Chapter 2 – Physiology and Biological Chemistry

Objectives

Given the synopsis in this chapter, competence in each objective will be demonstrated by responding to multiple choice, matching, put-in-order, or fill-in questions, at the level of 85% or greater proficiency for each student.

A. To explain the concept of processes in the study of physiology.
B. To explain the composition of body fluids and the role of water and electrolytes.
C. To explain the structure, features and roles of amino acids, peptides, and proteins.
D. To explain the structure, features and roles of lipids, including glycerol, fatty acids, glycerides, phospholipids, eicosanoids, and cholesterol.
E. To explain the structure, features and roles of carbohydrates, including monosaccharide, disaccharides, and polysaccharides.

What is Physiology?

Physiology is often defined as the study of the normal function of the body. (Pathophysiology is the study of abnormal function of the body.)

To be more precise, physiology focuses on how organisms, organ systems, organs, cells, and biomolecules carry out the physical and chemical functions that exist in living systems.

Central to an understanding of physiological functioning is the study of the fundamental biophysical and biochemical phenomena, that underlie the:

- Coordinated homeostatic control mechanisms within the body
- Continuous communication between cells, organs and organ systems

Biophysical and biochemical processes are responsible for controlling flow of chemical energy (metabolism) and for controlling information flow (cellular signaling),

- ➢ Physiology is the study of processes in the body and is critically intertwined with biophysics and biochemistry.

Why Study Physiology

Even after obtaining an appreciation of the structure of our organ systems and organs (as we did in anatomy), there is much more to learn about the processes that underlie the functioning of the body. Why study physiology?

- Physiology, biophysics, and biochemistry are fundamental to the medical sciences.
- Most disease states are caused by, or involve, abnormal biophysical and biochemical processes.
- Medical treatment regularly uses pharmacological interventions to modify biochemical processes.

Basic Chemistry

To review basic chemistry please see Appendix C. There you will find summaries of elements, orbitals, molecular bonds, water, electrolytes, molarity, osmolarity, pH, and buffers.

- The human body is made mainly of water, about 50%-70% (62%); and minerals, about 4-6%
- The human body is also made of proteins, about 16%; Fats, about 16% (healthy lean males) - 22% (healthy lean females); and sugars, about 1%

Body Fluids

Much of the body is composed of fluids, made mainly of water and various dissolved electrolytes and biomolecules. These fluids are located inside of cells (in intracellular spaces), between cells (in interstitial spaces), and in blood vessels (in vascular spaces), as shown in Figure 2-1.

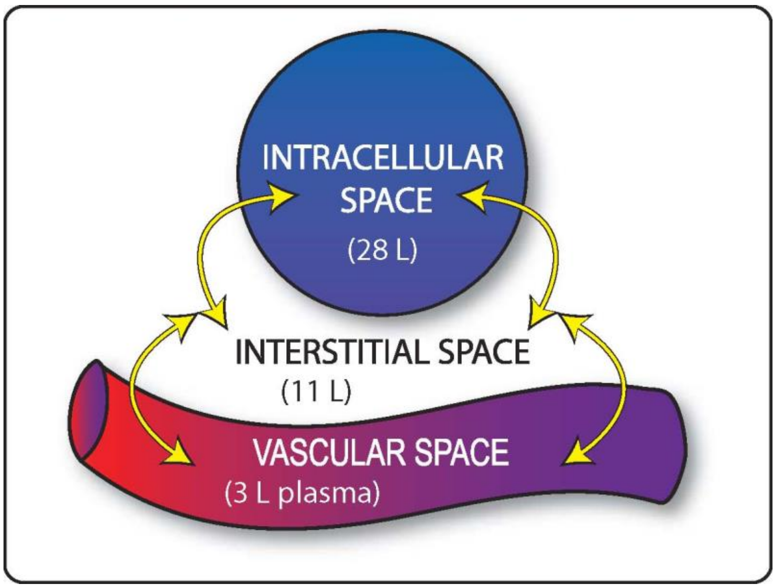

Figure 2-1 © 2007 David G. Ward, Ph.D.

- Intracellular fluid volume (in intracellular spaces) is about 28 L.
- Interstitial fluid volume (in interstitial spaces) is about 11 L.
- Vascular plasma volume (in vascular spaces) is about 3 L.
- Extracellular fluid volume is interstitial volume plus plasma volume, about 14 L
- Total body fluid is about 42 L in a 70 kg person.
- Thus an average person is about 60 percent fluid (42/70).

Composition of Body Fluids

Body fluids are composed mainly of water, electrolytes and various biomolecules. Electrolytes include primarily sodium, chloride, potassium, and calcium. Biomolecules include proteins, peptides, glycerides, fatty acids, and carbohydrates such as glucose. If we look at the composition of blood plasma, we are looking at a window into the composition of most of the extracellular fluids (blood plasma and interstitial fluid make up the extracellular fluid).

Blood is composed of plasma and cells (including cell fragments) as shown in Figure 2-2. Plasma makes up about 52% to 63% of blood in females and about 48% to 58% of blood in males. Red blood cells, white blood cells and platelets together make up about 37% to 48% of blood in females and about 42% to 52% of blood in males

