Chapter 3: Cytology

Cytology is the study of the cellular structures and their function.

A cell is an organized independent mass of protoplasm (nucleus and cytoplasm) which makes the basic primary structure of an organism.

CELL CONCEPT:

One of the most important concepts in biology is that a cell is a basic structural and functional unit of living organism.

This is known as a cell theory and was proposed jointly by two scientists; a Belgian botanist named Matthias Schleiden and the German zoologist named Theodore Schwann. They studied the plant cell and animal cell respectively and came up with the idea that plants and animals are made up by small individuals which perform different functions of the whole organism. This is the basis of the cell theory, which is listed below.

The cell theory embraces four ideas, these are:

1. Living organisms are made up of smallest sufficient unit of living matter called cell.
2. The new cell is derived from pre-existing ones by cell division.
3. Each cell is independent with others but function as integral part of the whole organism.
4. The cell contains the hereditary material which is passed from generation to generation.

Since we are focused on human studies – our cellular focus will be general in nature (not worrying about plant cells, bacterial cells, fungal...etc.) and become more focused in the next chapter when we study tissues.

But for now, we need to become familiar with the general descriptions of a cell and its primary components.

The study of cell structure includes the fields of CYTOLOGY (for cells) and HISTOLOGY (for tissues), whereas the function of cells is studied in CELL PHYSIOLOGY, BIOCHEMISTRY, and CYTOGENETICS.

The first instrument used in studying cell structure was the light microscope, which remains an important tool today.
The **TRANSMISSION ELECTRON MICROSCOPE** and the **SCANNING ELECTRON MICROSCOPE** have vastly increased our knowledge.

Before an object can be viewed, it is necessary to stain the material and cut it into samples thin enough for a light beam or an electron beam to penetrate them.

First, the tissue is treated, to “fix” the structures so they will not be altered by the staining and slicing. Usually this is done by using chemicals such as **ALCOHOL** and **FORMALDEHYDE**.

Stains have been developed that react differently with different cell structures, depending on their chemical composition or enzymatic activity. The use of stains containing radioactive atoms, known as **AUTORADIOGRAPHY**, often involves feeding cells specific compounds with radioactive atoms and then observing the distribution of radioactive events on a photographic film emulsion.

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**Organization of the Cell**

A cell has two major parts; they are the nucleus and the cytoplasm. We will discuss the organelles of the cell in greater detail a little later; but for now, consider these two components. The nucleus is separated from the cytoplasm by a nuclear membrane, and the cytoplasm is separated from the surrounding fluids by a cell membrane, also called the plasma membrane. The different substances that make up the cell are collectively called protoplasm. Protoplasm is composed mainly of five basic substances: water, electrolytes, proteins, lipids, and carbohydrates.

**Water.** The principal fluid medium of the cell is water, which is present in most cells, except for fat cells, in a concentration of 70 to 85%. Many cellular chemicals are dissolved in the water. Others are suspended in the water as solid particulates. Chemical reactions take place among the dissolved chemicals or at the surfaces of the suspended particles or membranes.

**Ions.** The most important ions in the cell are potassium, magnesium, phosphate, sulfate, bicarbonate, and smaller quantities of sodium, chloride, and calcium. The ions provide inorganic chemicals for cellular reactions. Also, they are necessary for operation of some of the cellular control mechanisms. For instance, ions acting at the cell membrane are required for transmission of electrochemical impulses in nerve and muscle fibers.

**Proteins.** After water, the most abundant substances in most cells are proteins, which normally constitute 10% to 20% of the cell mass. These can be divided into two types: **structural proteins and functional proteins**. Structural proteins are present in the cell mainly in the form of long filaments that themselves are polymers of many individual protein molecules. A prominent use of such intracellular filaments is to form microtubules that provide the “cytoskeletons” of such cellular organelles as cilia, nerve axons, the mitotic spindles of mitosing cells, and a tangled mass of thin filamentous tubules that hold the parts of the cytoplasm and nucleoplasm together in their respective compartments. Outside the cell, filamentous proteins are found especially in the collagen and elastin fibers of connective tissue and in blood vessel walls, tendons, ligaments, ...etc. The functional proteins are an entirely different type of protein, usually composed of combinations of a few molecules in tubular-globular form. These proteins are mainly the enzymes of the cell and, in contrast to the filamentous proteins, are often mobile in the cell fluid. Also, many of them are
adherent to membranous structures inside the cell. The enzymes come into direct contact with other substances in the cell fluid and thereby catalyze (speed up) specific intracellular chemical reactions. For instance, the chemical reactions that split glucose into its component parts and then combine these with oxygen to form carbon dioxide and water while simultaneously providing energy for cellular function are all catalyzed by a series of protein enzymes.

**Lipids.** Lipids are several types of substances that are grouped together because of their common property of being soluble in fat solvents. Especially important lipids are phospholipids and cholesterol, which together constitute only about 2% of the total cell mass. The significance of phospholipids and cholesterol is that they are mainly insoluble in water and, therefore, are used to form the cell membrane and intracellular membrane barriers that separate the different cell compartments. In addition to phospholipids and cholesterol, some cells contain large quantities of triglycerides, also called neutral fat. In the fat cells, triglycerides often account for as much as 95 per cent of the cell mass. The fat stored in these cells represents the body’s main storehouse of energy-giving nutrients that can later be dissolved and used to provide energy wherever in the body it is needed.

**Carbohydrates.** Carbohydrates have little structural function in the cell except as parts of glycoprotein molecules, but they play a major role in nutrition of the cell. Most human cells do not maintain large stores of carbohydrates; the amount usually averages about 1% of their total mass but increases to as much as 3% in muscle cells and, occasionally, 6% in liver cells. However, carbohydrate in the form of dissolved glucose is always present in the surrounding extracellular fluid so that it is readily available to the cell. Also, a small amount of carbohydrate is virtually always stored in the cells in the form of glycogen, which is an insoluble polymer of glucose that can be depolymerized and used rapidly to supply the cells’ energy needs.

**EUKARYOTIC CELL STRUCTURE**

Cells with a nucleus are known as **EUKARYOTIC** (True Nucleus). Most all human cells do have a nucleus and therefore we are classified as a eukaryotic organism. Living organisms that are composed of cells without nuclei are termed **PROKARYOTIC** (before nucleus) and are much more primitive in anatomy and physiology; examples of prokaryotic organisms would include bacteria and some blue-green algae.

At the most basic Level, the cell’s overall structure can be viewed as:

1. **Cell Membrane**
2. **Nucleus**
3. **Organelles**
4. **Cytoplasm**
1. **Cell Membrane**: the thin layer which separates the cell contents from its environment.
2. **Nucleus**: specialized structure within the cell which contains DNA and controls cell functioning and reproduction.
3. **Organelles**: small bodies with specific structures and functions within the cell.
4. **Cytoplasm**: called the cytosol in the diagram, it is the liquid substance between the nucleus and the cell membrane, in which the organelles are located.

Let us take a closer look at all of these structures.

**I) The CELL MEMBRANE and the “Fluid Mosaic” Model**

- The cell membrane functions in transport of materials in and out of cell, recognition, communication, and homeostasis.
- The Fluid Mosaic Model: Cells are surrounded by a thin membrane of lipid and protein, about 100 angstroms (100 x 10^-10 m) thick.
- Scientists today agree upon The Fluid Mosaic Model of membrane structure.
- The cell membrane is a remarkable structure that has properties of a solid and a liquid. It forms a "fluid sea" in which proteins and other molecules like other lipids or carbohydrates are suspended (like icebergs) or anchored at various points on its surface.
- The “sea” or “fluid” part is composed of side by side phospholipids arranged in a bilayer (called a lipid bilayer).
- The solid part (the “mosaic”) is the variety of proteins etc. embedded in the bilayer.
- Each phospholipid has a hydrophobic tail and a hydrophilic head.
- The membrane has consistency of light machine oil.
- The membrane is SELECTIVELY PERMEABLE (will let some substances in but not others of the same size).
This is a representation of the Fluid Mosaic Model of a cell. Notice the internal structure of the lipid bilayer with the hydrophobic tails oriented internally while the hydrophilic heads are oriented externally.

Other components of the Cell membrane: (see image above)

2. Integral membrane proteins
   a. float in or completely across lipid bilayer
   b. act as selective channels for transport
   c. act as receptor sites for messengers (hormones)

3. Peripheral membrane proteins
   a. lie on inner/outer surface of lipid bilayer
   b. many have enzymatic role
   c. structural function in tissue organization

II) THE NUCLEUS: the Cell’s CPU

- The nucleus is a large, centrally located organelle surrounded by nuclear envelope. The nuclear envelope is a double membrane (2 phospholipid bilayers thick) that has pores in it for molecules to enter and exit. The envelope is very porous and is a continuation of the membranes of the endoplasmic reticulum (discussed later).
- The pores, called nuclear pores, allow selected molecules into and out of the nucleus. It is also believed that these pores are the routes by which genetic messages (RNA) pass into the cytoplasm.
- The nucleus is the control center or "brain" of cell. It contains the DNA and is site of the manufacture of RNA. The DNA is contained by a number of chromosomes, which consist of
long strands of DNA tightly wound into coils with proteins called histones. The combination of DNA and histone proteins is known as **CHROMATIN**.

- Chromosomes function in packaging of DNA during nuclear division and control of gene expression. The nucleus, therefore, determines the metabolism, growth, differentiation, structure, and reproduction of cell.
- The nucleus contains one or more **DARK-STAINING** discrete structures, known as **NUCLEOLI**, which are sites of **RIBOSOMAL RIBONUCLEIC ACID (rRNA) SYNTHESIS**.

### III) ORGANELLES:

The following is a discussion of typical human cellular organelles and their functions.

#### A) ENDOPLASMIC RETICULUM (ER)

- The ER is a system of **MEMBRANOUS TUBULAR CANALS** that begins just outside the nucleus and branches throughout the cytoplasm.
- If ribosomes are attached to the ER, it is called **ROUGH Endoplasmic Reticulum**. The function of rough ER is protein synthesis.
- If no ribosomes are attached to the ER, it is called **SMOOTH Endoplasmic Reticulum**. The function of smooth ER is synthesis of lipids (Lipids are required for the growth of the cell membrane and for the membranes of the organelles within the cell and are often used to make hormones) and also to detoxify drugs and chemicals in the cell (takes place in peroxisome vesicles which are often attached to smooth ER).
- The endoplasmic reticulum membranes provide an increase in surface area where chemical reactions can occur.
- The channels of the reticulum provide both storage spaces for products synthesized by the cell and transportation routes through which material can travel through other parts of the cell. The endoplasmic reticulum is also the cell's membrane factory. Phospholipids and cholesterol, the main components of membranes throughout the cell, are synthesized in the smooth ER.
• Most of the proteins leaving the endoplasmic reticulum are still not mature. They must undergo further processing in another organelle, the Golgi apparatus, before they are ready to perform their functions within or outside the cell.

B) RIBOSOMES

• Ribosomes are the sites of protein synthesis. They are not membrane-bound and thus occur in both prokaryotes and eukaryotes.
• Eukaryotic ribosomes are slightly larger than prokaryotic ones. Structurally, the ribosome consists of a small and larger subunit.
• Biochemically, the ribosome consists of ribosomal RNA (rRNA) and some 50 structural proteins.
• Often ribosomes cluster on the endoplasmic reticulum, in which case they resemble a series of factories adjoining a railroad line.
• Ribosomes may be attached to the ER or floating free in the cytoplasm.
• They are by far the most numerous cellular organelle.

