First Session
Instructor: Dean Sheehy, MEd, CLS, WTII
Take Roll
Review Syllabus
  Grading for lecture.
  Grading for lab. No lab reports graded, only exams!
Prerequisites: Human Anatomy, Chemistry
Purpose for taking class.
How to succeed in Physiology.
  Time: 3 hours per lecture hour, 3 hours for lab per week.
  Demonstrated success in prerequisites.
  Family support.
  Read material.
  Learn as you go. Develop a foundation. Enjoy the subject.

Anoint your notes from text, review with others immediately following class sessions.
Get to know others. Study together.
Attend regularly. Be on time.
Make use of instructor. I want all of you to do well.

Introduction to Human Physiology

The Scope Of Physiology Chapter 1

Definition physiology = the study of how living things function. The functions of body systems and the basis of how they work.

Present day view is that all physiological processes can be explained according to the laws of chemistry and physics. Physiology draws on these fields to explain body functions. No supernatural forces or unexplained forces are considered.
The Basic Unit of Function of All Organisms = Cell

Characteristics of Living Cells (Life Processes) p. 7-8 Cells exhibit certain activities that can be considered the criteria of life.

1. **Intake of Materials**
   For energy to power cellular activities or, Materials synthesis.
   Origin: from breakdown products of food.

2. **Output of Materials**
   The elimination of wastes of metabolism.

3. **Metabolism**
   All chemical reactions in the body.
   Metabolic reactions are of 2 basic types:
   1. **Anabolism**: Metabolic processes that involve the building up or synthesis of complex (organic) molecules. This process requires energy.
      Example of anabolism: Taking in food and storing it.
   2. **Catabolism**
      The opposite of anabolism. Metabolic reaction in which complex molecules are broken down into simpler ones. This process yields energy.
      Example of catabolism: Breakdown of obtained or stored foods for energy.

4. **Reproduction**: 2 types:
   1. Replacement of worn out and damaged cells. Somatic cells. Duplicates of existing cells.
5. **Growth**: increase in size that results from 2 ways:
   1. Growth of an individual cell.
   2. Increase in number of cells.

6. **Movement**:
   Occurs within cells, entire cell can move, organs can move, or the whole organism can move.

7. **Responsiveness**
   Cells respond to changes in the internal or external environment. Homeostasis.

Since the body is made up of cells, the body exhibits these properties as a whole.

Levels of Structural Organization in the Human Body

**figure 1.1 page 3**

Chemical level: atoms, molecules, ions

Cellular level: the basic unit of life
   In our bodies there are about 40 trillion cells.
   The cells are organized into **tissues**.

Tissue level
   **Tissues** = groups of cells that work together to perform a similar function.

4 Elementary Tissues in the Human Body. page 4, 104

1. **Epithelial Tissues** = Function to cover the body and line its structures, forms glands. E.g. skin stratified squamous
2. **Connective Tissues** = Connecting and support, store energy, immunity. E.g. areolar C.T. just deep to the epidermis
3. **Muscular Tissue** = Contractile tissue causes movement. E.g. skeletal, cardiac, smooth
4. Nervous Tissue = Detect change, conduction of impulses. E.g. CNS and peripheral nerves

Organ Level
2 or more tissues that are organized for a specific function = Organ. Ex: stomach, heart, liver, kidney

System level
System = 2 or more related organs that are coordinated to perform a specific function. Ex: digestive system

Organismal level
Organism- one living individual. All systems functioning together to create a living human.

Homeostasis: homeo = sameness, statis = standing still
When systems work properly, they maintain the organism in an optimal state.

Homeostasis: Maintaining physiological limits at a set point. The maintenance of this state = homeostasis. Same state or steady state.

Homeostatic imbalance will cause disease or death. Ex: blood glucose, RBC level, blood pH.
Constant adjustments are made to maintain the steady state.

Are you aware of your body's homeostatic attempts? When you are hungry or hot, you become irritable or less efficient. So, you eat and sweat respectively.

Aging brings on aging and death of cells = slow drifting away from optimal condition of life. In other words, aging can be looked upon as a failure to maintain homeostasis.

Feedback Systems (Loops) to control homeostasis
figure 1.2 p. 9
A feedback system involves a cycle of events where the status of a condition is continually monitored and fed back to a central control.

Components of feedback loop:
1. **Stimulus** - change in environment that is sensed by:
2. **Receptors** - these sense changes and sends information to:
3. **Control center** - receives the input and provides output to:
4. **Effectors** - these bring about a change to return to homeostasis

**Negative feedback system** - the system that reverses the original stimulus. **Most systems use this type.** Used to maintain constant set points over long periods of time.

**Example:** Homeostasis of blood pressure. Set point: Keep blood pressure about 120/80.
If low, constrict arterioles to create more resistance, drink fluids to increase blood volume, slow heart rate, etc.
If too high, decrease heart rate. see fig 1.3 p. 10

**Positive feedback system** - The response enhances or intensifies the original stimulus until stimulus is removed. Rarely used in human physiology.

**Example:** Fig 1.4 p11 Homeostasis of labor contractions (oxytocin stimulates more uterus contraction). Want more and stronger contractions until birth occurs (the baby leaves and quits stretching the uterus that removes the stimulus).
**Systems of the Human Body**
see table 1.2 page 4-6.
An introductory review of the 11 body systems.

Body systems work together to bring about **homeostasis**.

**There are 2 Controlling Systems:** Monitor and detect changes in body components.

1. **Nervous System**- Components: brain, spinal cord, nerves, and sense organs.
   Functions: regulate body activity through nerve impulses.
   Consciousness, awareness.

2. **Endocrine System**- Components: All glands that produce hormones.
   Function: regulates body activity through hormones in the blood.

Both serve to coordinate all other body functions.

**Vegetative Systems:** Provide nutrition for cells and removal of wastes. Vegetative refers to a passive process.

1. **Digestive System**- Components: long tube with associated organs (gallbladder, liver, pancreas)
   Function: breakdown food mechanically and chemically, and elimination of solid waste.

2. **Respiratory System**- Components: Lungs and tubes leading to exterior environment.
   Function: supplies $O_2$, eliminates $CO_2$, and regulates acid-base balance of body (with kidneys).

3. **Urinary System**- Components: organs that produce and eliminate urine.
Function: eliminate metabolic wastes, regulate water balance, and maintains acid-base balance (with respiratory system).

   Function: Transportation.
   Distributes nutrients to cells (O₂, glucose), eliminates waste from cells (CO₂, ammonia, lactic acid).
   Maintains acid-base balance, protects against disease (non specific immunity), prevents hemorrhage by forming clots, regulates body temperature.

Protective Systems: Provide protection for the organism and its parts.

1. Integumentary (Skin) System- Components: skin and derivatives (hair, nails, sweat and oil glands).
   Function: mechanical protection, regulate body temperature, eliminates wastes.

2. Lymphatic and Immune System- components: lymph, lymphatic vessels, lymph nodes, spleen. Lymphatic tissues contain large numbers of white cells called lymphocytes.
   Function: protects body by filtering blood and production of proteins called antibodies and immune cells.

3. Cardiovascular System: blood also has cells that protect the body: phagocytes and neutrophils.

Other Systems

Function: protects and supports the body. Assists in body movements. Stores minerals.

2. **Muscular System**- Components: primarily skeletal muscle tissue which is attached to bones, also smooth and cardiac muscle.

   Function: Powers movements of the body and stabilize his body positions. Generates heat.

3. **Reproductive System**- Components: organs (testes and ovaries) that produce reproductive cells (gametes), and other organs that deliver and store reproductive cells.

   Function: Reproduce the species over time.

This brief review of the body systems helps demonstrate the dependence of the various systems on each other for functioning of the entire organism to maintain **homeostasis**.
Basis of Cell Structure and Function  Chapter 3 p 60

Introduction

The cell is the basic unit of function in humans. They are smaller than can be seen without a microscope so it's hard to relate to cells as life.

The 7 characteristics of living cells or what living cells do are:
- Intake, metabolism (anabolism and catabolism), output (elimination of wastes), reproduction, movement, growth, responsiveness.

Although each of your 100 trillion cells exhibit each of these characteristics that does not mean that all of your cells are exactly the same. In multicellular organisms we tend to see a division of labor, or specialization, amongst the cells. That is, the different cells within the body perform different jobs or functions. Ex: muscle cells and nerve cells.

Fig 3.1 p 60
Due to the differences in function of the cells we can see great diversity in cell:
1. **Size**
2. **Shape Of Cells**

Cell Size
Cells vary in size from the smallest bacteria (1 micrometer) to the largest cell, an ostrich egg. There are certain limits that are placed on cell size. They cannot be infinitely large or infinitely small. Information must pass from cell membrane to nucleus in a timely way for responses to be relevant. Human cells mostly between 7-30um across. However, RBCs are about 7 um where a nerve cell can be a meter long.
**Limits To Cell Size**

1. A cell must be at least large enough to contain the macromolecules (proteins and nucleic acids and their products) and organelles necessary to sustain life.

2. The upper size limit of cells depends on 2 things:
   
   a. Ability of the nucleus (eukaryotes) to control what takes place in the cytoplasm.
      
      Cells can sometime get around this by fudging a bit. If the cytoplasm is very large, you may find multinucleated cells (muscle cells).

   b. The extent to which nutrients and waste products can efficiently pass through the cytoplasm. The greater distance involved, the much greater the time involved in moving from one place to another.

**Differences in the shape of cells are obvious.** Some discussion on p. 107-8

The shape of cells depends on function.

Examples:

1. Cells that absorb things typically have microvilli. These increase the amount of absorptive or secretory area significantly without increasing the amount of cytoplasm.

2. Shape of RBC (erythrocytes), a biconcave disk, allows maximum surface area for rapid diffusion of $O_2$ and $CO_2$. No nucleus, just a sack of macromolecules, so very flexible for passage through capillaries.

3. Thin for allowing passage of materials. Squamous pulmonary epithelium of alveoli allows for diffusion of gasses to adjacent capillary endothelium.
Movement of Materials Across Plasma Membranes

How do cells acquire the materials necessary for activity?

Things may move into cells by passive processes that do not require energy use by the cell:
see table 3.1 page 74.

1. Diffusion.
2. Osmosis.
3. Bulk flow.

Or, they may move into the cell by active processes that require energy used by the cell:
1. Active transport.
2. Vesicular transport.
   a. Endocytosis
      1. Pinocytosis.
      2. Phagocytosis.
   b. Exocytosis.

**Passive Processes**
Movement of molecules due to differences in concentration gradient or pressure.
No energy is expended by the cell.
Molecules are always in motion (random) using kinetic energy obtained from their surroundings.

4 types of passive processes:

1. Diffusion (simple diffusion)- movement of molecules from an area of high concentration to an area of low concentration. See fig. 3.6 p.65
   Example: Smoking cigarette in a room. Smoke will first be concentrated around smoking person in room. Slowly the smoke moves away from the concentrated source (to our dismay) until the molecules become
equally distributed in the room at which time they are said to be in equilibrium. This called second hand smoke.

Have the molecules stopped moving? No. There are just as many molecules moving in one direction as another but no net movement. This called Dynamic equilibrium.

**Rate of Diffusion** p. 65-6
Rate of diffusion will be influenced by:

1. **Temperature**: increase temperature, increase kinetic energy, increase rate of diffusion.