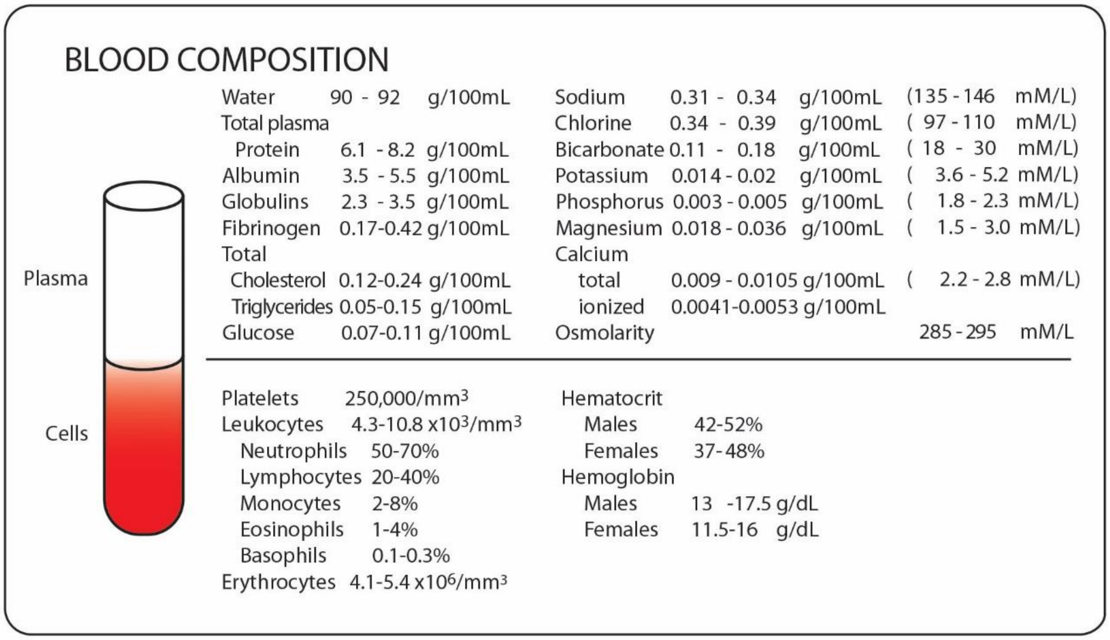

Figure 2-2 © 2016 David G. Ward, Ph.D.

- Plasma is about 93% to 90% water, with an osmolarity of 285 to 295 mOsm/L.
- About 6% to 8% of plasma is composed of three major groups of proteins.
    - Albumins boost osmolarity and transport lipids
    - Globulins transport ions, hormones lipids and form immune complexes
    - Fibrinogen is the precursor for fibrin in the clotting reaction
- About 0.2% to 0.6% of plasma is composed of cholesterol, triglycerides, and glucose.
- About 0.8% to 1.0% of plasma is composed of electrolytes such as sodium, chlorine, bicarbonate, potassium, phosphorus, magnesium, and calcium. The electrolytes are the major source of the osmolarity of the extracellular fluids.
- The remainder of plasma contains a wide variety of proteins, peptides, and lipids with critical roles as chemical messengers and enzymes.

Although the concentrations of electrolytes in interstitial fluid mimic blood plasma, the levels of electrolytes in intracellular fluid are markedly different, as shown in Table 2-2. The reason and function of these differences are explained in later chapters.

Table 2-2. Extracellular and Intracellular concentrations of common Electrolytes (Ions)

Electrolyte (Ion)	Extracellular concentration	Intracellular concentration
Na^+	140 mM/L	15 mM/L
K^+	5 mM/L	140 mM/L
Cl^-	105* mM/L	20* mM/L
Ca^{++}	3 mM/L	0.0001 mM/L

*different in nervous system

Biomolecules

In addition to water and electrolytes, the body is made of biomolecules, such as proteins (amino acids, peptides, and proteins), lipids (glycerol, fatty acids, triglycerides, phospholipids, eicosanoids, and cholesterol), carbohydrates (monosaccharides, disaccharides, polysaccharides), and nucleotides (nucleotides, and nucleic acids).

Amino Acids, Peptides, and Proteins

Amino acids, peptides and proteins are critical for the functioning of cells and include structural materials, enzymes, gene regulatory factors, transport agents, membrane receptors, hormones, neurotransmitters, and antibodies.

Amino Acids

Each amino acid contains an amino group (NH_2), a carboxyl group (COOH), and a variable group (R). There are 20 distinct amino acids (excluding selenocysteine – a unique 21st amino acid made from cysteine); 12 of the 20 can be synthesized in the body. However; 8 of the 20 must be in our diet and cannot be synthesized in the body.

When amino acids are free and not linked into peptides or proteins they have an uncharged amino group and an uncharged carboxyl group. When the amino acids are linked into a peptide or protein they are called amino acid residues because they lose H from the amino group and OH from the carboxyl group. When free amino acids are placed in water, the amino group and/or the carboxyl group may ionize, depending on the pH. For example, the amino group may gain H and the carboxyl group may lose H. The basic structures of free amino acids, amino acid residues, and ionized amino acids are shown in Figure 2-3.

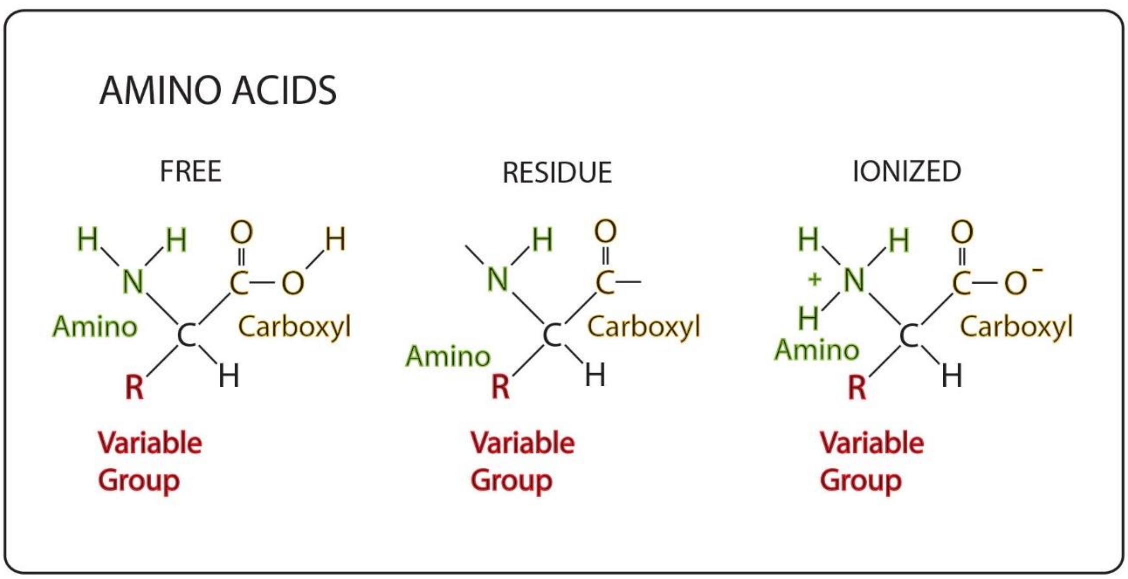

Figure 2-3 © 2014 David G. Ward, PhD

Amino acids vary in their organization and are grouped according to chemical properties of their side chains (R group). Pertinent examples of different categories of amino acids are shown in Figure 2-4. Furthermore, these specific amino acids were chosen because of their functions.