C) GOLGI COMPLEX
- Golgi Apparatus or Golgi Complexes, are flattened stacks of membrane-bound sacs.
- Golgi function as a packaging plant, modifying vesicles produced by the rough endoplasmic reticulum. New membrane material is assembled in various cisternae (layers) of the Golgi

**Structure**

1. cisternae - lined up in stacks next to nucleus
2. cis, medial, and trans parts. (Cis face receives material from the ER. The trans face forms transport vesicles that send material to the cell membrane for secretion)

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**D) MITOCHONDRIA**

Mitochondria are rod shaped or cylindrical organelles surrounded by an envelope of two membranes. The outer membrane is a smooth membrane and the inner membrane folded to form cristae. The cristae provide large surface area for biochemical activities. It enclose a matrix (mixture of protein, lipid and nucleic acid) with few ribosomes, a circular DNA molecule and phosphate granules.

**FUNCTIONS OF MITOCHONDRIA**

1. In aerobic respiration the cristae are the site of oxidative phosphorylation and electron transport.
2. The matrix which contains large number of hormones and enzymes in liquid form is the site of Krebs’s cycle.

Mitochondria are found in greater numbers in cells that readily require a higher amount
of ATP energy such as muscle and liver cells. This only makes sense as primary purpose is the oxidative respiration of glucose molecules to produce ATP for cellular energy.

E) LYSOSOMES

A simple spherical sac bounded by a single membrane and contains a mixture of digestive enzymes such as protease, nuclease and lipase which break down proteins, nucleic acids and lipids respectively.

The enzymes contained within lysosomes are synthesized on rough E.R and transported to the Golgi apparatus. Golgi vesicles containing the processed enzymes later bud off to form the lysosomes.

FUNCTIONS OF LYOSOME

- Lysosomes contain digestive enzymes which are used in digestion of reductant structure or damaged macromolecule from, within or outside the cell by autolysis.

- Lysosome destroys foreign particles such as bacteria by phagocytosis.

- It secretes the digestive enzymes.

- Lysosomes play part in autophagy, autolysis, endocytosis and exocytosis.
  - Autolysis is the self-digestion of a cell by releasing the contents of lysosome within the cell. For this reason, lysosomes sometimes called ‘suicide bags’ or ‘self-breaking down’.
  - Autophagy is the process by which unwanted structures within the cell are engulfed and digested within lysosome.
  - Endocytosis occurs by an in-folding or extension of the cell surface membrane to form vesicles or vacuoles. It is of two types, these are:
    - Phagocytosis – ‘cell eating’. Material taken up is in solid form.
    - Pinocytosis – ‘cell drinking’. Material taken up is in liquid form.
  - Exocytosis is the process in which waste materials may be removed from cells. It is the reverse of endocytosis.
F)

CENTRIOLES

Centrioles are small hollow cylinders that occur in pair in most animal cells.

In centrosomes (poorly defined structures which initiates the development of microtubules), the two centrioles lie right angle to each other. Each contains a 9+0 pattern of microtubule triplets, i.e: a ring having nine sets of triplets with none in the middle.

Before an animal cell divides, the centrioles replicate, then each pair becomes part of a separate centrosome. During cell division the centrosomes move apart so that each new cell has its own centrosome. Plant cells have the equivalent of a centrosome but it does not contain centrioles.
The function of the centriole is to be a microtubule organizing center in order to control separation of chromatids or chromosomes by a sliding motion. This is a mitotic process and therefore these organelles are discussed primarily in conjunction with that process.

**G) CYTOSKELETON**

The cytoskeleton is a network of interconnected filaments and tubules that extends from the nucleus to the plasma membrane in eukaryotic cells.

The cytoskeleton contains three types of elements, these are: Actin filaments, intermediate filaments and microtubules.
ACTIN FILAMENTS

Actin filaments or microfilaments are long extremely thin fibres that occur in bundles meshlike network. It contains two chains of globular actin monomers twisted about one another in a helical manner. It plays a structural role and involved in the movement of the cell and its organelles.

INTERMEDIATE FILAMENTS

They are rope like assembly of fibrous polypeptides but specific types varies according to the tissue. They are intermediate in size between the actin filaments and microtubules.

Intermediate filaments support the nuclear envelope and plasma membrane and take part in the formation of cell to cell junction.

In the skin, the intermediate filament is made up of protein keratin which gives mechanical strength to the skin cells.

MICROTUBULES

Microtubules are straight un-branched hollow cylinders which are usually short in length. They occur in most plant and animal cells.

Microtubules are involved in the movement of cytoplasmic components within the cell. They also occur in centrioles, in the spindle, in cilia and flagella and in the basal bodies.

Microtubules are made up of proteins. They help to maintain the shape of the cell and act as routes along which organelles can move.

H) CILIA AND FLAGELLA

Flagella and cilia are organelles that project from the surface of cells but are connected to a basal body just below the plasma membrane. Flagella occur singly or in small number where as cilia occur in large number on large cells and are typically shorter that flagella. Simultaneously, flagella and cilia are almost identical and both are able to move.

Flagella and cilia are enclosed to plasma membrane and internally they consist of microtubules arranged in an outer ring of nine pairs surrounding one central pair.

FUNCTIONS OF CILIA AND FLAGELLA

- They contain enzymes that produce energy to move a cell. E.g.: sperm or a unicellular organism such as Chlamydomonas.
- They propel fluids across cells, e.g.: the ciliated cells that move mucus along the bronchial lining.
- They are used to sense the environment, e.g: sensory hair cells.
These two images show ciliated cells in the human body. The first gives you a labeled diagram of what is termed “Ciliated Epithelia” while the second image shows an electron micrograph of some ciliated cells from the human trachea.

The only flagellated cells in the human are the male gametes, sperm cells. Here in this micrograph the “head” and “tail” regions are clearly visible with the tail being flagella.
I) CYTOPLASM

All of the preceding organelles are found within the fluid of the cell – the cytoplasm; an aqueous substance containing a variety of cell organelles and other structures such as insoluble wastes and storage products.

The soluble part of the cytoplasm forms the ‘background material’ or ‘ground substances’ between the cell organelles.

It contains about 90% water and forms a solution which contains all the fundamental biochemicals of life. Some of these are ions and small molecules in true solution; others are large molecules such as proteins which form colloidal solutions.
Reading Assignment #3-1: Disease at the Organelle Level

German physiologist Rudolph Virchow first hypothesized cellular pathology--disease at the cellular level--in the 1850s. Today, new treatments for many disorders are a direct result of understanding a disease process at the cellular level. Here, we take a look at how three abnormalities--in cell membranes, in peroxisomes, and in lysosomes--cause whole-body symptoms.

**Cystic Fibrosis and the Cell Membrane**

Cystic fibrosis (CF) was first described in medical journals in 1938 as a defect in the channels leading from certain glands, resulting in a variety of problems--chokingly thick mucus in the lungs and frequent infection there; a clogged pancreas, preventing digestive juices from reaching the intestines; and salty sweat. A child with CF is often small and sickly, and until the recent availability of biochemical tests, was often initially diagnosed simply as having failure to thrive.

Earlier descriptions of CF mentioned the characteristic of salty sweat. A seventeenth century English saying states, "A child that is salty to taste will die shortly after birth." But this symptom would be a telling clue in explaining how the genetic abnormality causes symptoms felt at a whole-body level.

Researchers identified the cellular defect behind cystic fibrosis in 1989 as abnormal channels in lung and pancreas cells that trap salt within cells. The salty cellular interiors draw moisture in from surrounding tissue, drying out the mucus until it is so sticky that it clogs organs. Several new treatments, including a healthy gene introduced into the lungs in a nasal spray, target the illness at the cellular source.

**Adrenoleukodystrophy (ALD) and Peroxisomes**

For young Lorenzo Odone, the first sign of adrenoleukodystrophy was disruptive behavior in school. When he became lethargic, weak, and dizzy, his teachers and parents realized that his problem was not just temper tantrums. His skin darkened, blood sugar levels plummeted, heart rhythm altered, and the levels of electrolytes in his body fluids became imbalanced. He lost control over his limbs as his nervous system continued to deteriorate. Lorenzo's parents took him to many doctors. Finally one of them tested for an enzyme normally manufactured in peroxisomes.

Lorenzo's peroxisomes lacked the second most abundant protein in the outer membrane of this organelle. Normally, the missing protein transports an enzyme into the peroxisome. The enzyme controls breakdown of a type of very long chain fatty acid. Without the enzyme, the fatty acid builds up in cells in the brain and spinal cord, eventually stripping these cells of their fatty sheaths, made of a substance called myelin, that are vital for nerve transmission. Death comes in a few years.

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For Lorenzo and many other sufferers of ALD, eating a type of triglyceride from rapeseed oil slows buildup of the very long chain fatty acids for a few years, stalling symptoms. But the treatment eventually impairs blood clotting and other vital functions, and fails to halt the progression of the illness.

**Tay-Sachs Disease and Lysosomes**

Michael was a pleasant, happy infant who seemed to be developing normally until about six months of age. Able to roll over and sit for a few seconds, suddenly he seemed to lose those abilities. Soon, he no longer turned and smiled at his mother's voice, as he had before, and he did not seem as interested in his mobile as he once was. Concerned about Michael's reversals in development, his anxious parents took him to the doctor. It took exams by several specialists to diagnose Michael's Tay-Sachs disease, because, thanks to screening programs in the population groups known to have this inherited illness, fewer than ten new cases appear each year. Michael's parents were not among those ethnic groups and previously had no idea that they both were carriers of the gene that causes this very rare illness.

A neurologist clinched her suspicion of Tay-Sachs by looking into Michael's eyes, where she saw the telltale cherry red spot indicating the illness. A look at his cells provided further clues—the lysosomes, tiny enzyme-filled sacs, were swollen to huge proportions. Michael's lysosomes lacked one of the forty types of lysosomal enzymes, resulting in a lysosomal storage disease that built up fatty material on his nerve cells. His nervous system would continue to fail, and he would be paralyzed and unable to see or hear by the time he died, before the age of four.

The cellular and molecular signs of Tay-Sachs disease—the swollen lysosomes and missing enzyme—had been present long before Michael began to lag developmentally. The next time his parents expected a child, they had her tested before birth for the enzyme deficiency. They learned, happily, that she would be a carrier like themselves, but not ill.

**Questions Based on the Reading:**

1. Why do CF sufferers usually die before adulthood?
2. What is it that the peroxisome does that is so vital for nervous system health?
3. Lysosomal activity is crucial to cellular function – in Tay-Sachs, what is it the lysosome cannot do?
Reading Assignment #3-2: World Health Organization – Cancer Factsheet 2015

Cancer

Key facts

- Cancers figure among the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases and 8.2 million cancer related deaths in 2012 (1).
- The number of new cases is expected to rise by about 70% over the next 2 decades.
- Among men, the 5 most common sites of cancer diagnosed in 2012 were lung, prostate, colorectum, stomach, and liver cancer.
- Among women the 5 most common sites diagnosed were breast, colorectum, lung, cervix, and stomach cancer.
- Around one third of cancer deaths are due to the 5 leading behavioural and dietary risks: high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use, alcohol use.
- Tobacco use is the most important risk factor for cancer causing around 20% of global cancer deaths and around 70% of global lung cancer deaths.
- Cancer causing viral infections such as HBV/HCV and HPV are responsible for up to 20% of cancer deaths in low- and middle-income countries (2).
- More than 60% of world’s total new annual cases occur in Africa, Asia and Central and South America. These regions account for 70% of the world’s cancer deaths (1).
- It is expected that annual cancer cases will rise from 14 million in 2012 to 22 within the next 2 decades (1).