2. **Concentration gradient (difference)**: increase gradient, increase diffusion. The rate of diffusion will slow as equilibrium is approached, or said another way the gradient decreases.

3. **Size of diffusing molecule**: increase size (molecular weight and radius of molecule), decrease diffusion. More friction with solvent.

Where does diffusion take place in the human body?
Anywhere solute is dissolved in solution (water based solvent in physiologic systems).

a. Selective movement across a lipid membrane permeable to: 
   H₂O, small non polar uncharged molecules, fat soluble.
   Ex: H₂O, O₂, CO₂, N₂, steroids, fat sol vitamins, small alcohols, ammonia.
   Ex: Passage of gases at lung surface (CO₂, O₂).
   Note: impermeable to ions and polar molecules. Water in an exception.

b. Selective movement across a membrane within a specialized transmembrane protein channel permeable to: small to medium polar and charged substances.
   Ex: Facilitated diffusion of glucose molecule, a polar molecule
   Note: larger molecules such as proteins are too large to diffuse through a membrane.
2. Osmosis - Is a specialized type of diffusion. Fig. 3.7 p.66

Osmosis is the movement of water (through a selectively permeable membrane) from an area of higher water concentration to an area of lower concentration.

In the case of osmosis, selectively permeable means the membrane will allow the passage of water molecules but not solutes. These solutes are general charged (electrolytes: Na+, Cl-) or polar (glucose). The selectively permeable membranes in our experiments mimic the phospholipid cell membranes of animal cells.

Examples of osmosis in the body:
   a. Kidney urine formation. Osmotic gradient established in nephron so water and salts can be selectively retained or removed.
   b. Movement of interstitial fluid back into capillaries after forced out by bulk flow of arterial pressure.
   c. Movement of water through the walls of the digestive tract as solutes are absorbed.

Remember: Body compartments, and cells and interstitial spaces are separated from each other by selectively permeable membranes. If osmotic balance gets disturbed, water will move to rebalance the concentration gradient. The results can be hazardous to the cell!

Example:
   Question: How do you wash red blood cells? Distilled water? No, use a saline solution.
   Tonicity and red blood cells. See figure 3.8 page 67

Isotonic saline = 0.9% NaCl. Isotonic saline has the same solute concentration as the cell contents of a red cell. Cell cytoplasm = 0.9% solutes and 99.1% water
Hypotonic saline or distilled water will cause the red cells to swell or burst. Hypotonic solution means there is less solute outside than inside the red cell.

Hypertonic solution will cause the red cell to shrink and become crenated. Hypertonic means the solution has more solutes outside than the inside of the red cell.

Example: Severe malnutrition in the human leads to loss of protein in the body and the blood plasma. The blood plasma has less solute so becomes hypotonic (less ability to pull water). Interstitial fluid water does not move back into the venules as it should, and can cause bloating and a large abdomen.

Think of the body as a series of compartments separated by membranes. If osmotic balance is off, fluid will move to one side or the other to balance the pressure. ECF (extra cellular fluid found in interstitial space and vascular space) versus ICF (intracellular fluid inside of cells). These concepts are important in successful IV therapy.

3. Bulk Flow: the movement in the same direction of large numbers of solute particles in solution due to differences in water or air pressure. Forces move particles in unison, not random motion.

   Example: Filtration- of materials through a permeable membrane, due to pressure.
   
   Example:
   a. Passage of materials through capillary walls due to blood pressure.
   b. Non-selective filtration that occurs in the nephron.
   c. Movement of air in and out of lungs due to changes in air pressure by lung expansion and contraction.

4. Facilitated diffusion Fig. 3.10 page 69
   Solutes (ions, glucose, urea, some vitamins) move down a concentration gradient from a region of higher concentration to a
region of lower concentration with the help of specific integral proteins in the phospholipid bilayer cell membrane. These are under genetic control.

These serve as water filled channels or transporters (carriers) for specific substances.

These substances maybe too lipid insoluble to diffuse through the plasma membrane.

Example: Glucose is moved across the plasma membrane by a transporter protein.
The glucose is phosphorylated as it moves into the cell and keeps the intracellular concentration of glucose very low to favor the concentration gradient.
Insulin can accelerate the facilitated diffusion by promoting the insertion of transporter proteins and thus helps to achieve homeostasis by moving glucose into cells quickly.

Active Processes for transmembrane transport

Active Transport: The movement of molecules across a cell membrane from an area of lower concentration to an area of higher concentration, requiring energy expenditure by the cell.

Opposite of osmosis. Fig 3.11 p 70
Energy is usually in the form of ATP that is used to change the shape of a transport protein in the plasma membrane. Fig 2.25 p 54
About 40% of the ATP generated in a cell is used for active transport.
70% in neuron.
This involves moving things against a concentration gradient. So they are often called pumps.

Example substances: Na⁺, K⁺, H⁺, Ca²⁺, Cl⁻, amino acids.

Example of active transport: Na⁺/K⁺/ATPase pump. Fig. 3.11, page 70
a. This pump expels Na⁺ (3) from cells and brings K⁺ (2) inside.
The pump maintains a low concentration of Na\(^+\) in the cytoplasm by pumping it out against the concentration gradient.

b. The K\(^+\) moves into cells against its concentration gradient.

All cells have hundreds of Na/K pumps in each square micrometer of membrane surface. This pump must work continually because K\(^+\) and Na\(^+\) slowly leak across the plasma membrane through leakage channels down their concentration gradients. These pumps help provide the gradients necessary for muscle contractions and nerve impulse transmission to occur.

**Drugs or poisons** can affect the active transport mechanism.

Example: Cyanide is lethal because it can shutdown active transport in cells throughout the body. Effects metal containing enzymes, esp. cytochrome oxidase and enzyme used in mitochondrial respiration to make ATP.

Example: p. 71 Digitalis slows the membrane bounq sodium pump as it binds to Na+K+ ATPase in cardiac myocytes so sodium accumulates in the cell. This causes more Ca\(^{2+}\) to stay in cell and results in a stronger heartbeat. The slower heartbeat allows time for more ventricular filling and blood ejection. Useful for congestive heart failure treatment or used on poison darts by native peoples.

The point: Ion balance inside and outside cell is crucial to normal functioning of nerve and heart cells, especially K+.

We won’t discuss symport (2 substances move in same direction) and antiport (2 substances move in opposite directions) activities of cellular membrane transport.

**Vesicular Transport**- large molecules cannot move directly across the cell membrane and must be transported in bulk processes.

We will discuss:
3 types of vesicular transport that bring materials into the cell, and, 1 type that moves materials outside the cell.

Endocytosis- processes that brings substances into cells using a segment of the plasma membrane to surround and enclose the substance to be taken in the cell. 3 types will be discussed:

1. **Phagocytosis- "cell eating".** Fig. 3.14 page 73
   Solid particles are surrounded by projections of the plasma membrane (pseudopods) and become enclosed within a sac of membrane (phagocytic vesicle) that moves into the cell. The solid material is digested by enzymes provided by lysosomes.
   
   Example: Phagocytes (neutrophils, macrophages) are cells present in most tissues that destroy bacteria and other foreign substances. Crawl around doing surveillance or signaled to aggregate at sites of infection or cellular damage.

2. **Pinocytosis- "cell drinking".** Fig 3.15 p 73
   Engulfed material (ECF and molecules) is a tiny droplet of extracellular fluid that becomes surrounded by cell membrane as it folds inward forming a pinocytic vesicle.
   Ex: Used to degrade macromolecules to amino acids for cell growth.

3. **Receptor-mediated endocytosis** Fig. 3.13 page 72
   Specific molecules or particles can bind to specific proteins receptors in the plasma membrane.
   Examples:
   a. Needed substances such as cholesterol, iron, and vitamins can be transported this way.
   Ex: Inherited lack of protein receptor = familial hypercholesterolemia. Cholesterol accumulates in blood, increasing coronary artery disease risk.
b. **Hormones** can deliver messages to target cells to perform a specific response.  
  Ex. insulin  
b. **Viruses** enter cells by this mechanism.  
  Ex: HIV (human immunodeficiency virus) enters human cells by binding to the receptor called **CD4** found on **helper T cells**.

**Exocytosis**  
Fig. 3.22 page 80  
The process that brings substances from inside the cell to the cell membrane where they are released to the outside.  
Membrane enclosed structures called **secretory vesicles** form inside the cell (golgi apparatus) and fuse with the plasma membrane.  
This process occurs in most cells.  
Example:  
1. **Nerve cells**: release neurotransmitters to influence another neuron or muscle cell.  
2. **Secretory cells**: digestive enzymes released to the GI tract and protein hormones (insulin) are released to the blood stream.

**Cell Structure and Function**  
fig. 3.1 p.60  
Two structures are apparent to us when we view cells with our microscope in the lab are:  

- **Nucleus**: Directs the cellular activity through genetic expression.  
- **Cytoplasm**: Substance or matrix between cell membrane and nucleus.  
  It contains many small factories type structures. These are called cell organelles and are responsible for synthesis, metabolism, and packaging of materials.  
  We will discuss a number of these organelles.

**Cell Membrane or Plasma Membrane**
The cell’s outer membrane limits the boundaries of cell, separating its contents from internal fluids of the body. The membrane must stay intact for its survival. We will find this is not the only membrane found in a cell. There are several others found in internal structures. The membrane systems serve to compartmentalize the various organelles and their functions within a cell.

**Membrane Systems**  
fig. 3.2 p 61
All membranes are composed of 2 major components:

1. Lipids
2. Protein

All membranes however are not alike; they vary the proportion (ratio) of lipid and protein.

Let's take a look at how the 2 components of a membrane (lipids, protein) are arranged with each other to form a membrane.

**Construction of a Membrane**

A lipid (phospholipid) could be diagrammed as follows:  
figure 2.18, p. 47
There are 2 major components:

1. The **head** is composed of a phosphate group linked to a small charged group that is **hydrophilic** ("water loving"). It occupies the 3rd position of the glycerol backbone of a triglyceride.

2. **Fatty acid tail**: the 2 fatty acids that make up the tail have **no polar charge** and are **hydrophobic** ("water fearing").

Lipids take on the following arrangement in the membrane:  
fig. 2.18 p47
Notice the hydrophobic tails pointing inward towards each other inside the membrane and hydrophilic heads pointing outward facing the interstitial and the intracellular areas. We can see from this arrangement that molecules not soluble in lipids will have a hard time getting through the lipid portion of the membrane. This creates a barrier to diffusion of most substances, especially those that are polar or charged.

**Membrane Proteins**

How do such polar molecules such as glucose (not soluble in lipids) get in? Or through membrane?

Protein subunits "float in a sea of lipids" within the membrane.

See figure 3.2 p. 61

Notice how the phospholipid bilayer membrane is embedded with many different proteins. These are generally not in a fixed position but can move in a fluid motion with the lipids. Some proteins extend from cytoplasm to extra cellular space while other are more in or outside the membrane.

**Functions of membrane proteins**  fig. 3.3 p.63

Fig 3.3 part 5

1. **Cell identity markers**

Some proteins are antigens that serve as self recognition cell markers (or cell identity markers). Tissue transplant antigens, blood types, immune functions, species barriers, etc.

Example: each person has their own specific antigens (major histocompatibility (MHC) antigens) that its body's immune system will recognize as being "self".

