

CHAPTER 25

LECTURE OUTLINE

I. INTRODUCTION

- A. The food we eat is our only source of energy for performing biological work.
- B. There are three major metabolic destinations for the principle nutrients. They will be used for energy for active processes, synthesized into structural or functional molecules, or synthesized as fat or glycogen for later use as energy

II. METABOLIC REACTIONS

- A. Metabolism refers to all the chemical reactions in the body.
- B. Coupling of catabolism and anabolism by ATP
 - 1. Catabolism includes all chemical reactions that break down complex organic molecules while anabolism refers to chemical reactions that combine simple molecules to form complex molecules.
 - 2. The chemical reactions of living systems depend on transfer of manageable amounts of energy from one molecule to another. This transfer is usually performed by ATP (Figure 25.1).

III. ENERGY TRANSFER

- A. All molecules (nutrient molecules included) have energy stored in the bonds between their atoms.
- B. Oxidation-Reduction Reactions
 - 1. Oxidation is the removal of electrons from a molecule and results in a decrease in the energy content of the molecule. Because most biological oxidations involve the loss of hydrogen atoms, they are called dehydrogenation reactions.
 - a. When a substance is oxidized, the liberated hydrogen atoms do not remain free in the cell but are transferred immediately by coenzymes to another compound.
 - b. Two coenzymes are commonly used by living cells to carry hydrogen atoms: nicotinamide adenine dinucleotide (NAD) and flavin adenine dinucleotide (FAD).
 - 2. Reduction is the opposite of oxidation, that is, the addition of electrons to a molecule and results in an increase in the energy content of the molecule.

3. An important point to remember about oxidation-reduction reactions is that oxidation is usually an energy-releasing reaction.

C. Mechanisms of ATP generation

1. ATP can be generated by any of three mechanisms of phosphorylation: substrate-level phosphorylation, oxidative phosphorylation, or photophosphorylation (if chlorophyll is present).

IV. CARBOHYDRATE METABOLISM

A. During digestion, polysaccharides and disaccharides are converted to monosaccharides (primarily glucose), which are absorbed through capillaries in villi and transported to the liver via the hepatic portal vein. Liver cells convert much of the remaining fructose and practically all of the galactose to glucose, so carbohydrate metabolism is primarily concerned with glucose metabolism.

B. Fate of Glucose

1. Since glucose is the body's preferred source for synthesizing ATP, the fate of absorbed glucose depends on the energy needs of body cells.
2. If the cells require immediate energy, glucose is oxidized by the cells to produce ATP.
3. Glucose can be used to form amino acids, which then can be incorporated into proteins.
4. Excess glucose can be stored by the liver and skeletal muscles as glycogen, a process called glycogenesis.
5. If glycogen storage areas are filled up, liver cells and fat cells can convert glucose to glycerol and fatty acids that can be used for synthesis of triglycerides (neutral fats) in the process of lipogenesis.

C. Glucose Movement into Cells

1. Glucose absorption in the GI tract is accomplished by secondary active transport (Na^+ - glucose symporters).
2. Glucose movement from blood into most other body cells occurs via facilitated diffusion transporters (Gly-T molecules). Insulin increases the insertion of Gly-T molecules into the plasma membranes, thus increasing the rate of facilitated diffusion of glucose.
3. Glucose is trapped in the cell when it becomes phosphorylated.

D. Glucose Catabolism

1. Glucose oxidation is also called cellular respiration. It occurs in every cell of the body (except red blood cells, which lack mitochondria) and provides the cell's chief source of energy.
2. The complete oxidation of glucose to CO₂ and H₂O produces large amounts of energy and occurs in four successive stages: glycolysis, formation of acetyl coenzyme A, the Krebs cycle, and the electron transport chain (Figure 25.2).
 - a. Glycolysis
 - 1) Glycolysis refers to the breakdown of the six-carbon molecule, glucose, into two three-carbon molecules of pyruvic acid
 - 2) The reactions of glycolysis use two ATP molecules, but produce four, a net gain of two (Figure 25.3).
 - 3) Figure 25.4 depicts the 10 reactions of Glycolysis.
 - b. Fate of pyruvic acid
 - 1) When oxygen is in short supply, pyruvic acid is reduced to lactic acid. Under aerobic conditions, pyruvic acid is converted to acetyl coenzyme A and enters the Krebs cycle (Figure 25.5). Thus the fate of pyruvic acid depends on the availability of O₂.
 - c. Formation of Acetyl Coenzyme A
 - 1) Pyruvic acid is prepared for entrance into the Krebs cycle by conversion to a two-carbon compound (acetyl group) followed by the addition of coenzyme A (CoA) to form acetyl coenzyme A (acetyl CoA) (Figure 25.5).
 - 2) Coenzyme A is derived from pantothenic acid, a B vitamin.
 - d. Krebs Cycle
 - 1) The Krebs cycle is also called the citric acid cycle, or the tricarboxylic acid (TCA) cycle. It is a series of biochemical reactions that occur in the matrix of mitochondria (Figure 25.6).
 - 2) The large amount of chemical potential energy stored in intermediate substances derived from pyruvic acid is released step by step.
 - 3) The Krebs cycle involves decarboxylations and oxidations and reductions of various organic acids.
 - 4) For every two molecules of acetyl CoA that enter the Krebs cycle, 6 NADH, 6 H⁺, and 2 FADH₂ are produced by oxidation-reduction

reactions, and two molecules of ATP are generated by substrate-level phosphorylation (Figure 25.6).

