sources** by the body. Actually what the body does is metabolize these energy sources and produces **ATP** (see below) or store the carbohydrate for later use either as **glycogen** or in the form of **lipids**.

Carbohydrates are also combined with other molecules. One important combination is carbohydrates and proteins to form **mucoproteins (glycoproteins)**. Among other things these contribute to the formation of mucus which lubricates various membranes in the body.

3. LIPIDS (Fig. 3). Lipids are the group of organic molecules which include **fats (solid) and oils (liquids)**. They are made up of two parts, **glycerol and fatty acids**. Fats and oils are a source of high energy (twice as much per gram as carbohydrates and proteins). If the fatty acid chain contains as much hydrogen as possible, the fat or oil is said to be **saturated**.

Associated with lipids are **steroids**. These include molecules like **cholesterol and sex hormones**. The latter group will be discussed in the chapter on the endocrine system.

4. NUCLEIC ACIDS (Fig. 4). These are the largest molecules in the body and are responsible for regulating manufacture of proteins. There are two kinds of nucleic acids, **DNA and RNA**.

DNA is found on the **chromosomes** (see below). It contains the information for all of our **inheritance**. With this information the cell knows exactly how to make proteins that your body requires for structural and enzymatic functions.

RNA is the workhorse of heredity. It takes the information found on DNA and translates it into specific sequences that dictate placement of amino acids in proteins. RNA also makes up the **ribosomes** (see below).

5. ADENOSINE TRIPHOSPHATE (ATP) (Fig. 5). This is a molecule found in mitochondria which stores energy. ATP is made cyclically from **ADP plus energy**. When ATP is used, it releases its **terminal phosphate** and becomes **ADP (Adenosine Diphosphate)**. The energy used to hold onto the terminal phosphate is released and your body uses this energy for all of the various things that you do that require energy expenditure (including reading this!). The ADP molecule is then built back into an ATP molecule in your **mitochondria** by the addition of a terminal phosphate. The phosphate is held in place with energy that you get from the foodstuffs you consume.

D. CELL ORGANELLES

1. CELL MEMBRANE (Fig. 6): This structure defines the three dimensional shape of the cell. It is composed of a "sandwich" of protein "bread" and lipid "butter". Because of its chemical makeup, it is **selectively permeable**. This means that some things can easily pass through the cell membrane at all times (water), some things are selectively able to pass at certain times and not at others (sodium ions), and other things cannot pass through at all unless they are specially prepared (proteins).

In a muscle cell, the cell membrane is called the **sarcolemma** ,

2. CYTOPLASM (Fig. 7): This is the cellular contents that lie between the nuclear membrane and the cell membrane. It consists of a viscous, semitransparent fluid environment in which are suspended both organelles and various inclusions. Organelles include the following:

a. Endoplasmic Reticulum (ER). This is a network of tubes throughout the cytoplasm. They form a tubular skeleton-like superstructure for the cytoplasm. The ER serves a number of functions. In a muscle (where it is called the **sarcoplasmic reticulum**) it plays a role in calcium ion storage and release during muscle contraction. In some parts of the cell it is **rough**, that is, it is covered with **ribosomes** (see below) for protein synthesis (in a neuron the rough ER is referred to as the **Nissl bodies**). In other parts it is **smooth**, eg., lacking ribosomes. **Smooth ER** is responsible for lipid and sex hormone synthesis, and drug detoxification, among other functions. It serves as an **intracellular circulatory system**, channeling items from one part of the cell to others or from the nucleus through the cytoplasm to the cell membrane.

b. Golgi apparatus. This organelle consists of a series of stacked membranous sacs that resemble a stack of pancakes. The major function of the Golgi is to **modify, package and concentrate proteins for specific cellular functions.** Proteins are complexed with carbohydrates in the Golgi to form various **glycoprotein molecules.** One of these, **mucus,** is very important to the speech mechanism in that it lubricates the voice-producing mechanisms as well as traps dust particles in the breathing tube.

c. Ribosomes. These are cytoplasmic organelles that are used to **manufacture proteins.** They consist of RNA that forms the "**workbench**" where proteins are assembled from the information supplied by the DNA of the chromosomes.

d. Mitochondrion (-dria). The mitochondrion is often called the "**powerhouse of the cell**" because of its function in **energy transformations within the cell.** Remember that **energy can neither be created nor destroyed** by living organisms, it is simply transformed from one form to another. The mitochondrion is able to take energy from **regular-sized energy bonds** of foodstuffs and convert that into the **high energy bonds** of the ATP molecule.

This organelle consists of two membranous sacs. The outer one is more-or-less sausage shaped. The inner one, the larger of the two, is folded inside of the outer one in such a way that it produces shelf-like projections, called **cristae.** It is on the cristae that the mitochondria go about their function of **producing ATP.** These organelles are more numerous in metabolically active cells (muscle and nerve cells) and less so in less active cells (adipose cells).

e. Centrosomes, centrioles and spindle fibers. A centriole is an organelle found near the nucleus. It consists of rod-like bundles of **microtubules.** The microtubules are arranged in groups of three in nine bundles that are evenly spaced around a center to form a hollow tube. **Two centrioles form a centrosome.** The two centrioles lie at right angles to each other to form the centrosome.