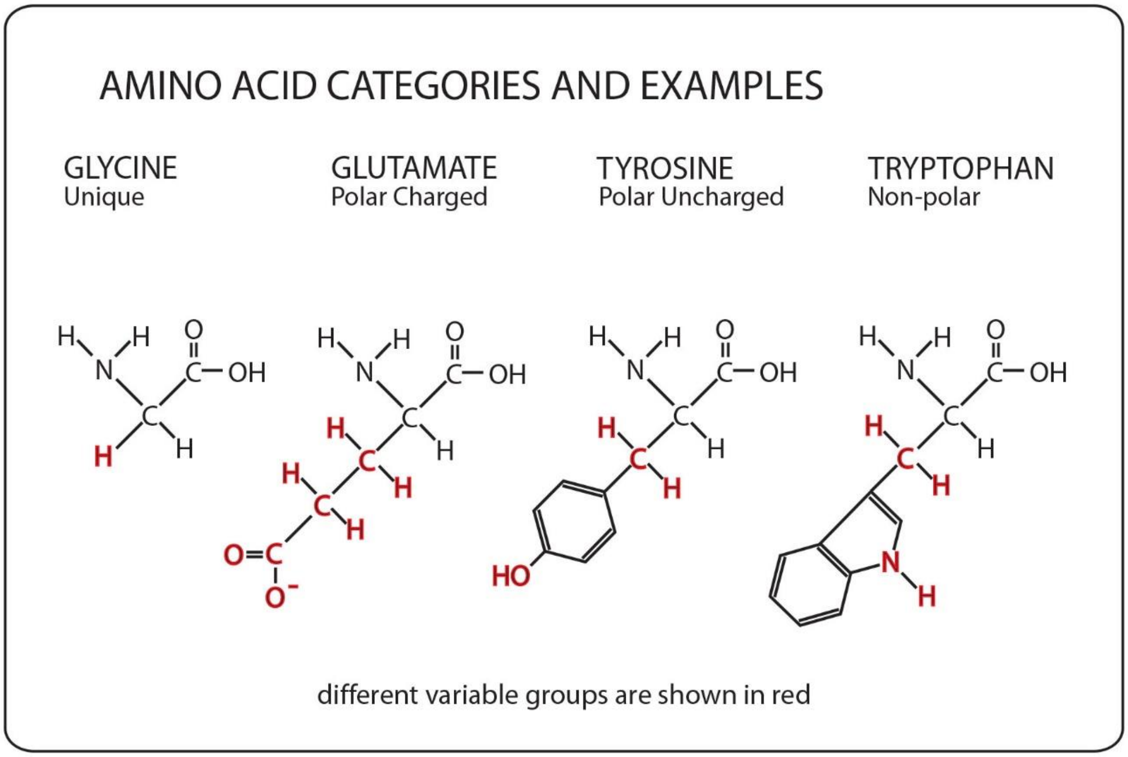

Figure 2-4 © 2014 David G. Ward, PhD

- Unique amino acids can be polar or non-polar.
- Polar charged amino acids are fully charged at normal pH and are able to form ionic attractions.
- Polar uncharged amino acids are capable of forming hydrogen bonds.
- Non-polar amino acids interact by means of van der Waals forces.

Functions of individual amino acids

Not only are amino acids linked together to form peptides and proteins, they function individually for many purposes, especially as chemical messengers. For example,

- Glycine functions as the second most common inhibitory neurotransmitter in the central nervous system.
- Glutamate functions as the most common excitatory neurotransmitter in the central nervous system.
- Glutamate is converted into gamma aminobutyric acid (GABA) which functions as the most common inhibitory neurotransmitter in the central nervous system.
- Aspartate is a common excitatory neurotransmitter in the central nervous system.

- Histidine is converted into histamine which is a common neurotransmitter in the GI tract and central nervous system, and is an inflammatory messenger in the immune system.
- Tyrosine is converted into dopamine, epinephrine, and norepinephrine which are common neurotransmitter in the central and peripheral nervous system, and are common hormones. Tyrosine is also converted into thyroid hormones which are major metabolic hormones.
- Tryptophan is converted into serotonin which is a common neurotransmitter in the GI tract and central and peripheral nervous system, and is a clotting messenger in blood.

Peptides and proteins

Amino acids are linked together to form peptides and proteins.

- The amino group (NH_2) and carboxyl group (COOH) of the amino acids form the **backbone** of a protein
- The variable group (R) of the amino acids form the **side chains** of a protein

Peptides and proteins consist of amino acids linked together by peptide bonds. Proteins vary in length and can be more than 1500 amino acids long. Peptides are relatively short chains of amino acids with the cut off for peptide *vs* protein at around 50 amino acids. Unfortunately, such definitions are often ambiguous and variable.

The sequence and interactions between the side chains (R groups) of the different amino acids allow each protein to fold into a specific three-dimensional **shape** and perform biological functions. Most proteins have an overall globular shape, and the specific shape of a protein is largely responsible for its specific function.

A protein has three levels of organization: primary, secondary, and tertiary structure. The term primary structure has two meanings and refers to: 1) the sequence of amino acid residues in the protein, and 2) the string like appearance of the backbone. The term secondary structure refers to the interaction between the backbone of the amino acids, causing coiling and/or pleating in the protein. The term tertiary structure refers to the interaction between the side chains of the amino acids, causing folding in the protein.

Figure 2-5 shows two views of the structure of aquaporin, a transmembrane protein that allows passage of water through plasma membranes in cells of the kidney, as well as many other cells. Note the complexity of the protein structure and the appearance of primary structure (strings), secondary structure (coiling), and tertiary structure (folding upon itself).