Cancer is a generic term for a large group of diseases that can affect any part of the body. Other terms used are malignant tumours and neoplasms. One defining feature of cancer is the rapid creation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs, the latter process is referred to as metastasizing. Metastases are the major cause of death from cancer.

The problem

Cancer is a leading cause of death worldwide, accounting for 8.2 million deaths in 2012 (1). The most common causes of cancer death are cancers of:

- lung (1.59 million deaths)
- liver (745 000 deaths)
- stomach (723 000 deaths)
- colorectal (694 000 deaths)
- breast (521 000 deaths)
- oesophageal cancer (400 000 deaths) (1).

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What causes cancer?

Cancer arises from one single cell. The transformation from a normal cell into a tumour cell is a multistage process, typically a progression from a pre-cancerous lesion to malignant tumours. These changes are the result of the interaction between a person's genetic factors and 3 categories of external agents, including:

- physical carcinogens, such as ultraviolet and ionizing radiation;
- chemical carcinogens, such as asbestos, components of tobacco smoke, aflatoxin (a food contaminant) and arsenic (a drinking water contaminant); and
- biological carcinogens, such as infections from certain viruses, bacteria or parasites.

WHO, through its cancer research agency, International Agency for Research on Cancer (IARC), maintains a classification of cancer causing agents.

Ageing is another fundamental factor for the development of cancer. The incidence of cancer rises dramatically with age, most likely due to a build up of risks for specific cancers that increase with age. The overall risk accumulation is combined with the tendency for cellular repair mechanisms to be less effective as a person grows older.

Risk factors for cancers

Tobacco use, alcohol use, unhealthy diet and physical inactivity are the main cancer risk factors worldwide. Some chronic infections are risk factors for cancer and have major relevance in low- and middle-income countries. Hepatitis B (HBV), hepatitis C virus (HCV) and some types of Human Papilloma Virus (HPV) increase the risk for liver and cervical cancer respectively. Infection with HIV substantially increases the risk of cancer such as cervical cancer.

How can the burden of cancer be reduced?

Knowledge about the causes of cancer, and interventions to prevent and manage the disease is extensive. Cancer can be reduced and controlled by implementing evidence-based strategies for cancer prevention, early detection of cancer and management of patients with cancer. Many cancers have a high chance of cure if detected early and treated adequately.

Modifying and avoiding risk factors

More than 30% of cancer deaths could be prevented by modifying or avoiding key risk factors, including:

- tobacco use
- being overweight or obese
- unhealthy diet with low fruit and vegetable intake
- lack of physical activity
- alcohol use
• sexually transmitted HPV-infection
• infection by HBV
• ionizing and non-ionizing radiation
• urban air pollution
• indoor smoke from household use of solid fuels.

Tobacco use is the single most important risk factor for cancer causing about 20% of global cancer deaths and around 70% of global lung cancer deaths. In many low-income countries, up to 20% of cancer deaths are due to infection by HBV and HPV.

**Prevention strategies**

• Increase avoidance of the risk factors listed above.
• Vaccinate against human papilloma virus (HPV) and hepatitis B virus (HBV).
• Control occupational hazards.
• Reduce exposure to non-ionizing radiation by sunlight. (UV)
• Reduce exposure to ionizing radiation (occupational or medical diagnostic imaging).

**Early detection**

Cancer mortality can be reduced if cases are detected and treated early. There are 2 components of early detection efforts:

**Early diagnosis**

The awareness of early signs and symptoms (for cancer types such as skin, cervical, breast, colorectal and oral) in order to get them diagnosed and treated at early stage. Early diagnosis is particularly relevant when there is no effective screening methods or – as in many low-resource settings– no screening and treatment interventions implemented. In absence of any early detection or screening and treatment intervention, patients are diagnosed at very late stages when curative treatment is no longer an option.

**Screening**

Screening aims to identify individuals with abnormalities suggestive of a specific cancer or pre-cancer and refer them promptly for treatment or when feasible for diagnosis and treatment. Screening programmes are especially effective for frequent cancer types for which cost-effective, affordable, acceptable and accessible screening tests are available to the majority of the population at risk.

Examples of screening methods are:
• visual inspection with acetic acid (VIA) for cervical cancer in low-resource settings;
• HPV testing for cervical cancer;
• PAP cytology test for cervical cancer in middle- and high-income settings;
• mammography screening for breast cancer in high-income settings.
Treatment

A correct cancer diagnosis is essential for adequate and effective treatment because every cancer type requires a specific treatment regimen which encompasses one or more modalities such as surgery, and/or radiotherapy, and/or chemotherapy. The primary goal is to cure cancer or to considerably prolong life. Improving the patient's quality of life is also an important goal. It can be achieved by supportive or palliative care and psychological support.

Potential for cure among early detectable cancers

Some of the most common cancer types, such as breast cancer, cervical cancer, oral cancer and colorectal cancer have high cure rates when detected early and treated according to best practices.

Potential for cure of some other cancers

Some cancer types, even though disseminated, such as leukaemias and lymphomas in children, and testicular seminoma, have high cure rates if appropriate treatment is provided.

Palliative care

Palliative care is treatment to relieve, rather than cure, symptoms caused by cancer. Palliative care can help people live more comfortably; it is an urgent humanitarian need for people worldwide with cancer and other chronic fatal diseases. It is particularly needed in places with a high proportion of patients in advanced stages where there is little chance of cure. Relief from physical, psychosocial and spiritual problems can be achieved in over 90% of advanced cancer patients through palliative care.

Palliative care strategies

Effective public health strategies, comprising of community- and home-based care are essential to provide pain relief and palliative care for patients and their families in low-resource settings. Improved access to oral morphine is mandatory for the treatment of moderate to severe cancer pain, suffered by over 80% of cancer patients in terminal phase.

WHO response

In 2013, WHO launched the Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020 that aims to reduce by 25% premature mortality from cancer, cardiovascular diseases, diabetes and chronic respiratory diseases by 2025. Some of the voluntary targets are most relevant for cancer prevention, including target 5 aimed at reducing the prevalence of tobacco use by 30%.

* Global action plan for the prevention and control of NCDs 2013-2020
WHO and the International Agency for Research on Cancer (IARC), collaborate with other United Nations organizations within the UN Noncommunicable Diseases Interagency taskforce (2014) and partners to:

- increase political commitment for cancer prevention and control;
- coordinate and conduct research on the causes of human cancer and the mechanisms of carcinogenesis;
- monitor the cancer burden (as part of the work of the Global Initiative on Cancer Registries GICR);
- develop scientific strategies for cancer prevention and control;
- generate new knowledge, and disseminate existing knowledge to facilitate the delivery of evidence-based approaches to cancer control;
- develop standards and tools to guide the planning and implementation of interventions for prevention, early detection, treatment and care;
- facilitate broad networks of cancer control partners and experts at global, regional and national levels;
- strengthen health systems at national and local levels to deliver cure and care for cancer patients; and
- provide technical assistance for rapid, effective transfer of best practice interventions to developing countries.

References
1. World Cancer Report 2014
Quiz: Cytology and Biochemistry

Name: _________________________________

1-7: Match the statement to the term — one answer per blank; repeats possible:

___ cellulose is an example                        a. monosaccharide
___ glucose is an example                          b. polysaccharide
___ has hydrophobic and hydrophilic regions       c. plant triglyceride
___ long sequence of amino acids                  d. animal triglyceride
___ major component of cell membranes             e. phospholipid
___ saturated                                      f. protein
___ stores genetic information                    g. DNA

8. The molecule sketched to the right is what type of molecule? (How were you able to tell?)
   a. carbohydrate
   b. lipid
   c. protein
   d. nucleic acid

9. Proteins that fold back onto themselves to form a globular arrangement have what type of structure?
   a. primary structure
   b. secondary structure
   c. tertiary structure

10. The tendency of water to resist changes in temperature is the result of water’s
    a. high density
    b. high specific heat
    c. being a good solvent
    d. high heat of vaporization

If the statement is true of prokaryote cells write “pro”, if the statement refers to eukaryote cells write “eu”, if the statement is true for both types of cells write “both”:

11. ____small, typically 1-5 um long                  12. ____has a defined nucleus with a double membrane
13. ____has mitochondria                              14. ____has a plasma membrane

15-21. Match the cell organelle to the statement - one answer per blank; no repeats:

   ___ ATP formation                                  a. chloroplast
   ___ final modification of protein, sorts and packages secretions b. cytoskeleton
   ___ initial modification and transport of newly made proteins   c. endoplasmic reticulum
   ___ network of tiny protein tubes and filaments               d. golgi body
   ___ photosynthesis                                            e. lysosome
   ___ reduced or used during endocytosis                      f. mitochondria
   ___ site of protein synthesis                             g. plasma membrane
   ___ network of tiny protein tubes and filaments               h. ribosome

22. Short Answer: If a cell has large amounts of rough endoplasmic reticulum and Golgi bodies, speculate on the kinds of cellular activities that might be going on.
Lab: pH, CELL STRUCTURE, DIFFUSION & OSMOSIS

**pH Effects in the Body**

**Acids** increase the concentration of $H^+$. They typically release $> 1$ $H^+$. Some examples are:

- hydrochloric acid $\text{HCl}$ -----> $H^+$ (hydrogen ion) + $\text{Cl}^-$ (chloride ion)
- carbonic acid $\text{H}_2\text{CO}_3$ -----> $H^+ + \text{HCO}_3^-$ (bicarbonate ion)
- acetic acid $\text{CH}_3\text{CHO}_2$ -----> $H^+ + \text{CH}_3\text{CO}_2^-$

**Bases (alkaline substances)** decrease the concentration of $H^+$ by binding to free $H^+$ they remove $H^+$ from solutions.

- (hydroxyl ion)$\text{OH}^- + H^+ -----> H$_2$O
- sodium hydroxide $\text{NaOH}$ readily ionizes in water $\text{NaOH}$ -----> $\text{Na}^+$ (sodium ion) + $\text{OH}^-$ (hydroxyl ion)

**Water** is both an acid and a base, if it ionizes. However, water ionizes rarely.

$\text{H}_2\text{O}$ -----> $\text{OH}^- + H^+$

The **pH scale** is a measure of the number of $H^+$ present in a solution. The symbol for $H^+$ concentration is [H$^+$]. pH is proportional to the inverse of the concentration of $H^+ \sim (1 / [H^+])$.

Which of the substances described above are organic molecules? Recall that organic molecules must have Carbon (C) & Hydrogen (H) atoms.

- Normal plasma has a pH = 7.35 - 7.45 so it is slightly alkaline.
- Neutral pH = 7 of pure water releases an equal number of $H^+$ & $\text{OH}^-$ ions
- Acidic pH < 7 means more $H^+$ are present or fewer $\text{OH}^-$ ions are present
- Basic/Alkaline pH > 7 means fewer $H^+$ are released or more $\text{OH}^-$ are present

The pH scale is log transformed, $\text{pH} = - \log[H^+]$. This means a 1 unit difference in value equals a 10X difference in the amount of hydrogen ions. Thus a pH of 3 is 10X more acidic than a pH of 4. A pH of 12 is 100X more alkaline than a pH = 10 because there is a 2 unit difference in the pH values, so it is a $10 \times 10 = 100$ difference in acidity.