Spindle fibers are protein strands that aid chromosome movement during mitosis and meiosis.

f. Lysosomes. These are **membranous sacs** within the cytoplasm that are formed by the **Golgi.** They consist of packages of specific enzymes formed on the rough ER, transported to and modified by the Golgi, and ultimately stored in the lysosomes. The function of these enzymes is to digest items within the cell. They destroy particles ingested by the cell as is one of the

major functions of **macrophages** (such as the **alveolar phagocytes** found in the lungs- discussed in chapter 2). They also digest defunct organelles so that their metabolic products can be used in other places by the cell.

An interesting embryological function of lysosomes is their function in digesting tissues that no longer are needed. Thus, the web between the fingers that is formed when the hands form embryologically is destroyed by the lysosomes during modeling of the hand (see chapter 5).

g. Vacuoles. These are spaces within the cell that contain lipid, water or in some cases, such things as food. The membrane of the vacuole is the same as the cell membrane. Adipose tissue consists of cells which have a large oil vacuole that takes up nearly all of the cell contents. We will discuss them when we talk about adipose tissue.

h. Cilia and flagella. While these technically are outward extensions of the cell membrane, we will discuss them as part of the cytoplasm since they are related to it. Cilia are multiple and short and flagellae are single, long hair-like structures that project from the cell surface. Both are composed of **protein microtubules** which are able to bend and move either the cell (single cells) or the fluid surrounding the cell (in tissues).

Cilia line the breathing tube and function to sweep mucus and trapped dust particles out of the lung. They are also found lining the top of the ependymal cells that form the lining for the ventricles and central canal of the central nervous system. Their function here is to propel cerebrospinal fluid through the central nervous system.

Flagellae make up the tails of sperm cells where they are responsible for propelling these cells to their "egg encounter".

3. Nucleus. The nucleus is the "control center" of the cell. It contains the chromosomes and nucleoli.

a. Chromosomes. These are the things on which the DNA is found. The DNA is responsible for providing the genetic information that allows the cell to produce proteins. Recall that proteins form enzymes which are necessary for regulation of all chemical reactions in the body. Without the enzymes the body would not be able to function. All of the **hereditary characteristics** that make you unique are regulated through your DNA makeup.

During the bulk of the life cycle of a cell the chromosomes are long and slender and are referred to as **chromatin material**. It is only when the

nucleus is ready to divide in mitosis or meiosis that the chromosomes appear as distinct, visible bodies.

b. Nucleolus(-i). These are bodies located within the nucleus that are composed of ribosomal RNA and proteins. They make ribosomes. They have no membrane.

E. CELL PROCESSES

1. CELL REPRODUCTION: Technically, a cell undergoes **cell division and nuclear division** as two separate and usually related events. Cell division involves the division of the cytoplasm whereas nuclear division involves division of only the nucleus. Nuclear division, mitosis or meiosis, may or may not occur with cell division. If they occur simultaneously, then multiple cells will be produced. If nuclear division occurs in the absence of cell division, then a multi-nuclear cell is formed.

a. Mitosis (Fig. 8): This nuclear event occurs with body cells when the need for new cells with the same chromosome complement as that of the parent (**diploid**) cells is present. If it is followed by cell division then one parent cell will produce **two daughter cells** which have the same chromosome complement as that of the parent cell (diploid).

b. Meiosis (Fig. 8): In this situation, the body is producing reproductive cells. These have half the chromosome complement of the parent cell (are **haploid**). Thus, when followed by cell division, each parent cell produces **4 daughter cells**. These cells are either sperm or egg cells. Thus, when a sperm cell unites with an egg cell during sexual reproduction, the chromosome number as found in the parent cell is restored.

2. TRANSLOCATION OF MATERIALS BY CELLS: In order for the cell to utilize items in its environment or to transport items from within the cell to the surrounding environment, these items must move through the cell membrane. There are two main processes whereby the cell moves things across its membrane, **active and passive transport**. Also, some things readily move across the membrane, some do it with difficulty, and some cannot move across the membrane at all.

a. Active processes (Fig. 9): These involve energy (carried on ATP) expenditure in order for them to happen. They will not occur in dead cells because the required energy is not there. In active processes the materials move through the cell membrane against a concentration gradient (eg., from a low to a high concentration). There are two active processes that we will study.

1). Active transport: In these processes an **ion moves from a low concentration to a high concentration across a cell membrane**. Since this **movement is against the concentration gradient**, it involves energy expenditure. Up to 40% of a cell's metabolic energy expenditure goes into this process. This process will be examined in some detail in Chapter 6 when we discuss the sodium and potassium pump involved in neural transmission.