In transplants from other people, rejection reactions happen because of the different ‘self’ antigens on the donor cell surface.

Foreign antigens stimulate an immune response (a cellular or antibody attack) in the recipient to combat the foreign material.
ABO and Rh blood groups are based on the presence of absence of membrane proteins.

Fig. 3.3 Part 1&2
2. Control Passage of Substances
Some proteins (transporters or ion channels) can act as transport devices, helping molecules to get into the cells. Most membranes are selective: they let some things through and not others.

Factors That Determine Membrane Selectivity other than proteins:

a. Thickness of Membrane- simply a greater distance to cover. E.g. diabetes, CF

b. Size of Substance Attempting to Penetrate- a few small, uncharged, non polar molecules (oxygen, CO₂) and a few small polar (for example, water and urea) can pass through the phospholipid bilayer.
   Pore size (7-8 angstroms) in a channel determines what will penetrate.
   Glycerol, ethyl alcohol are near the upper size limit for pore passage.

c. Lipid Solubility- membrane contains much lipid. The more lipid soluble (nonpolar, hydrophobic) a molecule is, the easier it will travel through the membrane.
   Ex:
   1. Lipid soluble antibiotics can enter CNS.
   2. Lipid soluble hormones go straight to nucleus to influence cell activities.

d. Electrical Charge on membrane in comparison to charge on molecule and ions.
   Like charges repel, opposites attract. Fig 3.4, p. 64
Most cell membrane membranes have a negative potential inside and relative positive outside. This aids inflow of positive ions (cations), and hinders the inflow of negative ions (anions). This electrical potential and a charged substance moves down its gradient.

Proteins act as transporters that pick up a substance on one side of the membrane and shuttle it through to the other side where it is released. These transporters (carriers) are very selective and control the transport of specific substances.

Fig 3.3 part 4
3. Membranes are involved in enzyme controlled reactions. Enzymes (organic catalysts) that alter rate of reaction, are present in membranes.
   Examples:
   a. Digestive enzymes in small intestine epithelium.
   b. Enzymes involved in electron transfer in mitochondria.

Fig 3.3 part 3
4. Membranes contain binding sites (receptors) for certain chemicals.
   Example: hormones, neurotransmitter, a nutrient.

Fig 3.3 part 6
5. Cytoskeleton anchor (linker)
Anchors cell filaments and tubules of cytoskeleton inside cell to membrane to aid in stability, shape, or movement.
Cell Organelles and Cell Organization  Chapter 3

see fig. 3.1, p.60

Introduction
All the structures within the cell boundaries are called organelles. They are all limited by or consist of a membrane. Each has a characteristic shape and specific function. They are dependent on each other for cell processes just as the organ systems of the human body must function together for survival.

Cell Organelles

**Nucleus** Fig. 3.25 p.84
Control center of the cell.
Contains DNA = heredity blueprints or the genome. We will discuss DNA and heredity later.

Functions:
1. Contains the information for the synthesis of protein (gene expression). Fig 3.27 p85 Proteins create structure and functions of the cell. Ex: contractile proteins, enzymes
2. Controls the cells ability to reproduce (divide).
3. Contains nucleoli- rRNA and ribosomes are manufactured here. Ribosomes are important structures for protein synthesis.

**Endoplasmic Reticulum (ER)** Fig. 3.20. p.78
An extensive system of membrane channels (cisterns) that are found throughout the cell. ER is continuous with the nuclear envelope and extends throughout the cytoplasm.

Functions:
1. **Rough ER** primary function is in protein synthesis. Membranes are studded with ribosomes (appear rough in EM pictures).
2. **Smooth ER** (without ribosomes) is a site for synthesis of lipids, steroids (a type of lipid), and carbohydrate, as well as a site to detoxify chemicals. Via enzymes.

3. ER provides an internal transport system for the cell to process and sort manufactured molecules and then move them where they are needed.

**Ribosomes**  
Fig. 3.19 p.78
A 2 subunit structure, one large, one small manufactured in the nucleus and move into the cytoplasm to function.

Ribosomes may be found free in the cytoplasm, mitochondria, or associated with the wall of ER.

**Functions:**
1. Is an organelle directly involved in protein synthesis (making of protein).
2. Rough ER produces protein to be used outside of the cell or in cell membrane.
3. Free ribosomes are also found in the cytoplasm not associated with ER. In this case they synthesize protein to be used inside of the cell.

**Golgi complex (apparatus)**  
Fig. 3.21 p.79, fig. 3.22 p.80
A membrane complex that processes, sorts, packages proteins and lipids into vesicles, especially in secretory cells.

**Function:**
Organizes the protein that has been produced in the rough ER and lipids into a membrane-bound package (secretory vesicle) for release to the outside of the cell. Molecules may be modified before release.

**Mitochondria**  
Fig. 3.24 p.83
“Powerhouses of the cell”.
This where a process called **cellular respiration** takes place. Cellular respiration is a universal process in all cells = aerobic chemical process that produces energy.

**Function:**
1. Mitochondria are the major source of energy for the cell. 
2. The energy is produced in the form of **ATP** and the number of mitochondria varies with the type of cell. 
Cells that are very active or synthesize a lot of protein (e.g. liver, muscle, kidney tubule cells, brown fat) will have more mitochondria than others.

Note: All mitochondria are of maternal origin (from the cytoplasm of the egg). Mitochondria contain their own DNA (mtDNA). Fathers only contribute nuclear DNA to their children. Can use to ID missing persons using a maternal relatives mtDNA.

**Lysosomes**  
Lysosomes contain digestive enzymes (60 or so) and low pH (5). Nickname = “garbage disposal of cell” capable of digesting large molecules, making smaller molecules of the larger ones.

**Functions**
1. Things like heat denature (inactivate) proteins so it is necessary to recycle of them and replace them with a new one. Lysosomes dispose of the denatured ones by digestion and return amino acids to the cytoplasm. A wide variety of molecules can be broken down by the enzymes found in lysosomes. Human liver cell recycles half its contents per week.

2. If a cell is injured in some way, lysosomes will digest damaged organelles. Clean up cellular debris in tissue (autophagy).

3. There are specialized cells in the blood stream called macrophages and neutrophils. When bacteria infect tissue, these phagocytes will engulf microorganisms and their lysosomes will digest them.

**What can happen if lysosomes don’t work right?**

*Tay-Sachs disease* is an inherited disease of a single faulty lysosome enzyme called HexA. Causes buildup of a membrane glycolipid in nerve cells that leads to early death (about 5 years of age).
Autolysis occurs at death due to release of lysosomes. It takes effort to keep lysosomes intact. This ends the rigor state of death after several hours as lysosomes dissolve cellular structures.

See table 3.2 p 86 for a quick review of cell parts and function.

**Cell Organization**

**Coordination of Cell Organelles**

Examining protein synthesis in a basic way will allow you to see the coordination of various organelles:

**Fig 3.27 p 85**

- a. Blueprint for protein synthesis is found in DNA of nucleus.
- b. mRNA carries message down the ER tunnel to a ribosome where protein is manufactured.
- c. Protein travels through ER to Golgi complex where protein is packaged and excreted to outside of cell through plasma membrane.
- d. Where does energy come from? Mitochondria that makes ATP for the entire cell.

**Reproduction of Cells**

**Normal Cell Division**

2 types: mitosis and meiosis

1. **Mitosis: Somatic Cell Division**

The Cell cycle  

**Fig 3.31 p 90**

**Mitosis**  

Fig 3.33 p 92

The reproduction of most cells takes place in a process known as mitosis = cell division. In the process of mitosis, 2 daughter cells are produced that are genetically identical to the parent cell. Same number and type of chromosomes,
Mitosis takes place in somatic (general body cells) cells, all body cells except gametes. The rate is different in for each tissue. Example: skin cells of epidermis, and lining of gut.

Note: We will not study the stages of cell division in this class.

2. **Meiosis- Reproductive Cell Division**

Sex cells reproduce differently than a somatic cell cells in a process known as meiosis.

Comparison of mitosis and meiosis  
fig. 28.2 p.1015

In meiosis the numbers of chromosomes are halved. Therefore, sperm and egg carry ½ the number of chromosomes as seen in the somatic cells of the species. For humans ½ = 23. However, when egg and sperm unite in fertilization, a zygote (fertilized egg) is produced and the chromosome number is restored, 46 in humans.

Cell reproduction Gone Wild (Astray)!

“Cancer”- a homeostatic imbalance. Uncontrolled cell proliferation. A lack of control of the cell cycle. p 95

Typically the number of cells produced by the body balance the number of cells that have died or are lost, a homeostatic balance. These processes are monitored in cells locally are under genetic control.

Ex: p53 is tumor suppressor gene on chromosome 17. It slows cell growth and may initiate cell death if the cell DNA is damaged. If this gene is damaged, a wide variety of cancers may results. It has been referred to as the ‘guardian angel of the genome’.

**Neoplasm**- Literally means "new formation" but it generally carries with it the connotation of non-beneficial formation of a cell mass. Cells divide without the normal controls.

Cells in a neoplasm have no useful function, but like all other cells require nutrients for nourishment (at the expense of other cells). Due to
rapid growth, they may out compete other cells in the area. This can lead to weight loss, organ dysfunction, fatigue, or other symptoms a the level of the human.

There are 2 major types of neoplasms: **benign** and **malignant**.

**Benign neoplasms**
1. Usually grow slowly.
2. Localized within a fibrous capsule that separates them from normal tissue.
Show no extreme structural differences from other cells.
Benign neoplasms can cause problems!
   - Create problems if they put pressure on delicate areas like the brain.
   - Or if cause excessive output of chemicals like hormones.

**Malignant neoplasm** - Differ from benign in that they:
1. Grow rapidly.
2. Usually lack fibrous capsules.
3. Commonly release cells into blood or lymph circulation.
   - Metastasis = movement from one part of body to another (e.g. cancer cells in this case). New tumors form where cancer filter out or deposit.
Malignant neoplasms are the **second leading cause of death**. (#1 = heart disease)
The word ‘tumor’ is used commonly but does not tell us much about the problem. Tumor means swelling or mass.

**Terminology of cancer** (optional discussion)

Neoplasms are named by adding suffix "oma" (tumor) to name of cell of origin.
Examples:
- Melanoma - cancerous neoplasm of melanocytes. Melanocytes produce skin pigment melanin.
- Osteoma - bone neoplasm.
- Lipoma - adipose tissue neoplasm. These cells contain fat or lipid.

**Causes of Cancer**
Neoplasms are believed to be caused by many agents.

Carcinogens are cancer causing agents. Cigarette tars, UV light, and many chemicals lead to mutations of cell growth mechanisms. Several mutations are required. A multi step process. It seems like everything is carcinogenic these days. Carcinogens are responsible for about 60-90% of cancers.

Hereditity is now being demonstrated to also play a major role in cancer development. Starts you off with mutations from birth that others might get through environmental exposure.

Viruses are responsible for about 25%. E.g. papillomavirus, hepatitis B, herpes simplex type II.

7 danger signals of cancer. From the American Cancer Society
1. Any unusual bleeding or discharge.
2. Sore that does not heal.
3. Any change in normal bowel habits lasting > 3 weeks.
4. Change in size or color of wart or mole.
5. Chronic indigestion or difficulty in swallowing. Esophageal reflux.
6. Lump or thickening in breast or elsewhere in body.
7. Persistent hoarseness or cough.