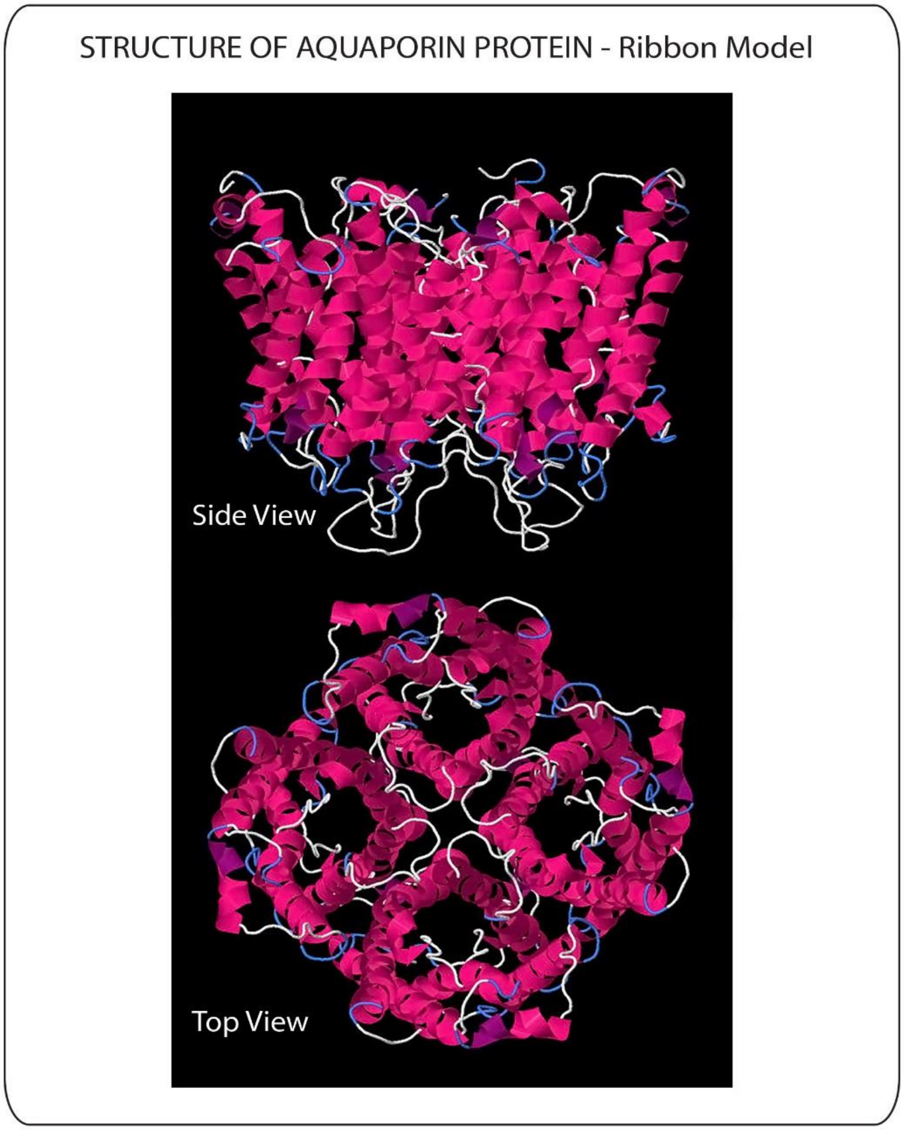

Figure 2-5 © 2014 David G. Ward, PhD

- Primary structure is the sequence of amino acids in the chain.
  - Determined by covalent bonds (peptide bonds) between the $-NH_2$ group and -COOH group of the amino acids
  - Peptide bonds are formed by dehydration synthesis (removal of H_2O) and broken by hydrolysis. (addition of H_2O)

- Secondary structure is the coiling (alpha helix) or bending (pleated sheet) of the amino acid chain.
  - Determined by hydrogen bonds between -CO and -NH groups of the backbone.

- Tertiary structure is the folding of the protein upon itself.
  - Determined by hydrogen bonds, ionic bonds, or disulfide bridges between side chains.

Functions and examples of peptides and protein

Peptides and proteins are ubiquitous (pervasive, abundant, everywhere). They do most of the work in cells and are required for the **structure**, **function**, and **regulation** of the cells, tissues, and organs of the body. There are tens of thousands of different peptides and proteins in the human body. Examples include:

- Structural proteins that are critical for the structure and function of chromosomes, the cytoskeleton, muscle cells, and connective tissues.
    - Histone
    - Actin
    - Myosin
    - Collagen
    - Elastin
- Enzymes that are critical for almost all of the thousands of chemical reactions that take place in our cells, and for the formation of new molecules by reading the genetic information stored in DNA.
    - Glycogen synthase
    - Glycogen phosphorylase
    - Phosphoglucomutase
    - Dopamine beta hydroxylase (DBH)
    - Phenylethanolamine N-methyltransferase (PNMT)
    - RNA polymerase
- Membrane transporters that are critical for allowing or causing the movement of most chemical substances into and out of cells.
    - Channels (Aquaporin)
    - Facilitated transporters (GLUT glucose transporters)
    - Co-transporter (Na/Glucose co-transporter [SGLT glucose transporters])
    - Counter-transporters (Na/H counter transporter)
    - Pumps (Na/K pumps)
- Chemical messengers, such as hormones and gene regulatory factors, that are critical for sending signals to genes and to cells.
    - Glucagon
    - Insulin
    - Thyrotropin
    - Triiodothyronin
    - CREB
- Membrane receptors that are critical for detecting chemical and physical messages.
    - Channel linked receptors (Cholinergic Nicotinic receptor)
    - Enzyme linked receptors (Tyrosine kinase linked receptor)
    - G-protein coupled receptors (Glucagon receptor)
    - Integrins
- Blood proteins that are critical for transporting oxygen and for the clotting of blood.
    - Hemoglobin
    - Fibrinogen
- Antibodies that bind to specific foreign particles, such as viruses and bacteria, to help protect the body.
    - Immunoglobulin G (IgG)
    - Immunoglobulin M (IgM)

Lipids

Lipids are critical sources of chemical energy, are a fundamental component of cell membranes, and serve in several types of chemical signaling. Lipids include fatty acids, glycerides, phospholipids, eicosanoids, and cholesterol.