2). Phagocytosis: This term means "cell eating" and involves the cell engulfing bacteria or other foreign materials. The cell "swallows" the foreign material into its "intestine", called a **vacuole**. Here the item is either digested through use of the enzymes provided by the lysosomes or is simply stored "out of harm's way". We will discuss **alveolar phagocytes** in Chapter 2.

b. Passive processes: These do not involve energy expenditure and will **happen with dead cells**. With passive processes the ions flow with the concentration gradient, eg., from a high to a low concentration through a cell membrane. Generally molecules must be small enough and soluble in the cell membrane for them to pass through the membrane. Large molecules like proteins are generally digested into their amino acid components in order to get through a cell membrane. They may also get through a membrane if they are in a vacuole and that vacuolar membrane joins with the cell membrane and expels them without their actually penetrating the membrane.

1) Diffusion: Movement of something (such as perfume) in the air from an area of high concentration (the just-opened bottle) to an area of low concentration (the air). When the cell is involved, **diffusion involves the molecule, ion or atoms moving across the cell membrane following the concentration gradient (eg. from high to low concentration through a membrane)**. Things that move across the cell membrane by diffusion either have specific "holes" in the membrane through which they pass (eg., ions such as sodium and potassium) or are lipid soluble, thus able to dissolve in the lipid of the membrane and move through in this fashion (eg. oxygen or carbon dioxide).

2). Osmosis (Fig. 9): This is the **diffusion of water molecules through a cell membrane**. The pressure created by this movement is called **osmotic pressure**. It is measurable using an osmometer. When comparing the osmotic properties of a cell to the solution in which it is placed, we check the quantity of dissolved materials in the solution or cell.

If we look first at the solution into which the cell is placed and examine the concentration of dissolved materials, it is obvious that there can be more, the same amount or less dissolved material in the solution than in the cell.

If we examine the situation in which there is more dissolved material in the solution than in the cell, it is obvious that there is less dissolved material in the cell than in the solution. If there is less dissolved material in the solution, then the cell has more. Also, very obviously, in a solution in which there is the same amount of dissolved material, it is the same as in the cell.

In the solution (or cell) with a higher amount of dissolved material, we call this a **hypertonic solution**. With a lesser amount of dissolved material (in either the solution or the cell), the solution is an **hypotonic solution**. With the same amount, both solutions are **isotonic**. If an animal cell is placed in an hypotonic solution, that cell will take on water, swell, and possibly burst. If it is placed in a hypertonic solution, it will lose water and shrink. In an isotonic solution the cell will neither swell nor shrink.

Since the cell membrane is permeable to both water and the dissolved materials, water will move in one direction and the dissolved materials will move in the opposite direction through the cell membrane. Thus, if a cell is placed in a hypertonic solution, the cell will lose water but gain dissolved materials.

3). Facilitated diffusion: Some molecules need help in diffusing through the cell membrane. In facilitated diffusion the molecule is not lipid soluble nor are there pores in the cell membrane through which it can pass. Thus, the molecule complexes with a special protein in the cell membrane which serves as a carrier across the membrane by making the molecule more soluble in the lipid of the membrane. Again, this is a legitimate type of diffusion in that the molecule moves from an area of high concentration to one of low concentration across the membrane. Glucose moves across the membrane in this fashion.

4) Filtration: We are not too interested in this one because it does not occur in areas under study in this course. In this case the molecule moves across the cell membrane due to **hydrostatic pressure**. This occurs in the kidneys.

3. HYDROGEN ION ACTIVITY

The **pH** (symbol written with a lower case p and upper case H) of a solution is a **measure of the hydrogen ion (H⁺) activity** (or acid-base balance) of that

solution. The pH scale (Fig. 10) is a logarithmic scale that runs from 0 to 14. A pH of 7 is neutral, below 7 is acidic, and above 7 is alkaline (a base). Because this is a logarithmic scale, a pH of 5 is 10 times more acidic than that of pH 6, one of 4 is 100 times more acidic than one of 6, one of 3 is 1,000 times more acidic than one of 6, and so on. It should be obvious from this that a pH change of one tenth of a pH unit is very significant. Look over the list of pH values for common solutions (Fig. 10).

The body has a series of **buffer systems** that are used to maintain appropriate pH values in and outside the cells. Buffers take up H⁺ or OH⁻ ions and neutralize them so they no longer have an influence on the pH of a solution. pH values can change dependent on addition or removal of hydrogen ions, hydroxide ions, or other ions from the solution.

Body fluid pH varies slightly but normally falls around the value of 7.0 to 7.4. Arterial blood is 7.4, venous blood is 7.35, and intracellular fluids average 7.0. If the pH of the blood goes above 7.45, a person is said to have **alkalosis**. A drop in arterial pH below 7.35 results in **acidosis**. **Respiratory acidosis or alkalosis** results when the breathing system fails to perform its normal function of stabilizing pH. Carbon dioxide concentrations in the blood have a major influence on blood pH and must be regulated by the breathing system. (CO₂ + H₂O -----> H₂CO₃ ----->H⁺ + HCO₃⁻-----> H⁺ + CO₃⁻). {carbon dioxide plus water yields carbonic acid yields hydrogen ions plus bicarbonate ions yields hydrogen ions plus carbonate ions}

Respiratory acidosis occurs when a person breathes shallowly or when gas exchange is hampered by diseases such as pneumonia, cystic fibrosis, or emphysema. When the blood pH falls below 7.0, the central nervous system becomes so severely depressed that the person goes into coma and death soon follows.