Detection Let’s review 4 techniques:
1. Biopsy - removal of tissue for microscopic exam by needle or surgery for diagnosis by a pathologist.
2. Imaging - X-ray, Cat scans, MRI scans.
3. Blood markers - PSA(prostatic specific antigen), CA125: used to detect and monitor ovarian cancer. These are proteins found in the blood that originates from cancerous tissue. They are readily accessible by venipuncture.

Treatment options
1. Surgery - surgical removal of a will defined tumor and possibly regional lymph nodes.
2. Chemotherapy- the chance to selectively damage neoplasm to a greater degree than normal tissues by administering cytotoxic drugs. Usually a multiple drug treatment by IV therapy.
3. Radiation therapy- focused beam of x-rays to region of tumor to kill malignant cells.
4. Immune therapy- target malignant cells with an antibody to a unique marker on tumor cells with adjunct therapy to induced a vigorous immune response (e.g. IL2).

Other terms
- Oncology- the study of tumors
- Oncologist- a physician that specializes in diagnosis and treatment of tumors.
Atoms
These extremely small particles are the smallest unit of chemical division to retain the properties and characteristics of an element. See periodic table of elements appendix B1

   Ex: Hydrogen atom = 10^-8 cm in diameter or 0.1 nm.

If an element is broken down by losing some subatomic particles, further it will change chemical characteristics.

There are dozens of types of subatomic particles, but we will study only the 3 that are involved in chemical reactions of molecules.

Fig 2.1 p 28

The subatomic particles are the proton, neutron, and electron. These 3 particles interact to form atoms.

Nucleus of the Atom
The core of the atom = nucleus. The nucleus contains the mass of the atom.
Within the nucleus are one or more of two type of subatomic particles.

1. Proton (p+)
   1. A positively (+) charged subatomic particle.
   2. # of protons in an atom determines its chemical characteristics and atomic number.
      On earth we see naturally occurring atoms made of 1-92 protons per atom. Synthetic elements have been made by humans.
3. Each of the atoms having various unique properties are called **elements**. Fig. 2.2 p.29

**Element**
A substance composed of atoms that are the same type.
92 natural + 19 or more created by scientists.
Example of elements:
- H = 1 proton
- C = 6 protons
- O = 8 protons

# of protons of an atom = **atomic number**.

2. **Neutron** (n⁰)
The other subatomic particle found in the nucleus of an atom is the neutron.
It has no (0) charge at all. But the mass = to that of a proton.

1. # of protons + # neutrons of atom = atomic weight
   Example:
   - carbon MW = 6p + 6n = 12
   - sodium MW = 11p + 12n = 23
2. Atomic weight is approximate since almost all of the mass of an atom is concentrated in the nucleus.
   a. Only a very small portion of mass is found outside the nucleus.
   c. Atomic weight on a periodic table also reflects the existence of **isotopes** of that element that contain **variable numbers of neutrons**.
   Example: carbon = 12.01 So, there are rare isotopes with more than 6 neutrons. Heavy isotopes tend to be unstable and degrade over time to more stable configurations.
   Note: Some isotopes are useful in medicine to aid in imaging scans of body systems, however they may be dangerous to handle because of their radioactive properties as they degrade.
d. Remember, neutrons do not change the chemical reactivity of an atom. So, you can have atoms of the same element with different molecular weights. But the number of protons must remain constant for the atom to retain its elemental qualities.

e. **Electrons (e⁻)**
A third type of subatomic particles exists outside of the nucleus, in what has been described as a type of cloud are smaller **electrons**.

Electrons are negative (-) in charge.
The negative charge is sufficient to balance the positive charge of a proton.
Therefore, if an atom has = number of protons and electrons it is said to be electrically neutral (0 charge) or a net charge of 0.

If atom contains more electrons than protons or vice versa, it will have a net charge.
Such an atom is called an **ion**.
Example: Na⁺ has 11p and 10e
Cl⁻ has 17p and 18e
Ca²⁺ has 20p and 18e
Note: Ions are very important in explaining physiologic functions, especially in muscle and neuron activity.

In comparison to the other subatomic particles mentioned, electrons have **almost no mass**.
Example: about one ounce of your body weight = electrons, rest is protons and neutrons.
Electron = 1/1,840 the mass of a proton or neutron.

Unit of measure of mass = daltons
proton = 1.007, neutron = 1.008, electron = 0.0005

**Molecule**
We know that atoms combine to form molecules. Molecules provide for much of the wide variety of characteristics of cells and their function.

2 or more atoms held together by some kind of chemical bond = molecule

**Introduction to chemical bonds**

Electron interactions are the basis of all chemical reactions. Electrons occupy a shell that will hold a maximum # of electrons. 

When the shells are completely filled, they are very stable and tend not to react with other atoms.

Example: shell #1 = 2, #2 = 8, #3 = 18, #4 = 18  fig 2.2 p 29

To achieve stability an atom tends to empty out or fill up their outer shell, which ever is more favorable.

Example:
1. Na (AT=11) wants to give up 1 electron, Cl (AT=17) wants to gain 1 electron. So, these 2 react together.
2. He (AT=2) is called inert (won’t readily react with other elements), as its outer shell is filled.
3. One major factor in predicting the chances of a chemical reaction occurring between molecules or atoms may be anticipated based on electronic configurations in these shells.

**Chemical bonds** p 31  3 types will be discussed:

1. **Ionic bonds**  Fig. 2.4 p. 31
   1. Atoms held together due to their net charges.
   2. Formed between strong electron donors (Ex: Na) and strong electron acceptors (Ex: Cl).
   3. Ions form readily in water solutions. Water interferes with the attraction between ions. Water is a polar molecule with positive and negative regions.
   4. Most ionic bonds in the human body are found in bones and teeth.

2. **Covalent bonds**  Fig. 2.5 p. 33
   1. Atoms held together by sharing pairs of electrons.
2. Usually 1, 2, or 3 pairs, noted as a single, double, or triple bond.

3. Electrons spend time around both bonded atoms in an attempt to complete their outer electron shells.

4. These are strong bonds that are present in all the macromolecules and water molecules in our cells.

5. Some molecules are polar to some degree and some are nonpolar.
   a. Polar means that the electrons are shared but spend more time around one atom than another because on atom pulls harder than the other on the electrons.
   b. A regional negative charge develops on the atom that pulls the hardest and a positive charge develops on the atom that is weaker.
   Example: water H₂O Fig 2.6 p 24 This makes water an excellent solvent for physiologic fluids.
   c. Nonpolar molecules have their electrons distributed evenly around its atoms and no regional charges form.

3. Hydrogen bonds fig. 2.6 and 7 p 34,
   1. Weak bonds where 2 atoms, usually oxygen or nitrogen on one molecule, associate with hydrogen on another molecule.
   2. These bonds do not form a molecule (only 5% as strong as covalent) but serve as weak links between molecules.
   3. They stabilize the structure of many large biomolecules when many hydrogen bonds are formed as the molecule folds.
      Note: These bonds are important to DNA and protein structure and function.
      The bonds act similar to a zipper in these large molecules with long repeating structures that can hydrogen bond with each other. 2.24 DNA p. 53
   4. H₂O molecules can form hydrogen bonds with itself and other polar molecules.
Atoms of a molecule may be the same. Examples: \(\text{H}_2\), \(\text{O}_2\) or different, \(\text{H}_2\text{O}\), \(\text{NaCl}\).

**Compound**

Atoms will also combine to form compounds. Molecules are made of 2 or more different kinds of atoms in definite proportions.

Is \(\text{H}_2\) or \(\text{O}_2\) a compound? No. \(\text{H}_2\text{O}\) or \(\text{NaCl}\)? Yes.

**Radical** table 2.5 p 42

A distinctive side chain that gives a biomolecule its individual identity. Called an R group or functional group.

**Chemical bonds and Energy Storage**

p 31 (chemical bonds), p 54-55 (ATP) p907-8 (anabolism catabolism and ATP)

Molecules and compounds are held together by chemical bonds. It takes energy to form bonds and a lot of the energy is stored in this bond as potential energy.

When bonds are broken, this potential energy is released. Example: ATP is the main energy source in living cells. It releases and transfers energy from high energy phosphate bonds to other biomolecules to do work in a cell.

\[
\text{ATP} \xrightleftharpoons{\text{Energy}} \text{ADP} + \text{Phosphate} + \text{Energy}
\]

When you eat sugar, bonds in the sugar are released providing energy. Fig 25.1 p908

Energy stored in a chemical compound is measured in terms of calories (lower case c). These are not the same as dietary calories. The relationship is: 1 dietary Calorie (Cal) or kilocalorie = 1000 chemical calories. Note upper case C in dietary calorie designation.
**Food Energy**
In terms of food energy, the food we eat has the following chemical equivalents:
In chemical calories:
- Carbohydrates = 4000 calories per gram
- Proteins = about same as carbohydrates.
- Fats = 9000 calories/gram

**The Composition of the Cell**
**Important Elements** table 2.1 p.28

Of 100 or so elements we know of, 4 elements makeup over 95% of the body.
These 4 elements are:

<table>
<thead>
<tr>
<th>Element</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>Carbon 18%</td>
</tr>
<tr>
<td>H</td>
<td>Hydrogen 10%</td>
</tr>
<tr>
<td>O</td>
<td>Oxygen 65%</td>
</tr>
<tr>
<td>N</td>
<td>Nitrogen 3%</td>
</tr>
</tbody>
</table>

These 4 = 96%

**Other important elements include** (each <2%):

<table>
<thead>
<tr>
<th>Element</th>
<th>Phosphorus</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>Sulfur</td>
</tr>
</tbody>
</table>

These 2 plus 4 above account for 99%

<table>
<thead>
<tr>
<th>Element</th>
<th>Magnesium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca</td>
<td>Calcium</td>
</tr>
<tr>
<td>Na</td>
<td>Sodium</td>
</tr>
<tr>
<td>K</td>
<td>Potassium</td>
</tr>
</tbody>
</table>

You can remember these by ‘mechanic’ (mgcanak)

<table>
<thead>
<tr>
<th>Element</th>
<th>Iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Iodine</td>
</tr>
</tbody>
</table>
6 of these elements, CHNOPS will combine in many ways to form most of the molecules found in living systems.

Important Molecules of Living Systems or Biomolecules

Only a few different kinds of molecules are found in large quantities in living systems.

<table>
<thead>
<tr>
<th>Biomolecule</th>
<th>% of body weight</th>
<th>male</th>
<th>female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water- H₂O</td>
<td>60%</td>
<td>62</td>
<td>59</td>
</tr>
<tr>
<td>Protein (amino acids)</td>
<td>17%</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>C,H,O,N,S</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(primarily muscle difference between sexes)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipids (fats) C,H,O</td>
<td>17%</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>Carbohydrates (sugars) C,H,O</td>
<td>1%</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>5%</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>(nucleic acids C,H,O,N,P + certain radicals, minerals, ions)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Important Molecules of Living Systems

Let’s take a closer look at these important biomolecules:

Water  p 38-39

Water is the most abundant substance in living systems even though it is inorganic in origin. It comprises from 60% in rbc's to 92% in plasma. Lean adult human bodies are 55-60% water. Its most important function is that of solvent of life’s chemicals.