- Lipids usually contain two or more H for every C, and less than one O for every C.
- Lipids generally are non-polar, hydrophobic, and do not dissolve in water.

Glycerol

Glycerol is not itself a lipid; but is critical in forming the backbone of glycerides (see next page). Glycerol is a chain of three carbons where all carbons have hydrogens and hydroxyls attached as shown is Figure 2-6. Because of the 3 OHs, glycerol is water soluble.

Fatty Acids

Fatty acids are long chain of carbons where the first carbon is attached to a carboxyl group (COOH) and the subsequent carbons have hydrogen(s) attached. The structure of saturated and unsaturated fatty acids is shown in Figure 2-6.

- Saturated fatty acids occur when there are no double bonds between adjacent carbon atoms. The *lack* of double bonds makes fat relatively solid.
- Unsaturated fatty acids occur when there are double bonds between adjacent carbon atoms. The *presence* of double bonds makes fat relatively liquid.

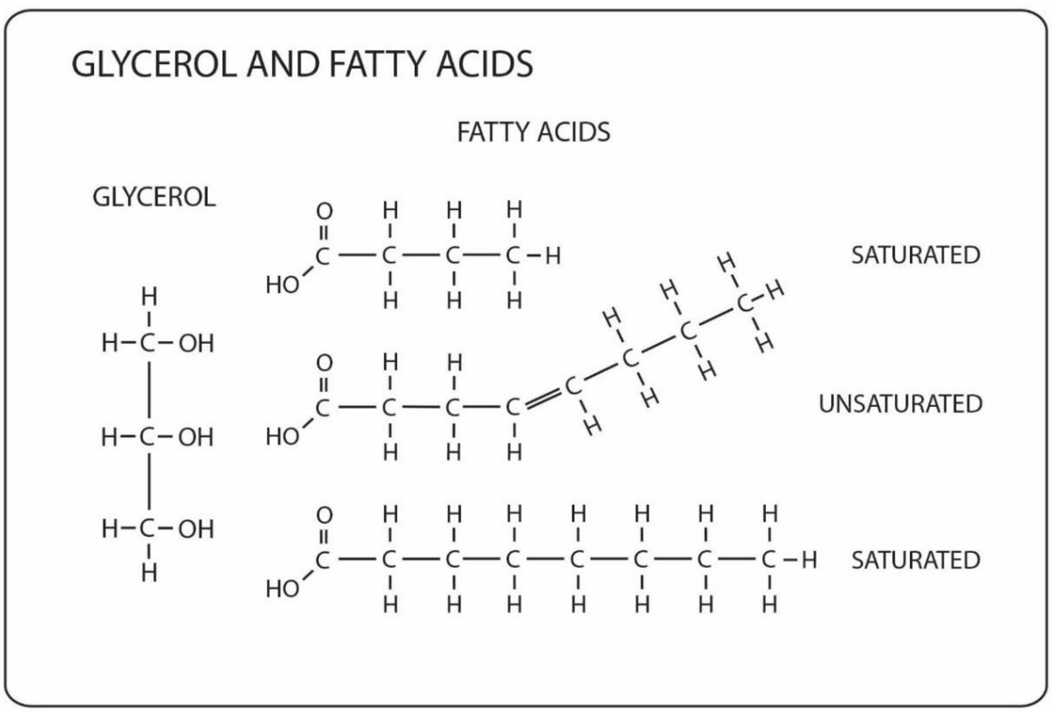

Figure 2-6 © 2016 David G. Ward, PhD

Glycerides

Glycerides are formed by linking glycerol to one, two, or three fatty acids. The basic structure of a triglyceride, where glycerol is linked to three fatty acids, is shown in Figure 2-7.

- Monoglycerides, Diglycerides and Triglycerides are formed by linking glycerol to one, two, or three fatty acids.
    - Glycerides can have any combination of saturated and unsaturated fatty acids.
- Glycerides are formed by dehydration synthesis (removal of water).
- Glycerides are broken apart by hydrolysis (addition of water).

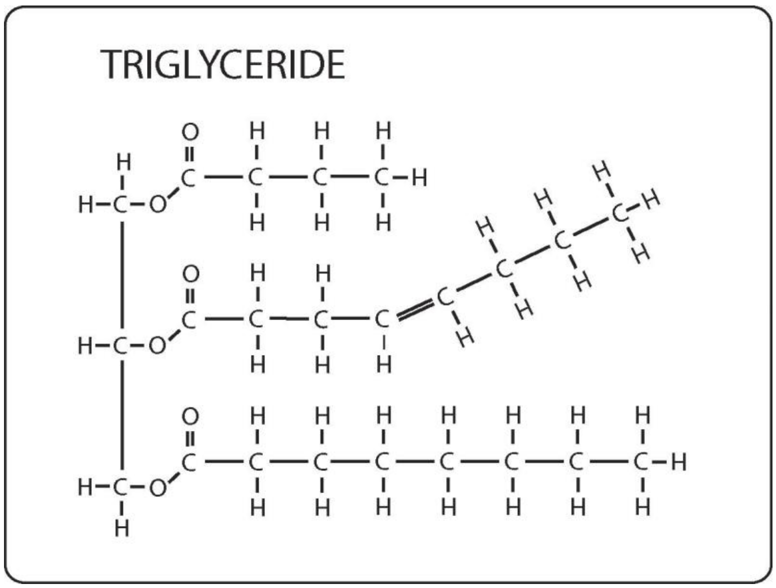

Figure 2-7 © 2007 David G. Ward, PhD

Functions of glycerides and fatty acids

Glycerides are abundant, and function, in part, as sources of chemical energy. In addition, glycerides and fatty acid, are the building blocks for other molecules.