Respiratory alkalosis results when carbon dioxide is eliminated from the body faster than it is produced, causing the blood to become more alkaline. This commonly happens when a person hyperventilates. Characteristic signs include muscle tetany, extreme nervousness, and convulsions. Death may result from respiratory arrest.

F. TISSUES: A tissue is a group of cells of a similar type performing a specific function in the body.

1. EPITHELIUM (Fig. 11): This type of tissue **covers organs**. It **always has one surface exposed to the environment and the other in contact with the underlying tissue**. There is no nervous or vascular tissue in an epithelium so it relies on a nutrient supply from the underlying tissue. Gas exchange occurs directly with the environment or with the underlying tissue. Because of the

lack of the vascular tissue, these tissues are either not very thick, or, if thick, have mostly dead cells on the surface exposed to the environment.

There are several types of epithelia and they are categorized based on cell shape and cell layering. **Simple epithelia** are one layer thick, **stratified** are multiple layers thick. **Pseudostratified epithelia** look as if they are stratified, however, the appearance is deceptive as the layered appearance is due to nuclear positions and cell shapes. **Squamous epithelia** are flat-celled. **Cuboidal epithelia** have cube-shaped cells. **Columnar epithelia** have cells that are tall, like columns.

a. **Simple squamous epithelium:** This tissue has fried-egg shaped cells. The nucleus bulges from the cell like an egg yolk. Since these cells have no protective cover and will dry out or be mechanically damaged easily, they are always found in protected places. This thin layered epithelium allows for rapid movement of gases or other items across the membrane, however, it must be kept moist at all times. We will discuss this epithelium where it occurs as a lining of the alveoli of the lung. Also, it forms the thin lining of the body cavities (parietal and visceral pleura, pericardium, and peritoneum). It forms the inner lining of the walls of capillaries, etc. We will see it in various places throughout this course.

b. **Stratified squamous epithelium:** This is a multiple-layered epithelium. It generates cells from its bottom layer (the **stratum germinativum**). These cells get pushed away from the basal layer where there is a nutrient source and ultimately die. As they move away they go through progressive stages of death until at the very outside of the epithelium they finally slough off. This tissue is found in places where abrasion or desiccation occurs. SSE provides a waterproof covering of the skin. In this situation the outer cells take on a waterproofing protein called keratin and help waterproof and friction proof the exposed skin surfaces. Stratified squamous epithelia are also found in places like the mouth and throat lining, vocal fold lining, and vaginal and anal canal linings among other places. In these places the multiple layers protect the underlying tissues from abrasion.

c. **Simple cuboidal epithelium:** This tissue has cube-shaped cells. Its functions are both secretion and absorption. We will see it in places like mucous glands of the larynx and trachea where it produces mucus that lubricates these structures. Cuboidal epithelium can also be stratified.

d. **Simple columnar epithelium:** This tissue has column-shaped cells. Often its free surface is ciliated. Also, **Goblet Cells** (which are goblet shaped and secrete mucus) are found at its base. We will find it in the nasopharynx and further down the respiratory tract in the bronchioles. It is

also found lining nearly the entire digestive tract (from stomach to rectum) and the oviducts.

e. **Pseudostratified Ciliated Columnar Epithelium (pcce)**: This tissue has some cells that reach its surface and some that don't. Coupled with the fact that the nuclei are in variable positions, it gives this tissue the appearance of being stratified. We will see it lining a great deal of the pharynx, larynx and trachea where its goblet cells produce mucus that traps dust particles and the cilia sweep the mucus and dust up into the throat to be disposed of.

2. Connective tissue (Fig. 12): This group of tissues consists of a number of diverse types that connect and support. These tissues have multiple components.

The cells are often scattered and sparse. **Cell types** include **fibroblasts** (produce fibers), **mast cells** (containing among other things, histamines which cause capillaries to be leaky during inflammatory reactions), **macrophages** (capable of phagocytizing foreign matter and dead or dying tissue cells), **chondroblasts and chondrocytes** (cartilage cells), **osteoblasts, osteocytes and osteoclasts** (bone cells) and **adipose** cells (cells specialized for storing lipid within an oil vacuole) among others.

Cells are placed in a **matrix** that contains a **ground substance and fibers**. The ground substance includes dense, hard materials (**hydroxyapatite crystals**) found in bone, gelatinous materials as found in cartilage, and watery materials such as found in blood. One of the most ubiquitous molecules found in the ground substance of connective tissues is **hyaluronic acid**. It is a polysaccharide that traps water in the tissue. The relative amount of hyaluronic acid in the various connective tissues determines the viscosity and permeability of the ground substance.

Fibers may be **white**, non-branched and composed of the protein collagen (**collagenous fibers**) or **yellow**, branched and composed of the protein elastin (**elastic fibers**). Reticular fibers, thought to be fine collagenous fibers with a slightly different chemistry, form a network (thus the name reticular) and are continuous with collagenous fibers in connective tissues. The blood supply may be well-established, scarce, or non-existent within the tissue.