1. **Solvent function of water.**  Fig 2.11 p 38

   Water is the solvent of our bodies. Solvent = aid dissolving medium. The reason it is such a good solvent is that it is a polar molecule.
The term "polar" means that one side of the molecule is slightly positively charged (hydrogen) and the other side is slightly negatively charged (oxygen).
In the case of water it looks like this:

\[ \text{H}_2\text{O} \]

See drawing of chemical structure of water showing regional polar charges: fig. 2.6 and 7 p.34.

The reason for the unequal distribution of charge is that the 2 H atoms share their electrons with the O atom in the formation of the bond (covalent).
However, the O keeps the hydrogen electrons more of the time than the hydrogens have them, making the oxygen side slightly negative and the hydrogen side slightly positive.

Water will dissolve NaCl because the positively charged sodium ion (Na\(^+\)) will be attracted to the O side (negatively charged) of a water molecule, and the Cl\(^-\) ion will be attracted to the H side (positively charged).

**Water has other important functions besides being a solvent:**

2. Water is the body’s medium for transport.
   Fluids are pumped or otherwise distributed throughout the body to transport nutrients and wastes.

3. Helps maintain cells at a constant temperature.
   Water is a good retainer of heat. Called ‘high heat capacity’.
   It is difficult to change the temperature of water (due to polar nature).
   In other words, it absorbs heat with modest change in temperature.

   This helps maintain homeostasis of body temperature.
   Much heat can be removed by sweating since water contains energy and it is dissipated as sweat evaporates.

4. Participates in chemical reactions.  Fig 2.15 p 44
Hydrolysis (breakdown) and dehydration synthesis (join smaller molecules) of biomolecules.

5. Serves as the body’s lubricant.
   Examples: Mucous and other lubricating fluids that lubes chest and abdomen, joints, moistens foods.

**Electrolytes**

Within the water of the body we will find ions collectively known as electrolytes. Substances that can dissociate into ions (electrically charged atoms) are electrolytes.

1. + charged ions = cations
   As they are attracted to a negatively charge pole (cathode).
   Note the ‘t’ in cation can viewed as ‘+’ sign.

2. - charged ions = anions
   As they are attracted to a positively charged pole (anode).

**Main electrolytes of the body:**

| Cations  |  |  |
|----------|  |  |
| Na⁺      |  |  |
| K⁺       |  |  |
| Ca²⁺     |  |  |
| Mg²⁺     |  |  |

| Anions   |  |  |
|----------|  |  |
| Cl⁻      |  |  |
| HPO₄⁻    |  |  |
| SO₄⁻     |  | sulfate |
| HCO₃⁻    |  | bicarbonate |

**Electrolytes are important in:** p 997

1. Osmotic gradients. Example: Na+, K-
2. Influence enzyme activity. Examples: Mg++
Will discuss this in muscular and nervous physiology chapters.

**pH Scale** fig. 2.13 p.41

Scale: 1-14  
7 = neutral, > 7 = basic, <7 = acid.
pH 7 means there is $1 \times 10^{-7}$ [H$^+$] in solution.
Note: the negative exponent is changed to a positive number in the pH scale.
pH of fluids in the body can vary by function.
Examples: table 2.4 p. 41
Blood pH must be stable between 7.35 to 7.45 or cellular functions cannot function properly. Death will occur if pH is not restored within minutes.

**Maintaining pH: buffer systems**

Weak acid/base + strong acid/base are components of a buffer system.
Buffers maintain pH in close limits in the presence of strong acids or bases. Strong acids and bases can contribute H+ or OH- that can change pH dramatically if not removed. Weak acids and bases act as chemical sponges to remove these ions.

See chemical equations for carbonic acid-bicarbonate buffer system. p. 41.

To remove excess of H$^+$, the weak base bicarbonate removes H$^+$.

\[
H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow H_2O + CO_2
\]

bicarbonate acts as a weak base
To increase $H^+$, carbonic acid, a weak acid, dissociates to provide $H^+$.

\[ \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \]
carbonic acid acts as a weak acid

Example: When a patient having a heart attack comes to the ER and their pH is 7.0, what buffer is given? Bicarbonate to remove the $H^+$ and move the pH toward 7.4.
Carbohydrates

Carbohydrates are compounds made of C, H, O. see fig. 2.14 for example structure
Close to the ratio of 1:2:1, or CH₂O.
Therefore, the term: carbo (C) hydrate = (H₂O) or ‘watered carbon’

Examples: sugars and starches (animal starch = glycogen, plant starch = cellulose).

Represents about 2-3 % body weight.
Mainly used for energy in humans but can be structural as in DNA, RNA.

Sugars are formed by photosynthesis. We cannot make them ourselves, so must consume in diet.

Note: Cellulose is the most abundant organic substance on earth.
It is the primary structural component of plant cell walls.
Humans lack the enzymes to digest cellulose but use it to help digest other food as dietary fiber.

Carbohydrates have 3 major properties:

1. Have a high caloric value and principal energy source for most living systems.
2. Are the basic materials from which many other types of molecules are made.
3. They are soluble in water (except polysaccharides).

There are 3 recognizable forms of carbohydrates: see table 2.6 p. 43

Monosaccharides, Disaccharides, Polysaccharides.
Mono = 1, Di = 2, Poly = many; saccharide = sugar.

1. Monosaccharides
   1. A monomer, the basic building block. 3-7 carbons, usually 5 or 6.
2. Sometimes called "single sugars" a term that includes both mono-
and di- saccharides

Example: glucose (main energy molecule), (deoxy)ribose, fructose,
galactose (in milk).

2. **Disaccharides** - "2 sugars". 2 sugar molecules bonded
together.
1. Formed by dehydration synthesis reaction between two
monosaccharides. Fig 2.15 p 44
2. Sucrose C\textsubscript{12}H\textsubscript{22}O\textsubscript{11} Ratio is not quite 1:2:1 because a water
molecule was removed.
   Examples:
   a. Maltose- malt sugar (2 glucoses joined)
   b. Lactose- milk sugar (glucose plus galactose). Some people are
      lactose intolerant.
   c. Sucrose- table sugar (glucose plus fructose) sugar most
      common in plants.
3. Find disaccharides primarily as intermediates in protein synthesis
   or breakdown of other carbohydrates in humans.

3. **Polysaccharides** - "many sugars".
1. Made of many 10s, 100s, 1000s? of monosaccharides linked
together in long chains that may branch.
2. Not soluble in H\textsubscript{2}O and not sweet.
3. They makeup a storage form of sugar: Glycogen (repeating
   glucose units) in liver and muscle.
4. Polysaccharides also play a structural role: Cellulose in plant
   cell walls. Not digestible in humans.
   Examples: cellulose and starches (glycogen- animals main storage
   form).
   DNA and RNA in humans and other organisms. Keeps the based
   lined up in a regular pattern.

**Lipids (fats)**  table 2.7 p. 45  p 45-48

**Lipids** are most commonly fats, waxes, or oily substances.
Contain C,H,O. Less O than sugar.
2 Major Characteristics of Lipids

1. Are water **insoluble** or hydrophobic.
   a. Are soluble in solvents like ether, alcohol, and chloroform, nonpolar solvents.
   b. Combined with proteins for blood transport to form water soluble lipoproteins.
2. Have C-H bonds in greater proportion than other organic compounds. Less O bonds means less polar bonding, means more storage of energy.

More C-H bonds leads to their ability to store more than 2x the energy than an equivalent amount of carbohydrates or protein.

Fats = 9kcal/g  Carbohydrates and Proteins = 4 kcal/g

Therefore, they are important sources of energy.

Lipids are stored in cell mostly as fat.
Lipid is synthesized from sugar.

In storage in skin, lipids insulate and are important to help maintain body temperature.
They give form to the body and cushion organs.

There are 3 major types of lipids we will discuss:

1. **Simple Lipids**- includes fats, waxes, and oils. Figure 2.17 p. 46
   These are the triglycerides, composed of 3 fatty acids bonded to a molecule of glycerol.
   Triglycerides are the major storage form of fat. Excess food energy ends up here.
   They compose the adipose tissue of the body and are the primary lipids to metabolize for energy by the body.

2. **Phospholipids**  See figure 2.18 p. 47
   A lipid portion and a non-lipid portion attached to a glycerol backbone.
   Phospholipids are the main component in cell membranes.
   Phospholipids are modified triglycerides with 2 fatty acid chains attached to a glycerol backbone with a phosphate group (which usually links a small charged group) in the 3rd position.
Lecithin is a good example.

3. **Steroids** - sterol and steroids. See figure 2.19 p. 48
Steroid structure differs considerably from the triglycerides but they are nonpolar, fat soluble molecules. They have 4 rings of carbon atoms.
   Examples: cholesterol, sex hormones, cortisol, bile salts, vitamin D.
Cholesterol can contribute to fatty build-up in atherosclerosis but also serves as the starting material for synthesis of other steroids.

(We will not discuss eicosanoids or other lipids)

**Emulsification of Fats**  (this topic not discussed in Chapter 2 Tortora)

In order for the body to digest fats it must find a way to make them soluble.

**Bile salts**
Which are made in the liver as cholesterol derivatives have this responsibility.
They work the same way that detergents do to get grease off of dishes, clothing, etc.
It’s important for us to look at how a detergents works.

**How Detergents Work**
Lipids in an aqueous solution will go to the top of the water as a film.

Note: Detergents are lipid salts (soap), so have a polar end.
The situation looks something like this:

- Draw figure showing lipid layer on top of water in a beaker with tails up, charged head down.
- Draw an individual phospholipid molecule showing the 2 tails (no charge) and charged head.
- Fig 2.18 p.47 shows a phospholipid with similar structure.

A **detergent molecule** looks like this:
Head Charged (+/-) CH₂-CH₂-CH₂-CH₂-CH₂-...CH₃
Hydrocarbon Chain

The head end is charged meaning it is soluble in water (water is a polar substance and charged molecules, ions, or parts of molecules will be soluble in it). The long hydrocarbon chain that forms the tail is not charged and will not be soluble and water.

However, when detergents are added to lipids in water, the detergent molecules will react with a lipid molecules to form microscopic droplets. This is how lipids are made soluble.

Draw a micelle first with the charged heads out and tails inward forming a sphere.

Now we can add some nonpolar (non charged) fats.

Draw figure showing fat molecules in center of radiating pattern of detergent molecules with detergent polar heads facing outward associating with water and tails facing inward associating with fats.

The lipids are protected inside the coating of detergent molecules. Like dissolves like, so hydrophobic tails go together and polar heads and water go together.

The fat droplets are emulsified and become soluble with water. This allows fats to be absorbed and digested in the body. They are transported in the plasma in this type of structure. Micelles are about 40-600 um in diameter. Fig 25.13 p. 920

Review Types of Lipids
1. **Simple lipids = triglycerides.**

   Triglycerides are composed of glycerol bound with 3 fatty acids. This happens as follows:

   Figure 2.17 p. 46. Or,

   Draw diagram of glycerol combining with three fatty acids by dehydration synthesis forming a triglyceride.

   \[
   \text{Glycerol} + 3 \text{ Fatty Acids} = \text{triglyceride}
   \]

   A fatty acid may be **saturated** or **unsaturated**.