A variety of homeostasis imbalance problems can lead to pH imbalances in the body's extracellular fluids (e.g. blood plasma pH). We will discuss more during the quarter, but digestive tract imbalances are relatively common & easily explained as follows:

**Diarrhea or chronic use of laxatives** causes the loss of alkaline fluids from the intestines. If this is severe or chronic, the blood pH becomes more acidic. An acidic shift (below the normal range) in plasma pH is called acidosis. **Acidosis** can inhibit activity of the brain & muscle tissues, which can lead to muscle weakness, fatigue, and finally a coma & death.

**Vomiting** caused by an illness or bulimia leads to loss of extremely acidic stomach fluids. Loss of acidic stomach fluid shifts your blood pH to a more alkaline range. Extreme alkaline shifts of blood plasma are referred to as alkalosis. This has the opposite effect on the brain & muscle tissue to acidosis. Severe alkalosis may trigger excessive muscle tension, a faster heart rate & ultimately convulsions & death.
**Enzymes & other cellular proteins** may begin to denature (unwind or lose normal shape) as a result of extreme shifts in extracellular pH (either acidosis or alkalosis). These changes result in the malfunction of many metabolic processes.

**Introduction to the Cell Membrane**

Cells are the basic building blocks of living systems. All living things are made up of cells and all cells come from preexisting cells. A watery environment that is called extracellular fluid surrounds cells. Examples of extracellular fluids include: **plasma** (the fluid portion of blood) and **interstitial fluid** (fluid that is in the small spaces or interstices that surround most cells).

Most animal cells are very similar in design. The outer surface of a cell is called the cell or plasma membrane. The cell or plasma membrane is made up primarily of phospholipids so that it is selectively permeable or semi-permeable. Most lipids or **non-polar** (uncharged) substances move easily through a cell membrane. An exception is water. Water is an extremely small molecule, in very high concentrations in all body fluids. There are almost always small water channels in the membrane that allow water to move freely into or out of a cell. Most **polar** (charged, or ionic) substances move more slowly than water if they move at all across a cell membrane, in part because they are not as numerous as water molecules. Some polar molecules require active transport (which includes the expenditure of cellular ATP & the presence of special carrier proteins) to enter or leave a cell. Substances that move via active transport move more slowly than water across a cell membrane, because carriers have “rate limits” or maximum speeds at which they function. Some polar molecules may not move at all if the necessary carriers are missing from that cell membrane.

Some cells increase the amount of membrane by forming a dense series of finger-like projections called **microvilli** on one side of a cell. Microvilli increase the rate of transport across the cell membrane by increasing the surface area of the cell.

The internal environment of a cell is called **cytoplasm**. Cytoplasm contains **intracellular fluid** & organelles such as the nucleus and mitochondria. Intracellular fluid is highly viscous (sticky).

**Experiments: pH Testing**

One or two groups of students will measure the pH of some common substances. First test each substance with a broad scale pH paper.

- These strips have a series of color bars that can be matched to standards on the box.
- The paper will indicate integer values from 0-14.

Second, if materials are available, test each substance with an appropriate more narrowly defined pH paper scaled to 1 decimal place.

- For example, if a substance had a pH = 6 on the broad scale paper, use the narrow range paper for values between 5 & 7.
- Record this more accurate value. For example the solution may have a pH = 6.4.

Was this substance acidic, basic or “relatively” close to neutral (>6.5 but < 7.5)? Check the results with your classmates’ data and with your instructor. Be sure your values are in the correct range.
Your group will answer the review questions on pH for the entire class.

<table>
<thead>
<tr>
<th>Solution</th>
<th>Broad Range pH</th>
<th>Acidic, Basic or Neutral</th>
</tr>
</thead>
<tbody>
<tr>
<td>tap water</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pepsi or Coca Cola</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinegar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>coffee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bleach (1:10 dilution)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>apple juice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>baking soda</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tomato juice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milk of Magnesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lemon juice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>egg white</td>
<td></td>
<td></td>
</tr>
<tr>
<td>liquid soap</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Diffusion Experiments**

All molecules are in constant motion. As molecules bump into each other, directions are changed, causing random dispersal of the molecules. The random movement of molecules results in diffusion. Diffusion occurs when molecules of substance X move away from an area or source of higher concentration towards an area of lower concentration of substance X. Molecules of substance X move away from the area of higher concentration because the molecules encounter fewer obstructing molecules in the area of lower concentration. The rate of diffusion is variable and depends on temperature, molecular weight, distance to travel, solvent density, and other factors.

In your experiment, we are using an agar or gelatin gel. Agar is a gel extracted from a type of red seaweed found along the Pacific coast. The methylene blue dye has a Molecular Wt. = 320, and thus is a very heavy molecule. Your experiments & information from the web links should help you understand the effect of molecular weight, concentration and temperature on diffusion.

**Directions for making the agar plates:**

The formula for the agar plates is 1.5g of agar in 100 ml of water, so this is a 1.5% agar solution.

1. Measure out 1.5g of agar using a balance of your choice.
2. While one person is measuring out the agar, another person should begin to heat 100 ml of water on a hot plate.
3. Slowly add the agar to the hot water and continue to stir the mixture to break up any large, clumping particles.
4. When the mixture is completely dissolved, slowly pour into a Petri dish. Be careful to not pour too quickly as this will cause air bubbles to form.
5. When each plate is approximately ¾ full, place them aside on a paper towel with your name on them. It usually takes about 30-40 min for the agar to set up.

**WARNINGS**

The methylene blue dye should not come in contact with your skin or clothes!

Wear latex or vinyl gloves while handling the dye solutions.

- Place paper towels on the table beneath your agar plates while they are filled.
- Obtain 2 Petri dishes prepared with agar &/or gelatin.
- Use a straw to remove 2 disks of agar or gelatin from each plate.
- Keep your holes away from the edge of the plate & at least 2 cm apart from each other.
- The holes should be cleanly cut, no nicks or cuts. If not, cut a new hole.
- Check afterwards to be sure the agar remains firmly stuck to the bottom of the dish.
Procedures
1. Fill 1 well on each of your plates with the 0.01M methylene blue dye.
2. Fill the other well on each plate with the 0.001M methylene blue dye.
3. Use the micropipettes to fill each well without spilling dye on the surface of the agar.
4. Be sure ALL wells are filled to the SAME height (nearly to the top of the agar).
5. Use a grease pencil to mark the Petri dish so that you will know which solution is used in each well.

- When both agar plates are ready, place 1 plate on a heating pad & 1 plate on ice.
- Leave the plates in position for 20-30 min., but measure all plates after the same time interval.
- Measure the maximum spread of dye from each well by measuring the outermost diameter of each dyed circle in mm, by placing a sheet of white paper under the Petri dish & then placing the ruler underneath the dish.
- After you have measured the dye wells, save your agar plates so the rest of the class can see your samples.
- Your group will answer the review questions on diffusion for the entire class.

Place your information in the following table:

<table>
<thead>
<tr>
<th>DYE CONCENTRATION</th>
<th>Max. Diameter (mm) Cold Agar</th>
<th>Max. Diameter (mm) Cold Agar</th>
<th>Max. Diameter (mm) Hot Agar</th>
<th>Max. Diameter (mm) Hot Agar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylene Blue Dye Conc.</td>
<td>0.010M</td>
<td>0.001M</td>
<td>0.010M</td>
<td>0.001M</td>
</tr>
<tr>
<td>Trial 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Osmosis Experiments

Water is a charged or polar molecule (H\(^+\) - O\(^-\) - H\(^+\)) that is always moving across cell membranes. Scientists theorize that this is possible because it is such a small molecule or because there are special gap or pores that allow water movement through the cell membrane. The predominant direction of water flow is determined by the concentration of the solutes (non-water molecules) inside and outside of the cell. Water molecules will show a new movement from an area of higher water concentration (& lower in solutes) to an area of lower water concentration (& higher in solutes). In other words the net water flow tends to dilute an area of higher solute concentration. When water moves by diffusion through a semi-permeable membrane it is called osmosis. This is a type of passive transport because no cellular energy (ATP) is involved in the movement of water.

For convenience we will use tonicity & osmolarity as interchangeable terms. In fact, there are exceptions when these terms do not have identical meaning. An extracellular solution is isotonic ["iso" = same, tonicity = tone or tension] or iso-osmotic to a cell if the cell has no net gain or loss of water. This is a dynamic equilibrium. The cell & the extracellular solution have the same concentration of water & the same concentration of solutes. Our extracellular fluids need to stay
isotonic in order for cells to survive. Iso-osmotic solutions can be used as intravenous solutions or during kidney dialysis because they maintain the osmotic balance of the body’s extracellular fluids.

If cells are placed in a solution that contains a higher concentration of solutes than the cell, cells suffer a net loss of water and appear crenated ["cren" = notched] or wrinkled. These cells are in a hypertonic or hyperosmotic solution. Cells in a highly hypertonic solution may die from this dehydration.

A solution that has a lower solute concentration than is present in cells is said to be a hypotonic or hypo-osmotic solution. In this case, excess water flows into the cells and the cells swell. Neurons begin to malfunction when overhydrated. Blood cells & other cells may eventually rupture or burst open in a process called lysis.

Although we simplify osmolarity problems by using the % of a solute to represent its concentration, two solutions with the same % of solutes may NOT have the same number of solutes. Accurate osmolarity calculations must use a more complex calculation as follows:

All molar solutions contain the same number of molecules:
- 1 mole unit of any molecule has $6.02 \times 10^{23}$ molecules in 1 liter of solution.
- 1 mole of a substance equals its molecular wt.

Osmolarity is calculated as $(n) \times$ moles, where $n$ = the number of dissociated particles that are present when a substance is placed in water. 1 mole of glucose has an osmolarity = 1 Osmole because glucose doesn't ionize in water. 1 mole of sodium chloride has an osmolarity = 2 Osmoles because it ionizes freely into two ions: Na+ and Cl- when placed in water.

0.30 Osmoles of any solute is isotonic with a normal plant or animal cell.

Be able to calculate the grams needed of a molecule to make an isotonic solution if you are given the molecular weight of a molecule & the number of particles into which it ionizes, as shown below:

**Example #1**
- Sodium chloride (NaCl): molecular weight = 58.5 g (Add the mass numbers)
  - 1 mole of sodium chloride (NaCl) = 58.5 g NaCl / 1000 ml water
  - Sodium chloride readily ionizes into Na+ and Cl- so its osmolarity is 1/2 X its molarity.
  - Isotonic NaCl = 0.30 osmoles of NaCl / 2 particles = 0.15 moles of NaCl
  - 0.15 moles of NaCl = 58.5g NaCl/1000 ml water (1 mole NaCl) * 0.15 = 8.8 g NaCl / 1000 ml
  - 8.8 g NaCl / 1000 ml water = 0.88 g NaCl/100 ml water = 0.88% NaCl solution
  - An isotonic NaCl solution has 0.88% NaCl

**Example #2**
- Glucose (C₆H₁₂O₆): molecular weight = 180 g
  - 1 mole of glucose = 180.0 g C₆H₁₂O₆ / 1000 ml water
  - Glucose rarely ionizes in water, so its osmolarity is 1 * its molarity.
  - Isotonic Glucose = 0.30 osmoles of glucose /1 particle = 0.30 moles of glucose
  - 0.30 moles of glucose = 180 g glucose/1000 ml water * 0.30 = 54 g glucose/1000 ml water
  - 54 g glucose/1000 ml water = 5.4 g glucose/ 100 ml water = 5.4 % glucose solution
  - An isotonic glucose solution has 5.40% glucose.
Experimental Procedure - Using Potato Sticks

You will be given 5 potato sticks that are 4-6 cm long with a 1 cm diameter. You will be provided with 5 vials each with a different salt or sugar solution.