- Triglycerides are the main form of storage of lipids in adipose tissue and liver.
    - Serve as a major source of stored energy
- Diglycerides serve as building blocks for construction of phospholipids
    - Phospholipids, in turn, are a major component of cell membranes
- Fatty acids, in addition to being building blocks for glycerides, serve as building blocks for eicosanoids and cholesterol
    - Eicosanoids include prostaglandins, thromboxanes, leukotrienes, and endocannabinoids
        - Those derived from omega-3 fatty acids are generally anti-inflammatory
        - Those derived from omega-6 fatty acids are generally pro-inflammatory
    - Cholesterol is critical for the synthesis of steroid hormones

Phospholipids

Phospholipids are diglycerides attached to phosphate, forming a hydrophobic tail with a hydrophilic head. There are many different phospholipids, and the structure of one of the most common, Phosphatidylcholine, is shown in Figure 2-8. The head of phosphatidylcholine is composed of choline and phosphate. The tail of phosphatidylcholine is composed of glycerol and two fatty acids. Phospholipids are a central and critical component of cell membranes.

- The **head** of the phospholipid contains phosphate and is **hydrophilic**.
- The **tail** of the phospholipid contains fatty acids and is **hydrophobic**.

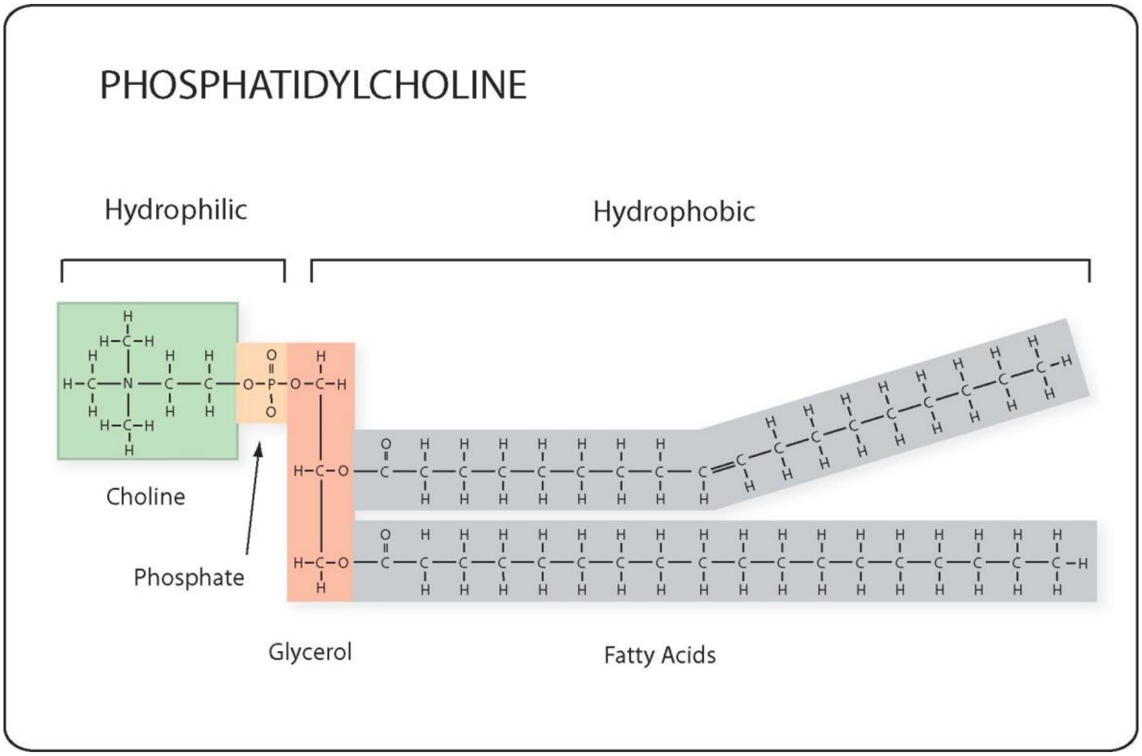

Figure 2-8 © 2007 David G. Ward, PhD

Functions of phospholipids

Phospholipids are a fundamental component of cell membranes.

- Phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, and phosphatidylserine are found in most cell membranes.
- Sphingomyelin is commonly found in the membranes of cells in the nervous system.
- Some phospholipids, including phosphatidylinositol (PIP2) are converted into arachidonic acid (an omega-6 family fatty acid), and into several chemical messengers, especially eicosanoids.

➢ Phospholipids are a fundamental component of cell membranes.

Eicosanoids

Eicosanoids are composed of two fatty acids connected by a carbon ring and are generally synthesized from omega-3 and omega-6 fatty acids. The most common eicosanoids are prostaglandins, thromboxanes, leukotrienes, and endocannabinoids.

- The enzymes cyclooxygenase and peroxidase are used to produce the prostaglandins and thromboxanes.
- The enzyme 5-lipoxygenase is used to produce the leukotrienes.
- The enzymes N- acylphosphatidylethanolamine-hydrolyzing phospholipase D (NAPE-PLD) and diacylglycerol (DAG) lipase are used to produce endocannabinoids, Arachidonylethanolamide (AEA) and 2-Arachidonoylglycerol (2-AG).
- Eicosanoids are important in cellular signaling, such as in the processes for blood clotting, inflammation, and neuromodulation.

We will explore eicosanoids further in subsequent chapters.

Cholesterol

Cholesterol is based on four rings of carbon based on fatty acids. The structure of cholesterol is shown in Figure 2-9.