There are many types of connective tissue found in the body. Following is a description of the more common types.

a. **Loose (or areolar) connective tissue**: This tissue has all three fiber types in relatively equal numbers in a semifluid ground substance. There are

several cell types present including fibroblasts, macrophages and frequently adipose cells. This tissue is a filler tissue that helps form the shape of organs, and forms the layer immediately underneath the epithelium (called the **lamina propria**) in a **mucous membrane** (such as in the trachea where it forms a large amount of tissue immediately under the pseudostratified ciliated columnar epithelium, columnar epithelium, and cuboidal epithelium). It also separates and cushions muscles, forms the subcutaneous tissue which attaches the skin to underlying tissues, surrounds glands, forms the bulk of the connective tissue of the trachea, etc. Because of the great amount of extracellular fluid in the ground substance, this tissue is subject to concentration of extra fluid, producing the condition called **edema**.

b. **Adipose tissue:** This tissue essentially is areolar tissue with a preponderance of adipose cells. It has the largest number of cells per volume of any of the connective tissues. The adipose cells are large, spherical cells with the bulk of the cell contents taken up by an oil vacuole. Since the oil vacuole displaces the contents of the cell, these cells have the nucleus near their edge and have the appearance of a **signet ring**. Other characteristics of this tissue are those of areolar tissue. This tissue is found in a number of places such as areas that produce body contours, behind the eye, around internal organs, etc. It also becomes more predominant in obesity.

c. **Elastic connective tissue:** The key characteristic of this tissue is the preponderance of elastic fibers in the matrix. Because of this, this tissue is extremely elastic. As with most other connective tissues, the fibers far outnumber cells. It is found in such places as the vocal folds and some very elastic ligaments.

d. **Dense connective tissue:** Collagen fibers predominate in this tissue. It has few cells or other components. This tissue forms tendons and ligaments as well as being an important component of the dermis of the skin.

e. **Cartilage:** Cartilage (Figure 12) is **avascular** and has **no nerve supply**. Due to the lack of the blood supply, these tissues are limited in size, not being able to form really thick structures. The **ground substance** consists of hyaluronic acid bound to proteins and chondroitin sulfate. Large numbers of collagenous, elastic or reticular fibers are found within the ground substance causing the matrix to be quite firm. Cells are scattered and found in **lacunae**. The individual cells are not in contact with each other. There are three types of cartilage: hyaline, fibrocartilage and elastic cartilage. The **perichondrium**, a membrane over the entire cartilage, is responsible for growth of the cartilage.

- 1). **Hyaline cartilage:** In this type, collagenous fibers predominate. The tissue itself has a white, glistening appearance. It is tough and resists wear. Of the three types, **this is the only one that will ossify**. This ossification may occur early (as with the embryonic skeleton), or later in life (as with laryngeal cartilages and tracheal rings) or not at all (depending on conditions). It is widely distributed in the body, being found in such places as in the embryonic skeleton, on the ends of bones, in parts of the larynx, trachea, etc., and in such places as the nose cartilages.
- 2). **Elastic cartilage:** The general appearance of this tissue is that of hyaline cartilage, however, elastic fibers predominate and give this tissue its elasticity, as well as an overall yellow color. **It will not ossify**. It is found in such places as the epiglottis, other laryngeal cartilages, the eustachian tube, and the pinna of the ear.
- 3). **Fibrocartilage:** In this cartilage, collagenous fibers predominate and form clearly defined bundles. It looks more like dense connective tissue than it does the other cartilage types. It is found in a few places, such as the intervertebral discs and the spongy cartilages of the knee.
- f. **Bone:** This is a hard, dense tissue that is built to support weight. Microscopically (Fig. 13) the cells are found in **lacunae**, as they are in cartilage, however, they are interconnected with tiny canals called **canaliculi** (which are not present in cartilage). There is a **well-developed vascular supply** which enables this tissue to be very dynamic. All three types of fibers are present. Bone consists of 35% organic matrix, called **osteoid**. **Osteoid is principally (95%) collagen with 5% extracellular fluid and hyaluronic acid**. The remaining 65% of the bone is inorganic salts, in the form of **hydroxyapatite crystals**.

You will study the microscopic structure of bone in lab. Briefly, there are two types, **compact bone and spongy bone** (Fig. 14). **Compact bone** is arranged in **Haversian systems (also called an osteon)**. The Haversian system consists of **concentric lamellae** of bone with **osteocyte-filled lacunae**. The lacunae are interconnected with **canaliculi**, providing communication among the various osteocytes. In the center of each Haversian system is the **Haversian canal** with its vascular and nerve supply. **Volkman's canals**, tiny canals that run at right angles to the long axis of the bone, connect the nerve and blood supply outside the bone with that of the Haversian canal. The individual Haversian systems run along the longitudinal axis of the bone. The hundreds of Haversian systems pack together to form the compact portion of the bone. Surrounding the bone is a membrane, called the **periosteum**. The periosteum provides the

blood and nerve supply for the Volkmann's canals. It also produces growth in girth for the bone.

Spongy bone (Fig. 14) is, as the name implies, much less dense than compact bone. The bone is arranged in **trabeculae** (beam-like shapes) which line up along lines of stress. This bone type does not have the Haversian system arrangement, however, the trabeculae contain lamellae with interconnected osteocytes.