1. Determine the initial mass (in g) of each potato stick. Your instructor will demonstrate how the balance is used.
2. Record this initial potato mass to 2 decimal places, for example: 3.15 g.
3. Immediately after each potato stick is massed, place it in one of the solution vials.

Predict which solutions SHOULD BE iso-osmotic, hyper-osmotic or hypo-osmotic to potato cells.

- Clue: We identified which solutions should be isotonic earlier in your notes.

Predict which solutions will cause the potato stick to gain or lose water & which solutions won't change.

THEN rank them by relative gain or loss:
0 = no change, +1 minimal gain, +2 moderate gain, +3 maximum gain
-1 minimal loss, -2 moderate loss, -3 maximum loss

- Predict (relatively) how much water potatoes will gain or lose in those solutions.

4. After 40 minutes mass each potato stick again & record the data.
5. Calculate the change in mass: final mass - initial mass = + or - change in mass.
6. Calculate the + or - %change as [change in mass (g) / initial mass (g)] X 100
Use the following tables to record your information.

### w/ NaCl

<table>
<thead>
<tr>
<th>Salt Conc.</th>
<th>INITIAL WT. of Potato</th>
<th>FINAL WT. of Potato</th>
<th>CHANGE IN WEIGHT (g) (show + or -)</th>
<th>CHANGE IN WEIGHT % (show + or -)</th>
<th>PREDICTED TONICITY RELATIVE TO LIVING CELL</th>
<th>RANK RELATIVE WATER LOSS OR GAIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>10% NaCl</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.5% NaCl</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.88% NaCl</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.50% NaCl</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>water</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### w/ Glucose

<table>
<thead>
<tr>
<th>Glucose Conc.</th>
<th>INITIAL WT. of Potato</th>
<th>FINAL WT. of Potato</th>
<th>CHANGE IN WEIGHT (g) (show + or -)</th>
<th>CHANGE IN WEIGHT % (show + or -)</th>
<th>PREDICTED TONICITY RELATIVE TO LIVING CELL</th>
<th>RANK RELATIVE WATER LOSS OR GAIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>30% Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10% Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.4% Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.5% Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>water</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**REVIEW QUESTIONS:** Answer the questions by typing in your response under the questions. Make sure you bold or highlight your answers.

**pH**

1. Explain the relative acidity of a pH = 5 vs. a pH = 7.

2. Give 2 reasons why the water sample you tested did NOT have a pH = 7.
   a.
   b.

3. Describe 1 event that may cause your extracellular fluid to become too acidic.

4. What physical symptoms do you suffer from when your body becomes too acidic (i.e. you suffer acidosis)?

5. Describe 1 event that may cause your extracellular fluid to become more alkaline.

6. What physical symptoms do you suffer from when your body becomes too alkaline (i.e. when you suffer alkalosis)?

7. How can you correct these pH imbalances? (We'll discuss the homeostatic regulation of pH later, so answer here what you might eat or drink to fix the problem).
   a. acidosis
   b. alkalosis

**Diffusion**

8. Describe 2 practical problems that can lead to measurement errors in the diffusion experiments.

9. Why should methylene blue travel farther in the agar if the dye concentration is higher?

10. Why should methylene blue travel farther under hot conditions?

11. Hypothesize what would happen if you used a lighter molecular weight dye.

**Osmosis**

12. Molecule X ionizes into 3 particles when it is placed in water, while substance Y does not ionize. If you are given solutions of molecule X & of molecule Y, each with a 0.2 molarity, what is the osmolarity of solution X & the osmolarity of Y? Show your work.

13. Which salt & glucose solutions should have been isotonic? Which hypertonic? Which hypotonic? Define these terms.

14. Potato slices in isotonic solutions should not show any weight change. Explain 2 practical measurement problems that could cause these potato slices to show a weight change.
15. Why do cells placed in hypertonic solutions lose water? How does the diffusion of water relate to solution tonicity?

16. Why do cells placed in hypotonic solutions gain water? How does the diffusion of water relate to solution tonicity?

17. Did the potato cells placed in more extremely hyper- or hypo-tonic solutions gain/lose even more water than less extreme solutions? Explain why they should or should not do this.

18. Explain how dehydration affects your body.

19. Explain how over-hydration affects your body.
Sweetness!

“Dear Lord!” exclaimed the nurse as she read off the patient’s lab report. Get the Doctor immediately she blurts out panickedly!

Your pager goes off. You dial the number. “This is Doctor (your name here) and I just got a page.” You listen to the nurse. “Oh really! I'll be right there!”

When you arrive at the nurses’ station she hands you the report. You immediately look over the numbers and rush towards the patient’s room. You burst in to find Mr. Sewell, calmly resting in his bed, watching the ballgame on ESPN. A quick battery of evaluations leads you to the conclusion that Mr. Sewell is not in any distress. So you look at the lab report again.

<table>
<thead>
<tr>
<th>Na</th>
<th>K</th>
<th>Cl</th>
<th>CO$_2$</th>
<th>O$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>212</td>
<td>9.8</td>
<td>90</td>
<td>35</td>
<td>97</td>
</tr>
<tr>
<td>mEq/L</td>
<td>mEq/L</td>
<td>mEq/L</td>
<td>mm Hg</td>
<td>mm Hg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Uric Acid</th>
<th>Creatine(CK)</th>
<th>Glucose</th>
<th>pH</th>
<th>Hematocrit</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.7</td>
<td>92</td>
<td>900</td>
<td>7.4</td>
<td>58%</td>
</tr>
<tr>
<td>mg/dL</td>
<td>units/L</td>
<td>mg/dL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This blood report was just taken this morning. As a matter of fact, you had drawn the blood when you checked up on him this morning on your way to another surgery. You were in a hurry and didn’t spend much time with Mr. Sewell, but he had seemed to be doing fine. He had wanted to know if he could get the IV out today. Said he was tired of his left arm being used for a pincushion. But otherwise he was in good spirits.

Mr. Sewell had a cholecystectomy just yesterday.

1) What is abnormal about the report?  
2) Can these readings be explained physiologically?  
3) What should you do next?

Use the values at [www.bloodbook.com/ranges.html](http://www.bloodbook.com/ranges.html) to analyze values.

**Directions:** Analyze the report, answer the questions and email your results to Mr. Sewell in the proper format.
Chapter 4: Histology

A complex organism, such as a human, is made of collections of cells working together in performing a specific function(s). These groups of cells are called Tissues. The study of tissues is called Histology.

There are four (4) basic types of tissue:

1. Epithelial:
   - covers body surfaces
   - lines hollow organs
   - lines body cavities and ducts
   - forms glands

2. Connective:
   - protection and support
   - binding together (like glue)
   - energy storage
   - immunity

3. Muscle:
   - movement and force

4. Nervous:
   - coordinates bodily activities

Let us begin to look at these tissues more in depth:

I) Epithelium:
Epithelium forms the coverings of surfaces of the body. As such, it serves many purposes, including protection, adsorption, excretion, secretion, filtration, and sensory reception. When considering the characteristics that make a tissue epithelium, it is important to think about the following:

- **Polarity**- Epithelium is arranged so there is one free surface (apical surface) and one attached surface (basal surface)
- **Cellular nature**- Cells in epithelium fit closely together side by side and sometimes atop each other to form sheets of cells. These sheets are held together by specialized junctions.
- **Supported by connective tissue**- Attachment to a layer of connective tissue at the basal surface forms a layer called the basement membrane, an adhesive layer formed by secretions from the epithelial cells and the connective tissue cells.
- **Avascular**- Epithelium typically lacks its own blood supply.
- **Regeneration**- Epithelium cells can regenerate if properly nourished.
Classification of epithelium is based on the shape of the cells and the arrangement of the cells within the tissue. Typically, the arrangement of the cells is stated first, then the shape, and is followed by “epithelium” to complete the naming (Ex. Simple Squamous Epithelium).

**Arrangements:**
- **Simple**- Cells are found in a single layer attached to the basement membrane.
- **Stratified**- Cells are found in 2 or more layers stacked atop each other.
- **Pseudostratified**- a single layer of cells that appears to be multiple layers due to variance in height and location of the nuclei in the cells.
- ** Transitional**- cells are rounded and can slide across one another to allow stretching.

**Shapes:**
- **Squamous**-(Latin, squama- scale)- flat, thin, scale-like cells
- **Cuboidal**- cells that have a basic cube shape. Typically the cell's height and width are about equal.
- **Columnar**- tall, rectangular or column shaped cells. Typically taller than they are wide.

**Classifications of Epithelia**

![Diagram of epithelia classification](image-url)
Using this criteria of classification, there are 6 basic classifications of epithelia based on shape....actually there are some others that we will learn later. These 6 basic types are as follows:

1. Simple squamous
2. Simple cuboidal
3. Simple columnar
4. Stratified squamous
5. Stratified cuboidal
6. Stratified columnar

Let us now take a look at each of these different types.
1) **Simple Squamous Epithelium**: a single sheet of flattened, scale-like cells.

1. "Squamous" means scale-like and refers to the fact that these cells are much wider than they are tall.
2. Simple squamous epithelium is found in areas such as:
   a. small glandular ducts
   b. the mesothelium lining the closed coelomic cavities (e.g.; pleural, pericardial, and peritoneal)
   c. the endothelium lining the blood vessels, heart, and lymph vessels
   d. respiratory bronchioles and alveoli
   e. Bowman's capsules and loops of Henle in the kidneys.
3. Functionally simple squamous epithelium is well suited for sites of fluid, metabolite, and gas exchange.

Simple Squamous Epithelium from the alveolar sacs on the lungs.

Here you can see the nature of a simple squamous epithelium as the single layer of flattened cells is pointed out. This is a slide from a uterine lining.
2) **Simple Cuboidal Epithelium**: a single sheet of hexagon-shaped cells; approximately the same height and width.

1. These cells are called "cuboidal" because they appear to be cube-shaped under the light microscope being of equal height and width.
   a. Cuboidal epithelial cells will typically have a centrally positioned nucleus.

2. Simple cuboidal epithelium is found in areas such as:
   a. glandular termini and ducts
   b. the parenchyma cells of the liver (i.e.; hepatocytes)
   c. rete testis (tubes in the testis)
   d. covering the free surface of the ovary (i.e.; germinal epithelium)
   e. certain portion of the renal tubules (i.e.; thick segments).

3. Functionally simple cuboidal epithelium may simply line conducting passageways (ex; glandular ducts) or may be structurally adapted to play important roles in secretion or absorption (ex; the proximal and distal convoluted tubules of the kidneys).

![Simple Cuboidal Epithelium forming individual tubules in the mammalian kidney. The Lumen can be clearly discerned as being surrounded by cuboidal cells.](image-url)
3) **Simple Columnar Epithelium:** a single sheet of polygon shaped cells – they are taller than they are wide.

1. These cells are called "columnar" because they appear to be column-shaped under the light microscope being of a much greater height than width.
   a. Typically, columnar epithelial cells will typically have a basally positioned, ovoid nucleus.
2. Simple columnar epithelium is found in places such as:
   a. the ducts of many glands
   b. lining the stomach, intestines, and gall bladder
   c. some of the small respiratory passageways
   d. portions of the oviducts and uterus.
3. Functionally simple columnar epithelium is well designed for absorption (ex; intestinal epithelium) and secretion (ex; uterine secretory cells).
   a. In some cases simple columnar epithelial cells will have cilia on their apical surfaces.