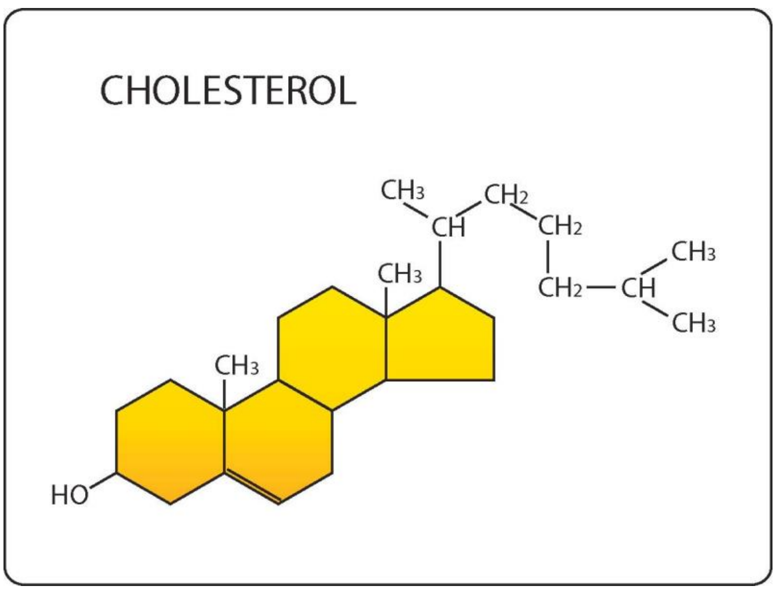

Figure 2-9 © 2007 David G. Ward, PhD

- Cholesterol is an integral part of cell membranes and forms the basis for the steroid hormones.
- Cholesterol is converted into the steroid hormones, which include progesterone, estrogen, testosterone, aldosterone, and cortisol.
- Cholesterol also forms the basis for vitamin D and bile salts.

We will explore steroid hormones further in the chapters about endocrine hormones, immunity, renal function, metabolism, and reproduction.

Carbohydrates

Carbohydrates function as sources of chemical energy and as building materials for other biomolecules making up cellular components. Carbohydrates range from simple sugars (monosaccharide and disaccharides) to complex carbohydrates (polysaccharides)

- Carbohydrates usually contain the ratio of 1C:2H:1O
  - Each carbon atom, except one, is linked to a hydroxyl group (OH); the remaining carbon is linked to a carbonyl group (C=O)
  - Sugars with 5 or more carbon atoms form ring-shaped molecules and lose the carbonyl group. The carbon to the right of the oxygen is numbered # 1
  - When forming a ring structure, one of the hydroxyl groups can take on a different orientation giving rise to alpha and beta forms of the same molecule (anomers).
- Carbohydrates generally are polar, hydrophilic and dissolve in water

Monosaccharides

Monosaccharides are simple sugars with 3 to 7 carbon atoms. The structures of Glucose, Galactose, Fructose, Ribose, and Deoxyribose are shown in Figure 2-10. Glucose is found in table sugar (sucrose), malt sugar (maltose), milk sugar (lactose), and starch.

- Glucose, Fructose, and Galactose are readily absorbed from the digestive tract. Glucose is the most common source of chemical energy.
- Ribose and Deoxyribose form the foundation of the nucleotides.
  - Ribose is essential for ribonucleic acid (RNA) and the high energy molecules adenosine triphosphate (ATP) and guanosine triphosphate (GTP).
  - Deoxyribose is essential for deoxyribonucleic acid (DNA).

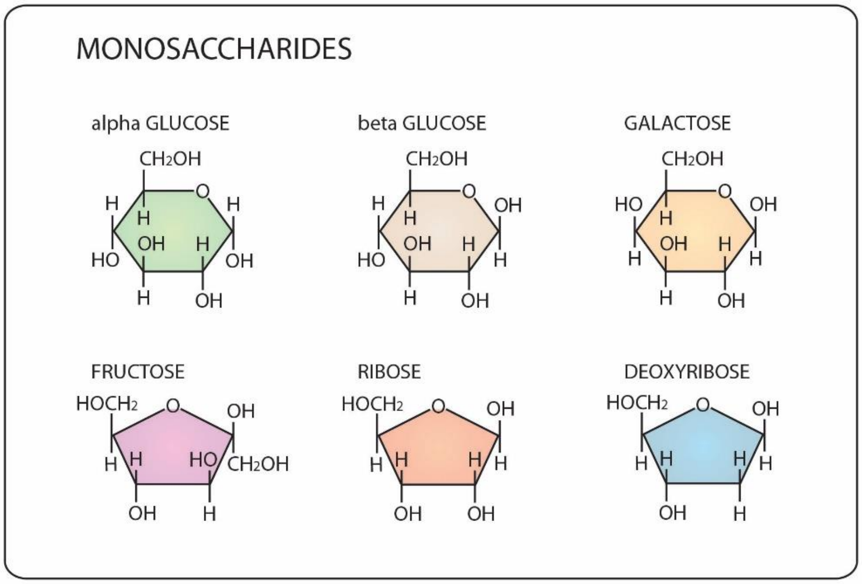

Figure 2-10 © 2016 David G. Ward, PhD

Disaccharides

Disaccharides are two simple sugars covalently bonded together. The structures of Maltose, Lactose, and Sucrose are shown in Figure 2-11. Maltose is malt sugar and is most commonly a breakdown product of starch. Lactose is milk sugar, and sucrose is table sugar.

- Maltose is made of two Alpha glucose molecules linked together
- Lactose is made, most commonly, of one Beta galactose molecule and one Alpha glucose molecule linked together.
- Sucrose is made of one Alpha glucose molecule and one fructose molecule linked together.
- Disaccharides are formed by dehydration synthesis (removal of water).
- Disaccharides are broken apart by hydrolysis (addition of water).

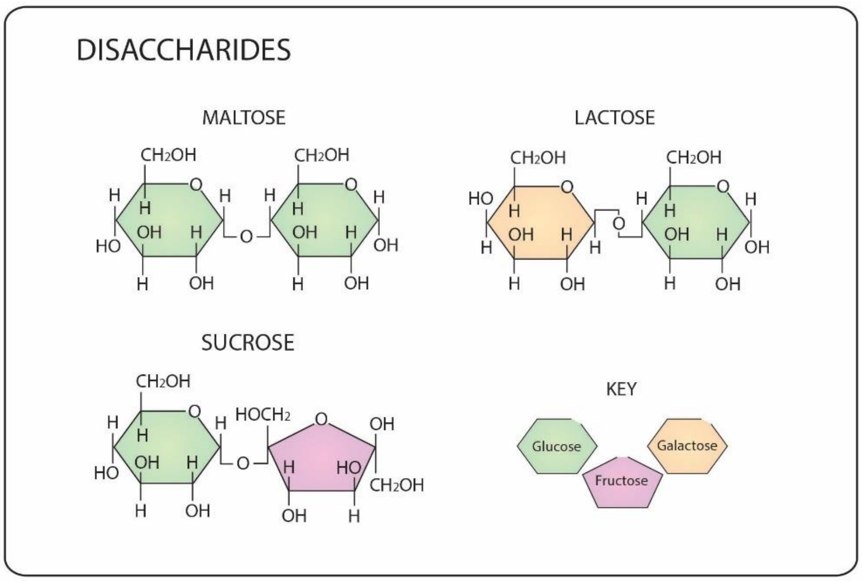

Figure 2-11 © 2018 David G. Ward, PhD

Functions of monosaccharides and disaccharides

Disaccharides are a major source of monosaccharides that, in turn, are major sources of chemical energy and major components of other biomolecules.