There are three cell types found in bone. **Osteoblasts** are free cells that form bone. As they form bone they become entrapped in the lacunae and become an **osteocyte**. Osteocytes maintain bone. A third cell type arises independently and is responsible for destruction of bone. These are the **osteoclasts**. When bone is being rearranged, osteoclasts destroy it and osteoblasts create new bone to replace that which was destroyed.

As bone forms during embryological and post-embryological development, it either replaces an existing piece of hyaline cartilage (**cartilage or replacement bone**) or it replaces an existing connective tissue membrane (**membrane bone**). Membrane bones are generally limited to the cranium and facial skeleton (plus a few other places), and cartilage bones are in the remainder of the skeleton. We will examine a fetal skull in lab. Here you will see membrane bone and the connective tissue membrane of the skull as it is being ossified. Where this membrane is not ossified it forms soft spots in the skull. Other bones in the body were originally hyaline cartilage and are replaced with bone as the skeleton ages. On the fetal skeleton you can see the yellow dried up cartilage that would have ossified. Ossification is completed at different times with various bones (Fig. 15, Fig. 16).

Macroscopic structure (Fig. 14) studies of bone will also be conducted in lab. **Long bones** are arranged to support weight. They are tubular with articular surfaces at either end. The bone has a **shaft (the diaphysis)**, with **epiphyses (epiphysis)** at either end. The epiphysis attaches to the diaphysis at the **epiphyseal plate**. Beneath the epiphysis is cartilage of the epiphyseal plate which will undergo a transition to bone in the epiphyseal plate. As new cartilage in the epiphyseal plate region grows and is ossified, the bone grows in length. Growth in length also occurs at the articular cartilage of the epiphysis. Once the bone reaches its definitive adult size, the epiphyseal plate disappears and the epiphysis fuses directly to the diaphysis. Generally each epiphysis articulates with another bone so is covered with an articular cartilage to provide for smooth operation of the joint. The diaphysis has a **medullary cavity** which is filled with yellow bone marrow. This **yellow marrow** is mostly adipose

tissue. Areas of spongy bone have **red bone marrow** which is a site of **hematopoiesis** (red blood cell formation).

A series of recent studies have shown that **smoking has a negative effect on bone fracture healing in humans**. Researchers at the University of Texas Southwestern Medical School looked at 76 fractures of the tibia. On the average those of non-smokers healed in 146 days. However, smokers bones took 276 days to heal. In fact, in two of the smoking patients the bones hadn't healed even after a full year!

It has been known for some time that **smoking increases the risk of osteoporosis and bone fractures**. **The fact that it also retards bone healing is especially significant for the smoker**. It is not clear yet what the mechanism is that retards bone healing but it is likely that somehow the smoking interferes with blood flow to the fracture.

In a separate study of spinal bone fusion in rabbits conducted at the Emory University School of Medicine, it was shown that **nicotine retards bone growth**. A month after fracturing the vertebrae, no bone fusion had occurred with the rabbits to which nicotine had been administered. However, in the control group which had no nicotine administered, 100% had complete fusion of the bone!

The amazing thing is that the cigarette manufactures still insist that smoking does not have harmful side effects! Hmmm, makes you want to go out and have a smoke!

g. **Blood**: Blood is considered to be a connective tissue because of the **cells and matrix**. There are **red blood cells** which carry oxygen and about 1/4 of the carbon dioxide on the **hemoglobin molecule**, and **white blood cells** which are responsible for protecting the body in a number of ways.

We will see one of the types of white blood cells (**lymphocytes**) in **lymph nodules** throughout the larynx, trachea, and lungs in labs. These lymph nodules are responsible for local immunological responses in the body. **Platelets** are cell fragments that participate in the clotting process.

The remainder of the blood, about 55%, consists of the **plasma**. Plasma is about 90% water with the remainder being various proteins, salts, and gases. Plasma leaks out of the blood system and has to be retrieved by the **lymph vessels of the lymph system** where it is called **lymphatic fluid**. This fluid is then dumped back into the blood circulatory system after having passed **lymph nodes** where bacteria, etc. are removed. Lymph nodes differ from lymph nodules in that the former have a capsule over them and are interconnected *via* the lymph vessels while the nodules have no capsule and no direct connections to the lymph vessels. The

respiratory gas, carbon dioxide is carried primarily in the plasma along with a small amount of oxygen.

3. MUSCLE: Muscle tissues have the ability to shorten and do **work**. There are three types of muscle, **skeletal, smooth, and cardiac** (Fig. 17). Most of our studies will deal with skeletal muscle, however, some knowledge of smooth muscle is warranted. Cardiac will be mentioned in passing as it is only found in the heart. Differentiation of muscle types is based on cell morphology, position in the body, whether or not it is under voluntary control and a number of other variables (Fig. 17).

a. **Skeletal muscle** (Fig. 18): Skeletal muscle is found attached to the skeleton, including both bone and cartilaginous structures. It is under willful (**voluntary**) control. The individual cells show **striations** (thus giving it one of its common names, striated skeletal muscle). Individual cells have fused into a long tubular arrangement called a **fiber** with the nuclei near the periphery of each cell.