4) **Stratified Squamous Epithelium:** this multilayered tissue's outermost cells have a flattened, squamous appearance.

1. The deeper cells may be less squamous in appearance, being cuboidal or even columnar in shape in certain cases, but classification is based on the outermost layer in stratified epithelia.
2. There are two groups of stratified squamous epithelia:
   a. **Stratified Squamous Nonkeratinized, or Mucus Type**
      i. The surface cells contain visible nuclei and lack keratin.
ii. It is found on the surfaces of moist cavities or passageways which open onto the body surface such as the: mouth, pharynx, esophagus, vagina, and anal canal.

b. Stratified Squamous Keratinized, or Cutaneous Type
   i. The surface cells are dead, being anucleated and filled with keratin.
   ii. It covers the entire exposed surface of the body (except for the cornea).
      1. It is well designed to deal with abrasion and desiccation.

Nonkeratinized, Stratified Squamous Epithelium: the tissue is identified by the cell structure at the apical surface. This tissue sample contains cells with nuclei at the apical surface, indicating that they are still alive and unkeratinized.

Keratinized, Stratified Squamous Epithelium: The Keratinization process fills the cells with the protein, making the layer and effective barrier against infections and dehydration.
5) **Stratified Cuboidal Epithelium:** multiple layers of epithelial cells where at least the surface cells are cuboidal.

1. Stratified cuboidal epithelium is of limited distribution throughout the body.
   a. Where it is found it is typically only two layers thick.
   b. It is found in areas such as larger glandular ducts.

The double layer of cuboidal cells can easily be seen forming these glandular ducts.

6) **Stratified Columnar Epithelium:** multiple layers of epithelial cells where at least the surface cells are columnar (the cells of the deeper layers are typically cuboidal in shape).

1. Stratified columnar epithelium is of limited distribution throughout the body.
   a. Where it is found it is typically only two layers thick.
   b. It lines small portions of the pharynx, larynx, the largest glandular ducts, and portions of the male urethra.
   i. It also occurs in certain regions of transition between two different types of epithelia.
There are two other types of epithelia that need to be mentioned here:

**A) Pseudostratified Epithelium:** This epithelium that looks like it is stratified, but really isn’t. It is one layer but not all the cells are the same height, yet all the cells are attached to the basal membrane. This height differential gives a layered appearance.

1. Pseudostratified columnar epithelium can be found in places such as:
   - a. most of the respiratory passageways
   - b. Eustachian tube and portions of the middle ear
   - c. portions of the male urethra
   - d. portions of the male accessory sex organs
2. Functionally pseudostratified columnar epithelium is designed for lining, secretory, and absorptive roles.
   - a. The pseudostratified columnar epithelium lining the respiratory tract are ciliated and the tissue will contain mucus producing goblet cells (see image below).

![Ciliated, Pseudostratified Columnar Epithelium: note the presence of cilia on the apical surface.](image-url)
B) Transitional Epithelium: multiple layers of variable appearing cells. The appearance of the cells is based upon the tissue's location and action.

1. It is a flexible layer which can expand and contract which is responsible for the variable appearance of the cells.
   a. The surface cells are typically dome-shaped while the underlying cells may be columnar, cuboidal, or even squamous in appearance.
      i. Occasionally two nuclei per surface cell are observed.
   b. Transitional epithelium is specifically adapted for flexibility and for stretching.
2. The distribution of transitional epithelium is limited primarily to the urinary system. It lines the renal pelvis, ureters, bladder, and portions of the urethra (based on gender).

Special Features of Epithelium:

- **Cilia**- (singular= cilium, Latin= eyelash)- hair-like appendages attached to the apical surface of cells that act as sensory structures or to produce movement.

- **Goblet cells** - specialized cells that produce mucus to lubricate and protect the surface of an organ

- **Villi**- (singular= villus, Latin= shaggy hair)- finger-like projections that arise from the epithelial layer in some organs. They help to increase surface area allowing for faster and more efficient adsorption.
• **Microvilli**- smaller projections that arise from the cell's surface that also increase surface area. Due to the bushy appearance that they sometimes produce, they are sometimes referred to as the brush border of an organ.

• **Tight Junctions** - Tight junctions are protein complexes that completely encircle a cell and thus connect it to all its neighboring cells and make it impossible for anything to pass between them. Common in lining of the stomach & intestines.

• **Desmosomes** - “spot weld” that holds cells together and enables a tissue to resist mechanical stress. Common in the epidermis and cervix.

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**I-b) Glandular Epithelia:**

- A gland is a cell or an organ that secretes substances for use inside or outside the body.
- Glands are composed predominantly of epithelial tissue.
- Glands are broadly classified as:
  - Endocrine
  - Exocrine
A) Exocrine Glands:

- Typically secrete material into ducts that lead to the body surface or to one of the cavities that is continuous with the body surface, i.e., digestive, reproductive, respiratory tract.
- *Exo* = outside and *crine* = secrete.
- Can be multicellular or unicellular.
  - **Multicellular**: Pancreas, stomach, sweat glands, salivary glands, mammary glands, sebaceous glands, etc.
  - **Unicellular**: Goblet cells

Multicellular Exocrine gland – the salivary gland.

A unicellular exocrine gland – the goblet cell. Often interspersed in epithelial tissue. These cells produce mucous defining the tissue as a mucosa.
B) Endocrine Glands:

- *Endo* = within.
- Do not secrete material into ducts.
- Secrete chemical signals called hormones into the bloodstream where they travel through the body and affect other cells.
- Examples include:
  - Thyroid, thymus, testes, ovaries, pituitary, pineal, adrenal, etc.
II) Connective Tissue

Connective tissues are the most diverse class of the four different tissues and include bone, blood, cartilage, adipose, and areolar c.t. The types of connective tissues are classified based on the relative proportions of three components: ground substance, fibers, and cells.

- The ground substance and fibers are the extracellular components of the c.t. and make up the Extracellular Matrix.
- As a point of terminology, the term “blast” refers to an immature cell and “cyte” refers to a mature cell type. You will see examples of these terms used later.

Functions of Connective Tissue:

1. Binding of organs
2. Support
3. Physical protection
4. Immune protection
5. Movement
6. Storage
7. Heat production
8. Transport

Categories of Connective Tissue:

1. Fibrous connective tissue (a.k.a. connective tissue proper)
2. Supporting connective tissue
3. Fluid connective tissue
Components of Connective Tissue:

Cell Types:

1. **Fibroblasts** – cells that produce fibers
2. **Macrophages** – phagocytic cells derived from monocytes of the blood with there being many specific ones: histiocytes (stationary macrophages) and wandering macrophages: Kupffer cells, alveolar cells, etc.
3. **Plasma cells** give rise to antibody-producing B-lymphocytes
4. **Mast cells** produce histamine which causes vasodilation and enhances white blood cell action
5. **Adipocytes** are fat cells which store lipids
6. **Chondroblasts/cytes** are cells which produce and maintain cartilage c.t.
7. **Osteoblasts/cytes** are cells which produce and maintain osseous c.t. (bone)
8. Blood cells: **Erythrocytes** (red blood cells) and **Leukocytes** (white blood cells) and **Thrombocytes** (platelets)

**Ground substance:** non-cellular material (mostly glycoproteins and proteoglycans such as hyaluronic acid, chondroitin sulfate, dextran sulfate, etc) secreted by the conn. tissue cells (may be fluid, semifluid, gelatinous or calcified to a small are large degree. This is the basis for allowing the c.t. to be classified according to their “texture” as either

- (1) Soft – aerolar, reticular, elastic, collagenous, adipose, pulp
- (2) Firm – the cartilages (hyaline, elastic, fibro-)
- (3) Rigid – bone and the dental tissues (enamel, dentin, cementum)
- (4) Fluid – blood and lymph

**Fibers:**

1. **Collagen fibers** – composed of collagen (which then polymerizes); very tough and resistant to stretching; found in collagenous c.t.’s, bone, cartilage, tendons, and ligaments.

2. **Elastic fibers** – composed of elastin; provide strength and stretching capacity; found in dermis of the skin, in elastic cartilage, blood vessels, and the lungs.

Because of their size, collagen fibers are sometimes referred to as “thick” fibers, and elastin fibers as “thin” fibers.
(3) **Reticular fibers** – composed of reticulin (simple collagen plus a glycoprotein), provide support in the walls of blood vessels and lymphatic organs and form a strong supporting network around collections of adipocytes, neuron processes, and muscle cells.

Reticular fibers have a rather unique and identifiable structure. They will usually stain dark and will be short and branched. This quality is why these fibers are found in the bulk of solid organs in the body – giving the organ the ability to be compressed and return to a normal shape.

II-a) **Classification of Connective Tissues:**

1. **Loose Connective Tissues** consist of fibers, cells and a semifluid ground substance
   a. **Areolar c.t.** – ground substance allows for passage of nutrients from the blood into adjacent cells and tissues; found in subcutaneous tissue
   b. **Adipose c.t.** - composed of adipocytes; associated with areolar c.t.; supports, protects, and generates heat (brown fat is used by infants to regulate their temperature)
   c. **Reticular c.t.** -
      i. Consists of fine interlacing reticular fibers and reticular cells
      ii. Forms the stroma of certain organs (lymph nodes)
      iii. Helps bind together the cells of smooth muscle
Areolar Tissues – found in the dermis of the skin.

Adipose c.t. Large anucleate cells that function mainly in fat storage.
2. **Dense Connective Tissues**: very little extracellular matrix.
   a. Dense tissues can be categorized as either “dense regular”, or “dense irregular” based upon the structural alignment of the protein fibers that make up the tissue.
      i. **Dense regular c.t.** will have parallel arrangements of protein fibers.
         1. Give great strength along the axis of fiber direction. Makes up such structures as tendons and ligaments.
      ii. **Denser irregular c.t.** will have fibers that are arranged in no specific pattern.
         1. Found in areas of the body that are exposed to tension in multiple directions.
         2. Usually found in sheets of tissue (dermis of the skin, heart valves, perichondrium, periosteum).

This image shows dense regular connective tissue. Notice how all the fibers are running parallel with each other. A bulk of the fibers are collagen, which provide great strength along the axis.

In dense irregular c.t. collagen fibers are arranged in multiple directions providing resistance to stretching in multiple planes. Does not have the strength of dense regular c.t.
b. **Elastic Connective Tissue:** Elastic tissue is a dense connective tissue where the predominant fiber type is the elastic fiber.
   i. It is found in areas that must be able to deal with a high degree of mechanical stress but also be highly resilient.
      1. Ex: elastic cartilage and elastic arteries.

The micrograph of this c.t. shows the pointer on the elastic layer of an artery. This tissue gives the artery the ability to expand and contract with variances in blood pressure and blood volume.

c. **Cartilages:**

**General Characteristics**

2. **Chondrocytes** are found in spaces called **lacunae**
3. **Perichondrium** is the dense irregular connective tissue layer which surrounds cartilage
4. Cartilages are avascular and chondrocytes depend on the diffusion of nutrients through the stiff, viscous matrix.
   a. Thus their metabolism and rate of division (a.k.a. mitosis) is low and healing of torn cartilage is a long process.
   b. Cartilage is avascular b/c chondrocytes produce a chemical called antiangiogenesis factor that, like its name suggests, prevents the growth of blood vessels.
5. Cartilage matrix collagenous fibers range in thickness from invisibly fine to conspicuously coarse.
Three types of Cartilage:

1) **Hyaline cartilage**
   a) most abundant form of cartilage
   b) fine collagen fibers embedded in a gel-type matrix
   c) weakest of the three types of cartilage.
   d) Forms a thin *articular cartilage* over the ends of bones at moveable joints.