   1. **Saturated**
      Means every carbon in the hydrocarbon tail has its full complement of hydrogens.
      In other words, all carbons are joined by single bonds as follows:
      Fig. 2.17 p.46
      Example: animal fats, palm oil, coconut oil.

   2. **Unsaturated fatty acid**
      Has doubled (2 pairs electrons shared) or triple bonds (3 pairs electrons shared) between 2 or more of the carbons in a chain.
      In other words, it doesn't have as many hydrogens as is possible or it could have.
      Polyunsaturates contain more than one double bond.
      Fig. 2.17 p.46
      Examples: corn, safflower, or canola oil.

      Saturated fats have a higher energy content (more calories) than unsaturated fats.
      They are also more solid at the given temperature.
      Most animal fats are saturated while most vegetable fats are unsaturated.
      Saturated fats and atherosclerosis are linked in diet studies. This leads to arteriosclerosis. In advanced cases, a heart attack will occur.

2. **Phospholipids**
A lipid portion and non-lipid portion.
There is a slight modification of triglycerides to form phospholipids: 1 fatty acid is replaced by a phosphate group with a small charged group.
Fig. 2.18 p. 47
Example: lecithin

3. **Steroids**
   1. Steroids are nonpolar, fat soluble molecules, that have 4 rings of carbon atoms that are derived from cholesterol.
   2. Cholesterol can be synthesized by the liver or received from your diet.
   3. Important derivatives of it included the sex hormones: estrogen, progesterone, testosterone.
   4. Cholesterol has definitely been implicated in one form of heart disease known as atherosclerosis where it clumps together in blood vessels to form crystals and is deposited there. The cholesterol crystals block the flow of blood.
Fig. 2.19 p 48

Optional Material  p 920-1
HDL- high-density lipoprotein. 50% protein, 37% triglycerides, 13% cholesterol.
   Considered good because it lowers cholesterol by soaking up cholesterol in the blood.
   Exercise can increase this beneficial form.

LDL- low density lipoprotein. 25% protein, 20% triglycerides, 55% cholesterol
   Considered bad because it increases circulating cholesterol that can cause deposits.
   Increased by high fat diet and little or no exercise.

High levels of serum cholesterol (>150mg/dl) are associated with increased risk of coronary disease.
For those with very high cholesterol (>200 mg/dl) that diet and exercise don’t correct can take drugs (e.g. Zocor, Lipitor blocks synthesis in liver or drugs that block adsorption in the GI tract).
Proteins are very large molecules composed of long chains of nitrogen containing molecules known as amino acids. They have a large range of function, both structural and physiological roles. Made from these elements: C, H, O, N, and S.

The major proteins functions include:

1. **Structure**
   - They can be structural elements within cells.
   - Examples: Collagen is a protein in bone and other C.T. Keratin is found in skin hair and nails. Silk, wool, horns, and antlers are made from structural proteins.

2. **Regulatory (hormones)**
   - Chemical messengers in the body that regulates various physiological processes, and, control growth and development.
   - Examples: Insulin regulates blood glucose level by controlling entry into cells and is a protein hormone.

3. **Contractile**
   - Allows shortening of muscle tissue that produces movement.
   - Examples: Myosin and actin form contractile filaments that pull against each other and shorten the muscle.

4. **Immunological**
   - Provides a specific response to protect the body against foreign substances and invading pathogens.
   - Examples: Antibodies and interleukins (IL2, TNF).

5. **Transport**
   - Carries vital substances throughout the body.
Example: Hemoglobin carries $O_2$ from the lungs to the body.

6. **Catalytic (enzymes)**  
   Fig. 2.23 p.52
   Enzymes are catalysts in cells. They speed up chemical reactions. These reactions can build up or breakdown biological compounds. Lock and key analogy: one enzyme for each reaction. Speeds up reaction $10^8$ to $10^{10}$ times more rapid than reaction without enzymes.
   All enzymes are proteins, but not all proteins are enzymes.
   Examples: named with suffix –ase.
   - Amylase breaks down starch.
   - Lipase breaks down lipids.
   - Lactase breaks down lactose.

**Amino Acids and Polypeptides**

Proteins are made of amino acids. There are 20 amino acids used to make proteins. Fig 2.20 p 49

Amino acids are strung together in **polymers** to form individual types of proteins.
   Polymers are larger molecules composed of many repeating molecular subunits.
   Example: Insulin is composed of 51 amino acids strung together. You can see that with 20 different amino acids, there are many different types of combinations possible.

The **sequence** in which the amino acids are arranged in the polypeptide chains(protein) determines the biological characteristics of the protein molecule.
   Even one small variation in this sequence can cause disaster. One change (substitution) of an amino acid in a protein can alter the shape of the protein and render it non-functional.
   Example: Sickle cell disease is the mutation of a hemoglobin gene at one amino acid.
   Hemoglobin has 574 amino acids in four chains (2 alpha chains (141 a.a.), 2 beta chains (146a.a.)). Fig 19.4 p 640
Valine (hydrophilic) replaces glutamic acid (hydrophobic) at position 6 of the beta chain that causes the hemoglobin to change shape under low oxygen levels to create sickle-cell shaped red blood cells. Fig 19.14 p 654
Cells get stuck in micro-circulation causing hypoxia and tissue damage. Can be deadly in the homozygous state (2 copies of the sickle gene, that is one inherited from each parent). The spleen can become quite enlarged.

**Amino Acid Structure:** figure 2.20 p. 49

Amino acids, since they make up proteins, are composed of the same elements as protein: C,H,O, as well as N.
Some amino acids (cysteine, methionine) will contain S that will bond with other S containing amino acids to create covalent bonds to reinforce the shape of the protein, as we will review later.

Every amino acids contains an amino group (-NH₂) and a carboxyl group (-COOH) bonded to a carbon atom:
figure 2.20.

```
R
H₂N – C C OH
|   ||
H O
```

Amino group – C – Carboxyl group

This is the basic structure of the molecule. It is the same in all amino acids.

R (side chain)
A group of atoms that acts as a single functional unit. The R group gives the amino acids its particular chemical behavior.
Examples: hydrogen bonding, sulfhydryl bonding (S-S), polar and nonpolar affinities. Remember what happened to hemoglobin with one change.
Examples: fig 2.20 p 49

- **Glycine (gly)**: When $R = H$, $H_2N\text{-C-C-OH}$
  - Structure: $H$ \_ \_ \_ \_ \_ \_ \_ $O$
  - When $R = \text{CH}_3$, $\text{Alanine (ala)}$, $H_2N\text{-C-C-OH}$
    - Structure: $H$ \_ \_ \_ \_ \_ \_ $O$
  - When $R = \text{CH}_2\text{-OH}$, $\text{Serine (ser)}$, $H_2N\text{-C-C-OH}$
    - Structure: $SH$ \_ \_ $O$
  - When $R = \text{CH}_2\text{-SH}$, $\text{Cysteine (cys)}$, $H_2N\text{-C-C-OH}$
    - Structure: $SH$ \_ \_ $O$

Since proteins are made of chains of amino acids, let's look at how amino acids are bound together to make proteins.

The amino "head" of the molecule can be linked to the carboxyl "tail" of another by the removal of a water molecule. This forms a covalent bond called a **peptide bond**. See figure 2.21 p. 49

This is called **dehydration synthesis**.
When several of these linkages form, combining several amino acids, the molecule is called a **polypeptide**. Polypeptides are assembled in the ribosome, linking the head of one amino acid to the tail of another, like a line of box cars.

The sequence of the box cars (amino acids) is determined by information from the nucleus of the cell.

As the amino acids produce a linear chain on the ribosome the **primary structure** of the protein is determined. See figure 2.22 p. 51

The **primary structure** is the unique sequence of amino acids making up a protein.

It will ultimately **determine the shape and function** of the protein. (Remember function changes as the shape changes, for better or worse)

3 other levels of protein organization are important to their function:

**Secondary structure**

The protein, commonly assumes an **alpha helix** (clockwise spirals similar to a phone cord) or a **pleated sheet** repeating pattern.

**Tertiary structure**

This level of protein structure describes the 3D shape of the protein molecule. It is determined by the side chain (R group) interactions that form hydrogen bonds, ionic bonds, covalent bonds, hydrophobic interactions. This level determines the proteins primary function. It is similar to the irritating secondary winding of the phone cord that occurs with use.

**Quaternary structure**

Some proteins contain more than 1 polypeptide chain. This level describes the bonding of individual polypeptide chains relative to each other. They are held in place by bonds as mentioned under tertiary structure.
Example: Hemoglobin consists of 2 alpha chains and 2 beta chains to form one functional protein.

Small changes in temperature, pH, or electrolyte concentrations in the body can cause protein structures to unravel and lose their characteristic shape. This process is called denaturation. This will affect the ability of the protein to perform its function. Example: cooking an egg, lowering the pH of milk, sunburn producing curdled or denatured proteins.
Nucleic Acids Chapter 2 p 52

Note- you should receive a handout copy of the genetic code in lecture

Nucleic acids include 2 types:

1. **Deoxyribonucleic acid or DNA**
   - Forms the inherited genetic information (material) inside the nucleus each cell, your DNA.
   - DNA = blueprints (genome) for the control of cellular activity.

2. **Ribonucleic acid or RNA**
   - RNA relays instructions from DNA to the cell to make amino acids into proteins.

Control by Nucleic Acids

DNA along with certain proteins (histones) make up chromosomes that contain the blueprint (genome) of life.
   - Humans have 46 (2x23) chromosomes, 23 from each parent.
   - There are about 30-38K genes in a human, so about 1500/chromosome.

The genetic information (genome) in chromosomes (DNA) has to get out of the nucleus and into the cytoplasm to control cell activities.
   - A certain type of RNA is responsible for this: messenger RNA or mRNA. mRNA carries the genetic message from DNA out of the nucleus to the ribosome in the cytoplasm.

   The end result being that the genetic message is taken from the mRNA and translated into a sequence of amino acids to make proteins.

   This is called the Dogma of Life.

   DNA ➔ mRNA ➔ protein

Chemistry of Nucleic Acids fig 2.24 p. 53
In order to understand how this works, it is necessary to take a closer look at nucleic acid chemistry.

The primary elements found in nucleic acids are C,H,O,N,P.

The basic unit of a nucleic acid = nucleotide.

DNA is made of thousands of nucleotide subunits strung together. DNA molecules are huge, the largest molecules in the cell. Molecular weight = 1 million to several billion. Up to 100,000 times the size of most proteins.

Each nucleotide is made of 3 components: figure 2.25 p. 54.

1. Phosphate group. \( \text{PO}_4^{3-} \)
2. Sugar- deoxyribose in DNA, ribose in RNA.
   
   Note: The base is the only chemical structure that differs from one nucleotide to another. The sugar and phosphate act as repeating structures in DNA and RNA to keep the bases exactly lined up opposite with each other. The bases determine the information in the genetic code.