A typical muscle (figure 19), such as the biceps, has an **origin** (attachment point which is at the relatively immovable skeletal structure), an **insertion** (attachment point on the movable skeletal structure), and a **belly** (the bulk of the muscle). If one carefully teases apart a whole muscle, the individual fibers become apparent.

The **fiber** is really a cell. However, the skeletal muscle cell is unusual in that it joins with others at its ends to form a long, continuous tube, the fiber. While most of the fibers range in length from 1 to 40 micrometers, some reach the length of 30 cm (a foot). The **nuclei** of these cells are pushed to the periphery by the large number of **myofibrils**. As with other types of muscle, there are large numbers of **mitochondria** within each cell.

Myofibrils are the individual proteinaceous contractile units of the muscle fiber. They are long filamentous structures that extend the entire length of the cell. There are typically thousands of myofibrils in each cell and they account for nearly 80% of the cell volume. When you exercise, it is by increasing the number of myofibrils and other muscle cell components such as mitochondria that you increase the size of each muscle fiber. Thus, a muscle gets bigger with exercise because you increase numbers of myofibrils, not the number of muscle fibers. Except for a few circumstances, the number of muscle fibers you have early in life is the number you finish with. If a muscle doesn't get used, the myofibril number reduces. It is estimated that muscle strength decreases at the rate of approximately 5% a day during periods of disuse! In severe cases such as what might occur with a quadraplegic, muscle cells irreversibly are replaced with fibrous connective tissue. Each myofibril is made of a chain of thousands of smaller units called **sarcomeres**.

The **sarcomere** is the smallest subunit of the myofibril. It shows a clear pattern of alternating light and dark banding. The dark bands are "**A**" **bands** (for anisotropic, meaning that they can polarize visible light). The light bands are "**I**" **bands** (for isotropic, meaning they do not polarize visible light). Because of the fact that A bands and I bands of each myofibril within a muscle fiber are aligned across the cell, the cell shows a characteristic banding pattern (**striations**). Within the A band is a lighter region, the "**H**" **zone** (for helle, meaning "bright"). Interrupting the middle of each I band is a narrow, dark, "**Z**" **line**. Thus, a sarcomere is the unit of a myofibril that extends from one Z line to the next Z line. The banding pattern of a sarcomere is made up from the organization of two protein filaments in the myofibril.

The two protein filaments are the **thick filaments** and **thin filaments**. The thick filaments extend the length of the A band. The thin filaments extend from the Z line to the H zone. The thick filaments are composed primarily of the protein **myosin**. The myosin protein has a rodlike tail and two heads (Fig. 20). The tails of the myosin's face toward the center of the sarcomere within the H zone, while the heads project outward from the thick filament and can contact the surrounding thin filaments. The resultant cross bridges formed with the myosin head/thin filaments are responsible for providing muscular contraction. The thin filaments are composed primarily of the protein **actin**. There are other significant proteins (such as **tropomyosin and troponin**) associated with the thin filaments which will not be discussed here.

Note that in **cross section the sarcomere** shows various views of the thin and thick filaments (Fig. 21, Fig. 22). In the H zone there are only thick filaments and they are arranged with each filament surrounded by six others in a regular hexagonal pattern. In the dark part of the A band, there are both thick and thin filaments. In this area the same pattern of thick filaments shows as we saw in the H zone, however, each thick filament is surrounded with six thin filaments. Note that each thin filament is surrounded with three thick filaments in a triangular pattern. In the I band, there are only thin filaments. These are arranged in hexagonal patterns as they were in the A band, without the corresponding thick filament.

Each muscle cell has thousands of myofibrils within it. The **sarcoplasmic reticulum (endoplasmic reticulum of a muscle cell)** of the cell extends among the myofibrils, providing an interconnection among them. At each **A-I junction** the sarcoplasmic reticulum forms a large sac-like structure called the **terminal cisternae**. The muscle cell membrane, called the **sarcolemma**,

covers the muscle cell. However, at each A-I junction, the sarcolemma penetrates into the muscle cell as a hollow tube, forming the **transverse tubule (T-tubule)**. The T tubule and two adjacent terminal cisternae of the sarcoplasmic reticulum form **triads**. All of the triads in a muscle cell are collectively referred to as the **T system**.

[TRIAD = T TUBULE + 2 TERMINAL CISTERNAE]

["T" SYSTEM = ALL TRIADS COLLECTIVELY]

Since the muscle cell is metabolically so active, the T system is essential in that it supplies the individual sarcomeres with oxygen, glucose and various ions. Also, the nerve stimulus can travel rapidly to all of the sarcomeres through the T system. **The sarcoplasmic reticulum regulates intracellular levels of calcium ions. When the muscle is stimulated to contract, the sarcoplasmic reticulum releases calcium ions that enable the contraction to occur.**

The mechanism of contraction of a muscle cell is interesting. First, when a muscle does work, it must contract. **Thus, a muscle always pulls as it shortens---never pushes!** Interestingly, even though the muscle shortens when it does work, the thick and thin filaments themselves do not shorten.