**Functions:**
- Keeps airways patent.
- Moves vocal cords.
- Precursor of bone in the fetal skeleton.
- Structural attachment.

2) **Fibrocartilage**: a combination of hyaline cartilage and dense regular connective tissue in both appearance and function.
   - Parallel collagenous fibers similar to those of tendon.
   - Rows of chondrocytes in lacunae between collagenous fibers.
   - Chondrocytes are fewer and smaller and are not in isogenous groups.
   - Never has a perichondrium

**Locations:**
- Pubic symphysis – the anterior joint between the 2 halves of the pelvic girdle.
- Intervertebral discs that separate the bones of the spinal column.
- Menisci (shock-absorbing pads of cartilage) in the knee joint.
- At points where tendons insert on bones near articular hyaline cartilage.

**Functions:**

- Resists compression and absorbs shock in some joints.
- Often a transitional structure between dense connective tissue and hyaline cartilage.
- For example, at some tendon-bone junctions.

(3) **Elastic Cartilage:** considered to be a modification of hyaline cartilage.

   a) The ground substance of elastic cartilage is sparse and extensively infiltrated with elastic fibers which are randomly arranged.
   b) Always covered by a perichondrium.
   c) Provides flexible, elastic support.
   d) Elastic cartilage is found in: the external ear, auditory tubes, eustachian tubes, epiglottis, corniculate cartilages, and cuneiform cartilages.

![Elastic fibers can be seen in between the chondrocytes.](image)
d. Bone (Osseous Tissue):

(1) Bone can be considered to consist of "bone tissue" and "bone organs".
   a. Bone tissue is the mineralized supportive connective tissue forming the framework of bone organs.
   b. Bone organs provide the supporting framework of the body.

(2) Bone Organs or Bones
   a. As organs bones consist of bone tissue, external and internal connective tissue investments, tendinous insertions, ligamentous attachments, blood vessels, nerves and bone marrow (which consists of either bone forming elements or adipose deposits).
      i. In certain bone organs there are additional specializations for articulation.
   b. Bone tissue consists of cells, fibers, and ground substance as does any c.t.
   c. However in bone tissue the matrix becomes mineralized with inorganic salts giving bone its rigidity.

(3) Morphologically bone tissue is organized in two ways:
   a. The two ways are:
      i. **Compact Bone** - when the tissue forms a compact solid mass with relatively few intervening spaces.
         1. **Compact bone** is composed of a basic unit called the **osteon** or **Haversian system**
         2. **Lamella** are concentric rings of matrix
         3. **Lacunae** are small spaces between lamellae that contain osteocytes (mature bone cells)
         4. **Canaliculi** are minute canals containing processes of osteocytes that provide routes for nutrient and waste transport
         5. **Central (Haversian) canal** contains blood vessels and nerves
      ii. **Spongy Bone** (aka; trabecular bone, cancellous bone) - when the tissue forms a three dimensional network of intercommunicating osseous projections termed "trabeculae".
          1. General distribution in a bone organ for these two morphologies of bone tissue:
             a) Compact bone forms an outer protective shell for bone organs. This is called Cortical Bone.
             b) Spongy bone forms a branching internal framework. This is called Medullary Bone.
      iii. **Functions of bone**
          (1) Supports
          (2) Protects
          (3) Helps provide movement
          (4) Stores minerals
          (5) Houses blood-forming tissue (marrow)
Perforating canal
Lamella
Canaliculi
Haversian canal
Lacuna

Compact Bone (100x)
e. Blood Vascular Connective Tissue:
1. Blood is a connective tissue composed of free cells in a fluid matrix. Unlike other types of connective tissues, blood lacks fibers except during the clotting response.
2. Blood can be looked at in terms of the extracellular material, the Plasma, and the cellular component, the Formed Elements.
   a. Plasma
      i. The plasma acts as a medium for the circulation of cells and metabolic substances.
      ii. The primary components of plasma are: water, inorganic salts, and the plasma proteins.
         1. Plasma Proteins - are special proteins unique to the blood. They include:
            a) Albumins - the most abundant class.
               1. They serve primarily to maintain blood viscosity and volume.
            b) Fibrinogens - serve primarily in clot formation.
            c) Globulins - a class of plasma proteins of diverse size and function.
               They include:
               1. Gamma Globulins such as the antibodies.
               2. Beta Globulins - used in the transport of hormones, lipids, and metal ions.
   b. Formed Elements (Blood Cells)
      2. There are three distinct classes: erythrocytes, leucocytes, and thrombocytes.
      3. All of the formed elements arise from hemopoietic tissue.
         a) In the embryos, fetus, and even the neonate there are a number of hemopoietic organs: spleen, liver, bone marrow, and yolk sac.
         b) In the adult hemopoiesis is restricted only to the red marrow.

Erythrocytes

1) The erythrocytes are the red blood cells and are the most numerous of the formed elements.
2) Appearance - erythrocytes are anucleated, red colored cells shaped like biconcave discs.
   a. They are 8 um by 2 um in dimension.
   b. Their shape increase surface area for gas exchange.
   c. The mature erythrocyte lacks most of the typical organelles to allow it to hold more Hemoglobin.
      i. Hemoglobin is a complex protein composed of four globular polypeptide chains, each bearing a Heme Group.
      ii. The heme group contains iron.
         1. Iron binds to oxygen allowing for its transport through the blood stream.
         2. It will also bind to carbon dioxide.
         3. The iron of the heme group gives the red color to erythrocytes.
            a. Since erythrocytes are by far the most abundant of the formed elements, they give the red color to blood.
   d. Erythrocytes are flexible cells which allow them to travel through the smaller capillaries.
**Leucocytes**

1) Leucocytes are the white blood cells.
2) They are the only complete cells of the formed elements.
3) Leucocytes can be described as connective tissue cells which utilize the blood stream for transport from the hemopoietic red marrow to areas where they are required.
4) Leucocytes are a variety of motile, nucleated cells which serve in the defense of the body from disease causing organisms (i.e.; the immune system).

**Thrombocytes**

1. Thrombocytes, also called "platelets", function to arrest bleeding and to cause thrombosis, clot formation.
2. Thrombocytes are the smallest of the formed elements.
3. Appearance - they are 2 to 4 um long and shaped like flattened discs.

The major formed elements of the blood can be seen above. The large cell with the lobular nucleus is a type of leukocyte; the dark fragments of cells that are smaller than everything else are thrombocytes; and the erythrocytes are the lightly stained cells that make up the bulk of the slide.
III) Muscle Tissue:

Specialized for contraction, cells of this tissue are referred to as **myofibers** due to their elongated shape.

**Functions of muscle tissue are:**

1. Provide motion
2. Maintenance of posture
3. Heat production

There are three types of muscle tissue found in the human body and each is unique in its physical characteristics. The three types are:

1. Skeletal muscle
2. Cardiac muscle

(1) Skeletal Muscle

Skeletal muscle is described as "**striated**" due to the intracellular arrangement of the contractile protein filaments which will form alternating bands when viewed under light microscopy in a longitudinal section.

1. The term "skeletal" comes from the muscle typically being attached to the skeleton.
   a. There are some exceptions such as the upper esophagus.
   b. As a result, skeletal muscle is primarily involved in the initiation of body movement and locomotion.
   c. Skeletal myofibers are long, cylindrical cells arranged parallel to one another along the long axis of the muscle organ.
      i. The longest of these cells will stretch the length of the muscle organ, from **origin** to **insertion**, (origin = point of attachment on fixed structure; insertion = attachment to structure to be moved) but shorter cells are more common.

**Characteristics of Skeletal Muscle:**

1. attached to bone
2. striated (light and dark banding)
3. voluntary
4. Multinucleated cells

![Diagram of Skeletal Muscle](Image)
(2) Cardiac Muscle
Cardiac muscle fibers possess many characteristics which are similar to those of skeletal muscle fibers but with modifications:

1. Cardiac muscle cells are typically uninucleated but can be binucleated.
2. They are smaller cells than are skeletal myofibers and they branch.
3. Myocardial cells are attached to one another at Intercalated Discs.
   a. Intercalated discs serve both to bind cells and to allow for communication between adjacent cells.

![Intercalated disc](image.jpg)

The arrow indicates an intercalated disc which can be seen throughout this tissue.

Characteristics of Cardiac Muscle:

1. Forms most of the heart wall
2. Striated
3. Involuntary
4. Single nucleus per myofiber
5. Presence of intercalated discs (junctions between myofibers)
(3) **Smooth Muscle:**

Smooth muscle forms the bulk of the visceral musculature.

1. Smooth muscle fibers can occur individually or, most often, in sheets.
   a. These sheets will be found in:
      i. the muscular walls of the digestive organs and the ducts of the associated glands,
      ii. lining portions of the respiratory tract,
      iii. lining the urinary and reproductive tracts,
      iv. the muscular walls of blood vessels and of the larger lymph vessels,
      v. the arector pili muscles.

**Characteristics of Smooth Muscle:**

1. Found in walls of hollow internal structures/organs.
2. Nonstriated
3. Involuntary
4. Single nucleus per cell
IV) Nervous Tissue:

The neuron is the functional and the structural unit of the nervous system. It displays two highly developed physiological traits:

1. **Irritability** - the capacity to generate a nervous impulse in response to various stimuli.
2. **Conductivity** - the ability to transmit these impulses along its cellular processes.
   a. Neurons allow for communication between the Central Nervous System (CNS) and the rest of the body via the Peripheral Nervous System (PNS).

Nerve tissue also includes a class of non-neuronal cells called the Supporting Cells. Supporting cells assist the neurons in their functioning.

**Functional Classes of Neurons and Characteristics of Neural Tissue:**

1. Three functional classes of neurons: **motor**, **sensory**, **interneurons**.
   a. The **cell bodies** (part of the cell containing the nucleus) of each of the neuron functional types are located in specific parts of the peripheral and central nervous system.
   b. Each neuron has three distinct structural parts:
      i. One soma (cell body)
      ii. Each neuron has only one axon (cytoplasmic extension or process along which the nerve action potential (impulse) travels away from the cell body.
      iii. Neurons may have only one dendrite or may have multiple dendrites (cytoplasmic extensions or processes along which the nerve action potentials (impulses) travel toward the cell body.
   c. Neurons respond to various stimuli and conduct nerve impulses to other neurons, to muscle cells, or to glands.
CONNECTIVE TISSUE MATRIX

Name _____________________________

Coloring Instructions

- Collagen fibers [A] yellow.
- Fibroblasts [B] blue.
- Mast cells [C] purple.
- Macrophages [D] orange.
- Elastic fibers [E] green (shade over the line).
- Blood vessel and blood cells [F] red.
- Fat cells [G] pink.