There are only 4 different kinds of bases in DNA:

- Adenine (A)
- Guanine (G)
- Cytosine (C)
- Thymine (T)

The 4 bases of RNA are:

- Adenine (A)
- Guanine (G)
- Cytosine (C)
- Uracil (U)

Note: only uracil differs from DNA bases
The organization of the components of a nucleotide is as follows:

where phosphate = P sugar = S base = B

\[
\begin{array}{c}
\text{P} \\
\text{\textbackslash} \\
\text{S-B} = \text{1 nucleotide}
\end{array}
\]

Nucleotides join together to form a strand of DNA like this:

\[
\begin{array}{c}
\text{P} \\
\text{\textbackslash} \\
\text{S-B} \quad = \text{1 nucleotide} \\
\text{\textbackslash} \\
\text{P} \\
\text{\textbackslash} \\
\text{S-B} \quad = \text{1 nucleotide} \\
\text{\textbackslash} \\
\text{P} \\
\text{\textbackslash} \\
\text{S-B} \quad = \text{1 nucleotide} \\
\end{array}
\]

= strand of nucleotides

Further simplification:
1 strand of nucleotide looks like 1/2 ladder, where: rungs = base, side of ladder = sugar + phosphate

\[
\begin{array}{c}
\text{|-B} \\
\text{|-B} \\
\text{|-B} \\
\text{|-B} \\
\text{|-B} \\
\end{array}
\]
In 1952, 2 men, Watson (American) and Crick (British) formulated current model of molecular of DNA.
They postulated that DNA is made up of 2 strands of nucleotides wrapped around each other.
Published in 1952, Nobel prize in 1962.
There work has been confirmed by decades of research.

The overall shape is a double helix (double coil), with the bases of each strand sticking inwards from the backbone and bonding with each other. see fig. 2.24 p.53

The 2 opposing strands appear bound by a ‘zipper’ of hydrogen bonds between bases.
DNA double helix has bases projecting inward from opposing twisted helix strands.
Looks like a twisted ladder. Consists of thousands of nucleotides strung together. How many are shown here? 1 for each B (base).
See diagram in a 3D helix view, and a 2nd, in a flat, unwound view.

Base Pairing of DNA Nucleotides

Bases = Adenine (A) Guanine (G) Cytosine (C) Thymine (T)

A will only pair with T: A-T or T-A

G will only pair with C: G-C or C-G

Note: A and G are larger bases while T and C are smaller bases. A large base must bind to a small base for the DNA molecule to fit together correctly.
Therefore, base pairs of DNA strand could look like this:

| -T  |
| -A  |
| -C  |
| -G  |
| -T  |
| -A  |

What are the base pairings for this example?

On an exam if you are given the bases in one strand of DNA you should be able to determine the nucleotide sequence of the complementary strand.

The strand of the DNA that contains the genetic information (gene) is called the "antisense" or "gene" strand. The strand of DNA complementary to the sense strand is called the "sense" strand because it is similar to the mRNA sequence. This will more sense after more discussion.

Base Pairing in RNA Nucleotides

Bases = Adenine (A) Guanine (G) Cytosine (C) Uracil (U) (uracil replaces thymine)

G will only pair with C: G-C or C-G This is the same as DNA.
U will only pair with A: U-A or A-U U takes the place of T in RNA.

Other Differences Between DNA and RNA

RNA sugar = Ribose
RNA consists of a single strand of nucleotides.
mRNA is smaller, containing 300-3000 nucleotides.
If only single-stranded, what does RNA bases pair with?
    RNA may twist upon itself to give a 2 stranded look (tRNA) or will exist as single-stranded, mRNA.
What does mRNA pair with?
mRNA takes the genetic message from DNA in the nucleus to the site of protein synthesis at the ribosome. An mRNA molecule represents the code for one protein. So, it is created on DNA in the nucleus at the site of a gene coding for a protein. And then it pairs with tRNA at the ribosome.

Where are ribosomes?
In the cytoplasm or ER. mRNA leaves the nucleus through a nuclear pore to enter the cytoplasm and then to free ribosomes or ER with ribosomes.

Transcription figure 3.28 p. 87
Transcription is the process where the directions found in DNA to make a protein are transcribed to create an mRNA molecule.

See below a nucleus showing double stranded DNA and mRNA leaving the nucleus through a nuclear pore. Note the nucleus with sense and anti-sense DNA strands. Identify the base pairing needed to create the mRNA. Explain how DNA acts as a template for mRNA.
The process where genetic information of DNA is used to specify base sequences of mRNA is called "transcription".

Be prepared to transcribe an mRNA strand from a DNA strand that I will provide for you.

How does each newly formed somatic cell in your body obtain genetic information?
Before mitosis, the cell creates a second set of chromosomes in a process called DNA replication. So, briefly there are 92 copies of the chromosomes, then one set of 46 goes to each daughter cell as mitosis proceeds.

The Genetic Code

Once the DNA is transcribed into mRNA it travels to the ribosome and tells ribosome what amino acids to connect together to make protein (translation).

Translation
The information in mRNA dictates the sequence of amino acids to be placed in protein molecules.

Example:
Initiator
AUG leu ser pro ala tyr
a.a - a.a- a.a- a.a.- a.a.- a.a. And so on. a.a
Terminator
UAA

How does DNA code for 1 of 20 specific amino acids in sequence to make protein?
Through tedious research it has been found that a 3 base sequence in DNA is transcribed into a 3 base code in mRNA, for a particular amino acid.

So, each group of three bases represents an amino acid in the building a protein.
The code for a particular amino acid has been termed a "codon".
Example:

<table>
<thead>
<tr>
<th>DNA (gene)</th>
<th>mRNA</th>
<th>Amino acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>U</td>
<td>phenylalanine</td>
</tr>
<tr>
<td>A</td>
<td>U</td>
<td>serine and</td>
</tr>
<tr>
<td>G</td>
<td>C</td>
<td>lysine</td>
</tr>
<tr>
<td>T</td>
<td>A</td>
<td>arginine</td>
</tr>
<tr>
<td>A</td>
<td>U</td>
<td></td>
</tr>
</tbody>
</table>

The bases are analogous to a 4 letter alphabet, and the codons are analogous to words spelled with 3 letters.

1. There are 64 different codons as follows:
   \[4^3 = 64\], where 4 = the four bases, 3 = 3 bases/codon.
2. So, there are 64 different ways that A,T,G,C can combine to form 3 letter codons.
3. Most (18/20) amino acids have more than 1 codon.
   Example:
   Valine: There are 4 codons for valine.
   GUU
   GUC
   GUA
   GUG
   Some amino acids have 6 codons (leucine, serine, arginine).
   Most amino acids have between 2-6 codons.

4. When different codons code for the same amino, demonstrating a redundant or degenerate code.
5. Some codons act as punctuation marks, 1 start, 3 stop codons, that tell the ribosome when to start and stop and amino acids chain.
   The stop codons are also known, less appropriately, as "nonsense" codons.
Control by Nucleic Acids in Protein Synthesis figure 3.30 p. 89

The synthesis of a protein requires that certain things are present within the cell:

In Nucleus
1. DNA
2. Free nucleotides floating around that can combine to form mRNA.

In Cytoplasm
1. Ribosomes
2. The 20 various amino acids that will eventually be joined together in proper sequence to form protein.
3. ATP = energy source (which is also a nucleotide).
4. tRNA = transfer RNA.
   tRNA is made in the nucleolus and moves out of the nucleus and into the cytoplasm through nuclear pores.

Anticodons

tRNA is a small molecule that looks like this:
fig. 3.30 p.89

See the tRNA molecule with one end for attachment of a specific amino acid, and the other end for the 3 base anticodon that is complementary to the mRNA codon.

Example: anticodon CGU = alanine a.a. end

The anticodon determines what amino will attach to tRNA.
1. In the presence of ATP, an amino acid is activated and attaches to tRNA.
2. Only the amino acid represented by the anticodon can attach to the tRNA.
So, there is an tRNA type for each codon representing an amino acid.
3. Where do amino acids come from?
   Your diet. If your diet does not contain all 20 amino acids, this causes a disease called kwashiorkor. It rarely occurs in developed
areas of the world. Mainly in areas where starchy foods are a staple of the diet. Meat and milk contain all 20 amino acids.

Now that we know what things must be present in the cell for protein synthesis, how do they work together?

**Sequence of Events for Protein Synthesis**

1. Free nucleotides are attracted to DNA strand where complementary base pairing occurs.

2. Nucleotides link to form mRNA strand.
   - Steps 1&2 are the process called Transcription.

3. mRNA separates from DNA and moves out of nucleus to associate with ribosomes.
   - Structurally, a ribosome consists of 2 subunits, one about half the size of the other.
   - The smaller ribosomal subunit complexes with tRNA, mRNA, and proteins to initiate reading of the mRNA message.

4. Free amino acids in cytoplasm combine with their respective tRNA carriers.

5. tRNA anticodon with associated amino acids, base pairs with mRNA codons at ribosome. The ribosome then moves along the mRNA strand.

6. Ribosome continues moving along mRNA strand to new codons, where amino acids are added to a growing polypeptide chain.
   - tRNA molecules are released as the amino acids are joined by a peptide bonds.
   - The next tRNA carrying an amino acid attaches by anticodon to the next mRNA codon to continue the process.
   - Steps 3-6 represent the translation process.
7. Polypeptide disconnects from the ribosome and mRNA strand when a "stop" codon is reached.
   One of three codons: UAA, UAG, or UGA.
   There are no tRNA that recognize these codons.

These proteins determine the physical and chemical characteristics of the cell.
   They have many functions:
   1. Structural: plasma membranes, microtubules, microfilaments, centrioles, flagella (cilia), mitochondria, etc.
   2. Enzymes that run the cell’s metabolism.

Proteins carry out life functions. DNA only contains codes for the potential for life. Life does not exist without protein.
Review of Protein Synthesis

Review of the 7 step process of protein synthesis starting with transcription of DNA to mRNA through the process of translation.

1. **Nucleotides to DNA.** Fig 3.28 p 87
   Draw nucleus with double stranded DNA showing complementary base pairing between the sense and anti-sense strands.
   Show free nucleotides beginning to base pair with sense strand.

2. **mRNA single-strand forms.** Fig 3.28 p 87
   Draw mRNA molecule alongside the sense strand of DNA demonstrating complementary base pairing between the sense strand and mRNA.
   Show free nucleotides in nucleus being attracted to the mRNA transcription process.

3. **mRNA separates and moves to ribosome.** Fig 3.28 p 87, fig 3.30-1 p 89
   Draw mRNA path as it would move from the nucleus via a nuclear pore to arrive at a ribosome.

4. **Amino acids bind to tRNA.** fig 3.30-2,3 p 89
   Draw a simple tRNA molecule reacting with an amino acid (valine, anticodon = CAU) and ATP to form an activated tRNA-amino acid complex.
   Show free amino acids floating in the cytoplasm.

5. **Translation begins.** Fig 3.30-3,4 p 89
   Draw 2 ribosomes attached to mRNA, reading codons. Codons sequence: AUG (start/methionine), UUC (leucine) show tRNA here with ribosome, GUA (valine), UAC (tyrosine), CGA (arginine), GAG (glutamic acid) show tRNA here with ribosome, UAA (stop codon).

6. **Translation continues** as ribosome moves along mRNA strand. Fig 3.30-5 p 89
   Draw a peptide forming behind the second ribosome with glutamine tRNA – arginine-tyrosine, valine, leucine, start/methionine.
7. **Stop codon is reached** and polypeptide disconnects from ribosome. Fig 3.30-6 p 89
Demonstrate effect of reaching the stop codon.