Back in 1954, Hugh Huxley proposed the **sliding filament theory of contraction**. Basically, what he proposed was that the thin filaments slide over the thick filaments, thus shortening each sarcomere. The collective shortening of thousands of sarcomeres allows the entire muscle to shorten an appreciable amount (roughly 35% to 50% of its relaxed length). Examination of the banding pattern of the sarcomeres substantiates this hypothesis (Fig. 20). When the muscle contracts, each sarcomere becomes visibly shorter (that is, visible with an electron microscope). Examination of the shortened sarcomere (Fig. 20) reveals that the H zone and I band disappear and the Z lines move closer together. The A band remains the same length, however, its medially located H zone has disappeared. When the muscle relaxes, the sarcomere reverts to its normal appearance (described above).

Further studies have shown that the myosin heads are responsible for the movements observed in the sarcomere. When the muscle is initially stimulated by the nervous system, the myosin heads contact the actin. They then bend away from the center of the sarcomere, thus sliding the thin filament over the thick filament. During a single contractile event, a single bending of the myosin head will shorten the muscle approximately 1% of its length. Since the muscle can shorten up to 50% of its length, it is obvious that multiple attaching/bending events must occur. Thus the myosin heads "walk" over the actin effecting the total observed contraction.

The obvious next question is "**what causes the contraction of the skeletal muscle?**" A great deal is known about this subject and I will briefly outline it below (Fig. 23).

Initially, the neuron associated with the specific muscle will stimulate that muscle to contract by providing the neural impulse to the muscle at the neuromuscular junction (Fig. 21). We will address the nature of this neural impulse later (Chapter 6). However, it is important to know at this time that a neurotransmitter at the neuromuscular junction triggers the event. This event initiates the release of bound Ca^+ ions from the membrane of the T system. This Ca^+ rapidly permeates the entire fiber to start the contraction. The free Ca^+ ions enable the activated myosin heads to bind to the actin filaments. (An activated myosin head is one in which ATP energy is present and available for the contraction event). Once the binding of the activated myosin head occurs, the head bends, using energy supplied by ATP. The cell resupplies ATP which allows the bound, bent myosin head to detach from the actin. At this time the ATP splits into ADP and P with its resultant energy being supplied to form the activated myosin head.

A single power stroke of myosin cross bridges contracts the muscle about 1%. Thus, the above contraction must be repeated many times for the muscle to contract its full 35-50%. Relaxation occurs when the sarcoplasmic reticulum reclaims Ca^+ ions from the cell. This inhibits the contraction by preventing the establishment of cross bridges.

Rigor mortis, the death rigor, occurs in a muscle at death. At this time, the cell is no longer able to exclude Ca^+ from the cytoplasm. The Ca^+ promotes establishment of cross bridges (Fig. 24). Since no ATP is available to allow for breakage of these cross bridges, the myosin heads can no longer release their grip on the actin and the muscle remains in a fixed rigor. Muscles begin to go into rigor mortis after 3 to 4 hours. They reach their peak at about 12 hours but gradually diminish stiffness through the next 2 days.

Muscle fibers will be either individually or collectively stimulated by a neuron. Those muscles, such as finger or tongue muscles, in which most of the fibers have their own neuron, have fine control. Those, such as large leg muscles, which have a single neuron serving multiple fibers, have more crude control.

When a fiber is stimulated by a neuron, it will contract according to the **all-or-none response**. That is, the fiber will contract to its maximal amount with the stimulus. It won't partially contract. In order to provide graded strength

to a muscle, what happens is various numbers of fibers will fire dependent on the strength required of the muscle. Thus, several hundred fibers will be fired if a light workload is required, whereas thousands will be fired with a heavy workload.

Muscles do different things. Some are **prime movers**, meaning they are the main one involved in a specific action. Some are **antagonists**, meaning they work against prime movers. Many are **synergists**, meaning they work in tandem with others to effect a response.

When we begin our studies of specific muscles, it is important to consider their **origin and insertion**. Also, keep in mind that a **muscle's name is not randomly assigned**. There is a specific reason that name is applied to the muscle. The sartorius muscle of the upper thigh is so named because tailors (in Latin, a sartor) use this muscle to cross their legs. **Also, each muscle has a particular action which will be studied.**

b. **Smooth muscle** (Fig. 17): This type of muscle is found in the viscera, thus is also called **visceral muscle**. It differs from skeletal muscle in a number of ways. First, it is **involuntary**, that is, it is not under willful control. (It is under control of the **autonomic nervous system, not the voluntary nervous system**). Secondly, the individual cells are elongate, nonstriated, single nucleated, and tapered at each end. Third, it is found in places such as the internal organs, blood vessels, and the arrector pilus muscle of the skin. We will see it in trachea and other breathing tubes as the **trachealis muscle**.

c. **Cardiac muscle** (Fig. 17): This type of muscle is only found in the heart. Like smooth muscle, these muscle fibers are under autonomic nervous system control. The cells have a single nucleus, are striated, and branched. Again, remember that I don't have a heart!

4. **Nervous tissue**: This tissue is discussed in great detail in Chapters 6, 7 and 8 so we will not cover it here.