Match the structure to the function (use letters)

1. ____ Store energy
2. ____ Production of fibers
3. ____ Consume debris and foreign objects
4. ____ Fiber that makes up tendons
5. ____ Prevention of blood clots
Directions: Complete the chart by filling in the missing information

<table>
<thead>
<tr>
<th>TISSUE TYPES</th>
<th>SPECIFIC TYPES OF TISSUE</th>
<th>WHERE ITS FOUND IN YOUR BODY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lining of air sacs in the lungs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIMPLe CUBOIDAL</td>
<td>Digestive tract (intestinal wall)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Air passages (trachea, etc)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Outer layer of skin</td>
<td></td>
</tr>
<tr>
<td>TRANSITIONAL</td>
<td>Binds skin to internal organs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Layer beneath the skin</td>
<td></td>
</tr>
<tr>
<td>CONNECTIVE TISSUE</td>
<td>Covers ends of bones at joints</td>
<td></td>
</tr>
<tr>
<td>ELASTIC CARTILAGE</td>
<td>Skeleton</td>
<td></td>
</tr>
<tr>
<td>FIBROCELLULAR</td>
<td>Circulates throughout body</td>
<td></td>
</tr>
<tr>
<td>ELASTIC CARTILAGE</td>
<td>Muscles connected to bones</td>
<td></td>
</tr>
<tr>
<td>FIBROCELLULAR</td>
<td>Walls of many internal organs</td>
<td></td>
</tr>
<tr>
<td>FIBROCELLULAR</td>
<td>Walls of the heart</td>
<td></td>
</tr>
</tbody>
</table>

NERVE TISSUE

NERVE TISSUE
**Skin and Connective Tissue Diseases**

The skin is the largest organ in the body — both in weight and in surface area — and separates the body's internal environment from the external environment. The skin has many diverse roles. It acts as a channel of communication with the outside world; protects the body from water loss; uses specialized pigment cells, called melanocytes, to protect the body from ultraviolet radiation; participates in calcium homeostasis by contributing to the body's supply of vitamin D; and helps regulate body temperature and metabolism.

Elastic tissues such as the skin require a strong and resilient structural framework. This framework is called the extracellular matrix, or connective tissue. The orientation of the connective tissues — adipose (fat cells), cartilage, bone, tendons, and ligaments — found beneath the skin are also key for tissue appearance and function. All connective tissue is composed of three major classes of biomolecules: structural proteins (collagen and elastin), specialized proteins (fibrillin, fibronectin, and laminin), and proteoglycans.

Some skin and connective tissue diseases, such as those discussed in this section of genes and disease, are due strictly to genetic inheritance, while others do not have specific gene abnormalities as their sole cause. Many features of skin and connective tissue disorders overlap with each other, and with other disorders, even though they have unique genetic causes.

**MALE PATTERN BALDNESS**

5-alpha reductase is an enzyme that was first discovered in the male prostate. Here it catalyzes the conversion of testosterone to dihydrotestosterone, which in turn binds to the androgen receptor and initiates development of the external genitalia and prostate. The gene for 5-alpha reductase has been mapped to chromosome 5.

More recently, 5-alpha reductase was found in human scalp and elsewhere in the skin, where it carries out the same reaction as in the prostate. It is thought that disturbances in 5-alpha reductase activity in skin cells might contribute to male pattern baldness, acne, or hirsutism. The discovery of a plant homolog of human 5-alpha reductase may lead to new drugs, and the race is now on to find inhibitors of 5-alpha reductase.
**DIASTROPHIC DYSPLASIA**

Diastrophic dysplasia (DTD) is a rare growth disorder in which patients are usually short, have club feet, and have malformed hands and joints.

Although found in all populations, it is particularly prevalent in Finland.

The gene whose mutation results in DTD maps to chromosome 5 and encodes a novel sulfate transporter. This ties in with the observation of unusual concentrations of sulfate in various tissues of DTD patients. Sulfate is important for skeletal joints because cartilage—the shock-absorber of joints—requires sulfur during its manufacture.

Adding sulfur increases the negative charge within cartilage, which contributes to its shock-absorbing properties.

A great deal of further research must be done before this condition is fully understood and effective therapies are developed.

**ELLIS-VAN CREVELD SYNDROME**

Ellis-van Creveld syndrome, also known as "chondroectodermal dysplasia," is a rare genetic disorder characterized by short-limb dwarfism, polydactyly (additional fingers or toes), malformation of the bones of the wrist, dystrophy of the fingernails, partial hare-lip, cardiac malformation, and often prenatal eruption of the teeth.

The gene causing Ellis-van Creveld syndrome, EVC, has been mapped to the short arm of chromosome 4. As yet, the function of a healthy EVC gene is not known; this is one of the most important questions that must be answered about the disease, since it would give an indication as to the molecular mechanism of the disease. Ellis-van Creveld syndrome is often seen among the Old Order Amish community in Lancaster County, Pennsylvania. Because this group of people is small and isolated, it affords a rare opportunity to observe the passage of this particular disorder from generation to generation. A pattern of inheritance can be observed that has indicated the disease is autosomal-recessive (i.e. a mutated gene form both parents is required before the effects of the disease to become apparent).

**MARFAN SYNDROME**

Marfan syndrome is a connective tissue disorder, so affects many structures, including the skeleton, lungs, eyes, heart and blood vessels. The disease is characterized by unusually long limbs, and is believed to have affected Abraham Lincoln.
Marfan syndrome is an autosomal dominant disorder that has been linked to the FBN1 gene on chromosome 15. FBN1 encodes a protein called fibrillin, which is essential for the formation of elastic fibres found in connective tissue. Without the structural support provided by fibrillin, many tissues are weakened, which can have severe consequences, for example, ruptures in the walls of major arteries.

Beta blockers have been used to control some of the cardiovascular symptoms of Marfan syndrome; however, they are not effective against the skeletal and ocular problems, which can also be serious. A related disease has been found in mice, and it is hoped that the study of mouse fibrillin synthesis and secretion, and connective tissue formation, will further our understanding Marfan syndrome in humans.

MALIGNANT MELANOMA

In 1997, it was expected that about 40,300 Americans would be diagnosed with malignant melanoma, the most aggressive kind of skin cancer. Melanomas are more common in people with lightly pigmented skin, and people who have had melanoma once have a high risk of developing new melanomas.

In some cases, the risk of developing melanoma runs in families, where a mutation in the CDKN2 gene on chromosome 9 can underlie susceptibility to melanoma. CDKN2 codes for a protein called p16 that is an important regulator of the cell division cycle; it stops the cell from synthesizing DNA before it divides. If p16 is not working properly, the skin cell does not have this brake on the cell division cycle and so can go on to proliferate unchecked. At some point this proliferation can be seen as a sudden change in skin growth or the appearance of a mole.

The most powerful weapons against melanoma are therefore 1) prevention, by using protective clothing and sun screen and 2) early detection, by recognizing changes in skin growths or the appearance of new growths. Insight may also be drawn for other cancer types by studying the molecular biology of p16, since the malfunction of other components of the p16 pathway have also been implicated in other cancers.

MENKES SYNDROME

Menkes syndrome is an inborn error of metabolism that markedly decreases the cells' ability to absorb copper. The disorder causes severe cerebral degeneration and arterial changes, resulting in death in infancy. The disease can often be diagnosed by looking at a victim's hair, which appears to be both whitish and kinked when viewed under a microscope.
Menkes' disease is transmitted as an X-linked recessive trait. Sufferers cannot transport copper, which is needed by enzymes involved in making bone, nerve and other structures. A number of other diseases, including type IX Ehlers-Danlos syndrome, may be the result of allelic mutations (i.e. mutations in the same gene, but having slightly different symptoms) and it is hoped that research into these diseases may prove useful in fighting Menkes' disease.

If administered within the first few months of life, copper histidinate appears to be effective in increasing the life expectancy of some patients. However, this treatment only increases life expectancy from three to thirteen years of age, so can only be considered a palliative. A similar condition to Menkes' disease exists in mice; working with these model organisms will help give insight into human copper transport mechanisms, so helping to develop effective treatments for Menkes' sufferers.

**PORPHYRIA**

Porphyria is a diverse group of diseases in which production of heme is disrupted. Porphyria is derived from the Greek word "porphyra", which means purple. When heme production is faulty, porphyrins are overproduced and lend a reddish-purple color to urine.

Heme is composed of porphyrin, a large circular molecule made from four rings linked together with an iron atom at its center. Heme is the oxygen-binding part of hemoglobin, giving red blood cells their color. It is also a component of several vital enzymes in the liver including the group known as cytochrome P450. This enzyme family is important in converting potentially harmful substances such as drugs to inactive products destined for excretion.

Heme synthesis takes place in several steps, each of which requires a specific enzyme of which there are 8 in total. The genes that encode these enzymes are located on different chromosomes, and mutations of these genes can be inherited in either an autosomal dominant or autosomal recessive fashion, depending on the gene concerned. Affected individuals are unable to complete heme synthesis, and intermediate products, porphyrin or its precursors, accumulate.

Environmental triggers are important in many attacks of porphyria. Example triggers include certain medications, fasting, or hormonal changes. Genetic carriers who avoid a triggering exposure may never experience symptoms.

The cutaneous porphyrias cause sun sensitivity, with blistering typically on the face, back of the hands, and other sun-exposed areas. The most common of these is porphyria cutanea tarda (PCT).

Triggering factors are alcohol use, estrogen, iron, and liver disease, particularly hepatitis C. The acute porphyrias typically cause abdominal pain and nausea. Some patients have personality
changes and seizures at the outset. With time the illness can involve weakness in many different muscles.

The cutaneous and acute forms are treated differently.

Cure of these genetic diseases awaits the results of ongoing research on the safest and most effective means of gene transfer or correction.
Name: ___________________________________________

I)  **Organelle Matching Section:** Please match the correct statement to each organelle function:

<table>
<thead>
<tr>
<th>a. cell membrane</th>
<th>i. lysosome</th>
</tr>
</thead>
<tbody>
<tr>
<td>b. Granular</td>
<td>j. mitochondria</td>
</tr>
<tr>
<td>c. peroxisome</td>
<td>k. nuclear membrane</td>
</tr>
<tr>
<td>e. Microtubules/microfilaments</td>
<td>l. Smooth</td>
</tr>
<tr>
<td>f. cytoplasm</td>
<td>m. nucleus</td>
</tr>
<tr>
<td>g. endoplasmic reticulum</td>
<td>n. ribosome</td>
</tr>
<tr>
<td>h. Golgi apparatus</td>
<td>o. Chromatin</td>
</tr>
</tbody>
</table>

**What are their functions?**

1. ____ Liquid inside the cell, mostly water

2. ____ It is the boundary of the cell; it controls what substances enter or leave the cell.

3. ____ "Control center of the cell" where genetic material (DNA) is found.

4. ____ Term used to describe the endoplasmic reticulum if it has attached ribosomes.

5. ____ Very small organelles that are the sites of protein synthesis.

6. ____ System of tubes through the cytoplasm involved in transporting materials

7. ____ A flat stack of tubes involved in "packaging" materials that will exit the cell; UPS.

8. ____ Site of cellular respiration (where energy is released from nutrients); powerhouse.

9. ____ Term used to describe the ER that is more concerned with the synthesis of lipid-based products.

10. ____ Controls what enters or exits the nucleus.

11. ____ Long, thin, invisible strands of DNA.

12. ____ Specialized vacuole that stores digestive enzymes.

13. ____ Protein structures that form the cytoskeleton.

14. ____ Contains catalase for the denaturing of peroxide.
II) Label the Animal Cell correctly:

A) Its the little “dot”.

B) The cell “fluid.”

C)

D)

E)

F)
Internet Activity:
I) Go to the following website: http://www.kumc.edu/instruction/medicine/anatomy/histoweb/

Review the slides of the 4 tissue types:
- Epithelial
- Connective
- Muscle
- Nervous

This will assist you in learning the tissues that you will need to identify for the lab practical in class.

II) Digital flashcards of tissues can be found at the following site: https://quizlet.com/2621787/histology-lab-photo-quiz-flash-cards/