This is an amazing process when you think about it.
- Protein synthesis progresses at a rate of about 15 amino acids per second.
- Several ribosomes may be attached to the same mRNA forming the same protein simultaneously.
- Humans have DNA to code for about 30K-40K genes.
  - Some proteins can be modified several ways after translation in the cell so one gene can code for more than one function.

Every cell of the body contains the same information in the form of DNA.
- Example: A skin cell contains the part of the DNA that tells the skin cell how to function as well as how a muscle cell is supposed to function.

To put it another way, each cell contains the genetic information necessary to reproduce a new organism.
- This has been demonstrated recently by the cloning of mammals from somatic cells.

The fact that each cell does not reproduce a whole new organism shows that there are many other factors besides nucleic acids that determine what a cell does or does not do. This will be discussed soon.

The genes of eukaryotes, such as humans, contain stretches of bases called exons and introns. p. 88

**Exons**: stretches of DNA that code for protein.
**Introns**: intervening stretches of DNA that do not code for protein.

When an mRNA transcript is made, the introns must be removed and the molecule spliced back together.
Prokaryotes read their genes directly into functional mRNA. In other words, prokaryotes only have coding sequences. This creates a problem for cloning human genes into prokaryotes. Prokaryotes have no cellular machinery to remove introns from eukaryotic genes. So, yeasts, plants, and other animals (all eukaryotes) are becoming popular human gene recipients.

**DNA Replication**

How does a cell initially receive genetic information?
During cell division (mitosis).

DNA doubles itself by a process known as **DNA replication**. This is not a copy but a mirror image replication by complementary base pairing.
The Human Genome Project is currently mapping out the 3 billion base nucleotide pairs in the human genome.

Replication takes place as follows:

Make these drawings side by side as we go through lecture.
Make stick figure with DNA backbones and rungs.
Use different color each DNA strand in double helix.
Fig 3.32 p 91

Draw a double helix.
Draw a double helix unwound (ladder-like).
Draw the DNA strands separated.
Draw each strand and show how free nucleotides base pair with each strand.
   Draw 2 new strands of DNA pairing with the existing strands.
   Draw 2 new strands coiled up in separate double helix structures.

These 2 chromosomes are identical to the parent chromosome. In other words the genetic information is the same.
If mistakes are made in the DNA sequence, the cell could die or cause a problem such as cancer.

Each new chromosome goes to 1 of the new daughter cells formed during mitosis. Fig 3.33d p92

One theory on aging is chromosomes get shorter due to erosion of their tips (telomeres).
Each cell division shortens the telomere until it is completely gone and function is lost.

**Mutations** (Not covered in Tortora textbook)

**Introduction**
A mutation is a mistake at some point in the DNA message. Think of DNA as a structure that has shape and form. If the structure is altered, the message is changed, and therefore the protein(s) will change.

We can view mutations at the molecular level now that we know the structure of DNA.

**Mutation**
An alteration in genetic makeup (**genotype**) of an organism at the molecular level.
- It is an alteration in the base sequence of DNA that gets transcribed into RNA and then translated into protein.
- Such alterations may or may not affect the appearance (**phenotype**) of an organism. The mutation can result in an improvement, a weakness, or no change in the function of the proteins(s).

**Mutagens** Is an agent that increases likelihood of mutation.

**Mutagenic Agents**
Examples:
- **Radiation** 2 types
1. Ionizing: High energy x-rays and gamma rays strike molecules and cause them to ionize. Reactive radicals cause changes at the molecular level, such as base changes, chromosome breakage.
   Examples: x-rays
   Use a lead shield for protection of sex organs of patient and operator.

2. Non-ionizing: UV light from the sun (especially at 260 nm that is mostly filtered by the ozone layer) cause harmful covalent bonds between adjacent thymines, forming thymine dimers. This causes mistakes in transcription and replication.
   Example: UV rays- from sun causes thymine dimers in skin cells and leads to skin cancers. Light repair enzymes act to separate the dimer into separate thymines.
   Humans with xeroderma pigmentosum have genetic defects in their light repair enzymes and are at great risk of skin cancer.

Chemicals
A long list goes and new ones identified every day.
Examples: mustard gas, phenol, and formaldehyde.
In medicine: base analogs such as AZT used to treat HIV virus to create base pair substitutions.

Can these mutations be passed onto future generations?
Only if they occur in the germ cells, sperm or egg.
The atomic bomb irradiation in Japan lead to high incidents of leukemia in offspring.

Spontaneous mutations- "naturally occurring"?
Mutations occur at a slow rate all the time in all organisms.
   The normal rate is estimated at once in $10^{-6}$ replicated genes.
   Or once in $10^9$ replicated base pairs ($10^{-9}$mutation rate).
   An average gene has $10^3$ base pairs.
   A mutagen increases this rate by a factor of 10-1000 times.

Are all mutations harmful?
No! That is how evolution takes place.
Diversity provides the raw material for evolution.
Look around the classroom and see all the genetic diversity among your classmates. Some of us are better adapted to different environments. Evolution represents a combination of changes in the genotype and natural selection acting upon it.

As the environment changes, the value of a particular gene will be increased or decreased.

**Types of Mutations**
At the molecular level, all mutations are changes in the genetic code of an organism. In some way, the sequence of bases (A,T,G,C) has been altered and one or more codons has changed.

Mutagens may cause:

1. **Substitutions**
   Substitutions of an incorrect for a correct nucleotide.
   Analogy: say it with g(f)lowers.
   Literally: CAT
   (GUA valine codon)
   Becomes: CAG
   (GUC valine codon)

2. **Inversion**
   2 nucleotides have been reversed.
   Analogy: We put our trust in the untied nations.
   Literally: CAT (GUA valine codon)
   Becomes: CTA (GAU aspartic acid codon)

Substitutions and inversions are types of point mutations, as they only alter the message for 1 or maybe 2 amino acids in the sequence.

3. **Deletion**
   Missing nucleotide in sequence.
   Analogy: The Prime Minister spent the weekend in the country shooting p(h)easants. or,
   Delete the letter F from FAT make the sentence meaningless.
   THE FAT CAT ATE THE RAT
THE ACT ATA TET HER AT
Remove A in first codon in a three codon sequence

Literally:  CAT    TTA    GCA
            valine  leucine  arginine
            GUA codon AAU codon CGU codon

Becomes:  CTT    TAG    CA?  every codon after this altered.
            glutamic acid  isoleucine  different a.a.
            GAA codon AUC codon GU? codon

4. Insertion
Additional nucleotide is added to sequence.
Analogy: The Treasury controls the public monkeys. Or,
Insert the letter C before FAT make the sentence meaningless.
THE FAT CAT ATE THE RAT
THE CFA CTA TAT ETH ERA T

Add G in first codon in three codon sequence

Literally:  CAT    TTA    GCA
            valine  leucine  arginine
            GUA codon AAU codon CGU codon

Becomes:  CGA    TTT    AGC A  every codon after this altered.
            alanine  lysine  serine
            GCU codon AAA codon UCG codon C??

Deletion and insertions are more drastic and are called frame-shift mutations.
They alter entire amino acid sequence following the mutation, causing a dysfunctional protein.
They also may lead to the insertion of nonsense (stop) codon substitutions.

Why are visible mutations so rare?
Most mutations usually affect only 1 member of a pair of alleles.
Alleles represent 1 of 2 or more genes responsible for a certain trait.
Example:
Usually the normal allele exerts its effect more strongly (dominant).
Most mutations are recessive.
Example:
Cystic fibrosis: a disease of a cell membrane protein.
   Cc or  Cc = Normal membrane function,
   cc = faulty Cl⁻ transport protein in membranes.

But the defect is still carried as a recessive trait.
(These recessive traits often have a hidden advantage. CF gene is protective against Salmonella infection.)
May be expressed in future matings, especially when inbreeding is common.

Only if a DNA mutations occur in the germ cells (egg or sperm), will they be passed on to the next generation.

**Operon Theory of Gene Control by Nucleic Acids**
What controls when protein made or not?

Regulation of protein synthesis is important to the cell’s energy economy.
The cell can save energy by only making proteins for particular need.

Most genes are **constitutive** (60-80%), meaning their products are produced at a constant rate.
These gene products are needed in large amounts for essential processes common to all cells.

Some genes are **conservative**, meaning that their product production is regulated so they are present when needed.
   Example: Insulin is made after meals to let glucose enter cells.

According to this theory there are 3 segments (genes) of the DNA strand involved in the production and control of the production of proteins.
The 3 segments are the:

**Structural gene**- the gene(s) segment that codes for the functional protein.

**Operator segment**- the short segment of DNA that contains the operator/promoter complex that acts as attachment site for RNA polymerase and initiation of transcription.

**Regulator gene**- codes for repressor protein that binds tightly to operator site.
A DNA strand with an operon (promoter/operator, structural genes) and regulator gene. Show inducer protein, repressor protein.

**Operon**
Combination of the control region and structural gene.

Note: *Regulator gene* may be near the operon or located somewhere else on DNA strand.

Operation of the Operon:
In this example, the cell only makes proteins to metabolize lactose when it is present and needed for cellular metabolism. The cell needs 3 proteins to digest lactose (1, 2, 3)

When lactose is present in the cell, a small portion is converted to an inducer substance that can bind to the repressor protein.

It changes the shape of the repressor protein and it releases form the operon and allows for the transcription of the structural genes needed to metabolize lactose.

When the inducer is not present, the repressor protein will again bind and block the structural genes from being transcribed. This is known as an inducible system of control.

This demonstrates the role of nucleic acids in the control of cell activity.
Recombinant DNA  (cover if time permits)  p 90

Recombinants
Organisms that have another organisms gene(s) inserted into its genome. The organisms takes on the characteristic(s) contained in the gene(s).

Transgenic
Inserting a gene from one species into another species genome.

Products
There are 2 products that can be useful in the transgenic organism.

1. Genes-: Genes can be manufactured in large numbers so that they can be inserted in the original species to correct genetic defects.
   Example: CF gene can be replaced with a normal gene in a person born with CF.

2. Protein: Proteins can be harvested that have a wide variety of uses.
   Examples: Many modern medicines are made by genetically modified organisms, usually yeast or bacteria.
   Growth hormone (hGH), insulin, clotting factors, interferon (INF), erythropoietin (EPO), vaccines (HepB)

Other control of cell activity.  (Cover if time permits)

Hormonal Control

Hormones = chemical messengers produced by endocrine glands. Travel by means of bloodstream, a shotgun approach.

Hormonal control at areas sites:

1. Influence cell membranes.
   Example: Influence permeability. Insulin acts to accelerate facilitated diffusion of glucose into cells.

2. Influence activity of enzymes.  Fig 18.4 p 593
Water soluble hormones typically bind a membrane protein (G–protein) that will activate a secondary messenger (usually cAMP) inside the cell. The secondary messenger will activate or inactivate enzymes in the cell. Examples: Epinephrine binds to liver cells and causes inactivation of an enzyme needed for glycogen synthesis.

In vitro- in test tube.
In vivo- in living organism.

3. Influence genes. Fig 18.3 p 592
Lipid soluble hormones enter the cell through the phospholipid membrane where they bind to receptors that alter gene expression (turn gene on or off).
The resulting protein (or loss) will have an effect on cellular metabolism.
Example: estradiol, progesterone

Exam 1 Notes
Multiple choice- 50 points
Matching- 10 points
Fill in- 5 points
Essay- 10 points