- Glucose is the most common source of chemical energy.
- Deoxyribose is the sugar in deoxyribonucleic acids (DNA)
- Ribose is the sugar in ribonucleic acids (RNA)
- Ribose is also the sugar in ribonucleotides, such as ATP and GTP

Polysaccharides

Polysaccharides are formed when more than two simple sugars are covalently bonded together. The most common polysaccharides are glycogen, starch, and cellulose

- Glycogen and starch are made of alpha glucose linked by alpha-1, 4 glycosidic bonds, with additional alpha-1, 6 glycosidic bonds creating branches. Glycogen has marked branching about every 10-12 molecules. Starch is composed of amylose (no branching) and amylopectin (branching, less than in glycogen). An abbreviated illustration of glycogen with branching is shown in Figure 2-12.
    - Glycogen is the form of glucose storage in humans and animals.
    - Starch is the form of glucose storage in plants.
- Cellulose is made of multiple molecules of beta-glucose linked by beta-1, 4 glycosidic binds and is a critical structural molecule in plants. Humans cannot digest cellulose.
- Polysaccharides are formed by dehydration synthesis (removal of water).
- Polysaccharides are broken apart by hydrolysis (addition of water).

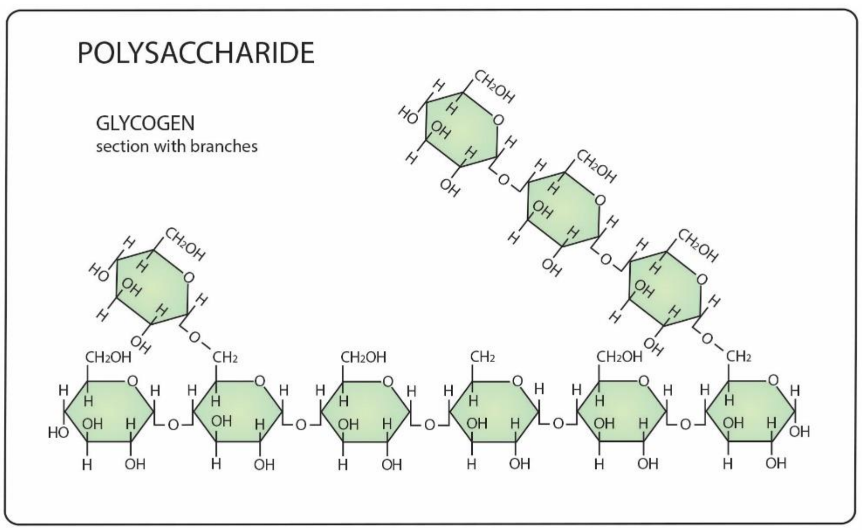

Figure 2-12 © 2018 David G. Ward, PhD

Functions of polysaccharides

Polysaccharides are constructed from monosaccharides; and are a major means to store carbohydrates for use as chemical energy and for incorporation into other biomolecules.

- Glycogen is the polysaccharide for storage of glucose in animals.
- Polysaccharides are a primary source of sugars that are conjugated with proteins and lipids.
    - Glycoproteins and glycolipids are major components of cell membranes.
    - Glycoproteins and glycolipids often are used in cellular metabolism or cell signaling

Quiz Yourself

1-5. Matching

A) Intracellular fluid	Contain(s) electrolytes	1) _____
B) Interstitial fluid	Composed mainly of water	2) _____
C) Vascular fluid	Found in blood vessels (about 3L)	3) _____
D) All of the above	Found in interstitial fluid (about 11 L)	4) _____
	Found in cytoplasm of cells (about 28 L)	5) _____

6-10. Matching (Typically)

A) Carbohydrates	Water soluble	6) _____
B) Proteins	Eicosanoids are example	7) _____
C) Lipids	H, (NH2), (COOH), and (R	8) _____
D) A&B	Twice as many H as C; same number of O as C	9) _____
E) B&C	Two or more times H than C; much less O than C	10) _____

11-15. Matching

A) Disaccharides	starch or glycogen	11) _____
B) Monosaccharides	deoxyribose	12) _____
C) Polysaccharides	glucose	13) _____
	maltose	14) _____
	ribose	15) _____

16-20. Matching

A) Glycerol	a chain of three carbons with hydrogens and hydroxyl	16) _____
B) Fatty acids	carbons with hydrogen attached and a carboxyl group	17) _____
C) Glycerides	two fatty acids connected by a carbon ring	18) _____
D) Eicosanoids	glycerol with one, two or three fatty acids	19) _____
E) Phospholipids	glyceride with phosphate attached	20) _____

Fill in

21. Hydrogen bonds represent the attraction of a hydrogen atom with ____________.

22. Water is an excellent solvent due to ____________ bonding between water molecules.

23. Fats and steroids exhibit ____________ solubility in water.

24. The more unsaturated a fat, the more ____________ ____________ there are.

25. In fat synthesis ____________ and fatty acids combine to make glycerides plus ____________.

Study Questions

1. Describe the location and composition of body fluids.
2. Describe the organization of electrolytes; and explain their behavior in water.
3. Compare and contrast the composition of carbohydrates, lipids and proteins.
4. Compare and contrast the primary, secondary, and tertiary structure of proteins; and explain their significance.