5) The energy originally in glucose and then pyruvic acid is primarily in the reduced coenzymes NADH + H⁺ and FADH₂.

6) Figure 25.7 summarizes the eight reactions of the Krebs cycle

e. Electron Transport Chain

1) The electron transport chain involves a sequence of electron carrier molecules on the inner mitochondrial membrane, capable of a series of oxidation-reduction reactions.

a) As electrons are passed through the chain, there is a stepwise release of energy from the electrons for the generation of ATP.

b) In aerobic cellular respiration, the last electron receptor of the chain is molecular oxygen (O₂). This final oxidation is irreversible.

2) The process involves a series of oxidation-reduction reactions in which the energy in NADH + H⁺ and FADH₂ is liberated and transferred to ATP for storage.

a) This mechanism of ATP generation links chemical reactions (electrons passing along the electron chain) with pumping of hydrogen ion.

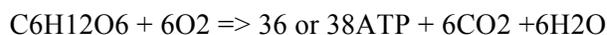
b) It is called chemiosmosis and is shown in Figure 25.8.

3) The carrier molecules involved include flavin mononucleotide, cytochromes, iron-sulfur centers, copper atoms, and ubiquinones (also coenzyme Q).

4) Within the inner mitochondrial membrane, the carriers of the electron transport chain cluster into three complexes, each of which acts as a proton pump that expels H⁺ from the mitochondrial matrix and helps create an electrochemical gradient of H⁺ (Figure 25.9).

f. Summary of Cellular Respiration

1) The complete oxidation of glucose can be represented as follows:



2) During aerobic respiration, 36 or 38 ATPs can be generated from one molecule of glucose. Two of those ATPs come from substrate-

level phosphorylation in glycolysis and two come from substrate-level phosphorylation in the Krebs cycle.

- 3) Table 25.1 summarizes the ATP yield during aerobic respiration.
- 4) Figure 25.10 summarizes the sites of the principal events of the various stages of cellular respiration.

E. Glucose Anabolism

1. The conversion of glucose to glycogen for storage in the liver and skeletal muscle is called glycogenesis. The process occurs in the liver and is stimulated by insulin (Figure 25.11).
2. The conversion of glycogen back to glucose is called glycogenolysis. This process occurs between meals and is stimulated by glucagon and epinephrine (Figure 25.11).
3. Carbohydrate loading by eating large amounts of complex carbohydrates maximizes the amount of energy available for exercise.(Clinical Connection)
4. Gluconeogenesis is the conversion of protein or fat molecules into glucose (Figure 25.12).
 - a. Glycerol (from fats) may be converted to glyceraldehyde-3-phosphate and some amino acids may be converted to pyruvic acid. Both of these compounds may enter the Krebs cycle to provide energy.
 - b. Gluconeogenesis is stimulated by cortisol, thyroid hormone, epinephrine, glucagon, and human growth hormone.

V. LIPID METABOLISM

A. Transport of Lipids by Lipoproteins

1. Most lipids are transported in the blood in combination with proteins as lipoproteins (Figure 25.13). Four classes of lipoproteins are chylomicrons, very low-density lipoproteins (VLDLs), low-density lipoproteins (LDLs), and high-density lipoproteins (HDLs).
 - a. Chylomicrons form in small intestinal mucosal cells and contain exogenous (dietary) lipids. They enter villi lacteals, are carried into the systemic circulation into adipose tissue where their triglyceride fatty acids are released and stored in the adipocytes and used by muscle cells for ATP production.

- b. VLDLs contain endogenous triglycerides. They are transport vehicles that carry triglycerides synthesized in hepatocytes to adipocytes for storage. VLDLs are converted to LDLs.
 - c. LDLs carry about 75% of total blood cholesterol and deliver it to cells throughout the body. When present in excessive numbers, LDLs deposit cholesterol in and around smooth muscle fibers in arteries.
 - d. HDLs remove excess cholesterol from body cells and transport it to the liver for elimination.
 2. There are two sources of cholesterol in the body: food we eat and liver synthesis.
 - a. For adults, desirable levels of blood cholesterol are TC (total cholesterol) under 200 mg/dl, LDL under 130 mg/dl, and HDL over 40 mg/dl. Normally, triglycerides are in the range of 10-190 mg/dl.
 - b. Among the therapies used to reduce blood cholesterol level are exercise, diet, and drugs.

B. Fate of Lipids

1. Some lipids may be oxidized to produce ATP.
2. Some lipids are stored in adipose tissue.
3. Other lipids are used as structural molecules or to synthesize essential molecules. Examples include phospholipids of plasma membranes, lipoproteins that transport cholesterol, thromboplastin for blood clotting, and cholesterol used to synthesize bile salts and steroid hormones.
4. The various functions of lipids in the body may be reviewed in Table 2.7.

C. Triglyceride Storage

1. Triglycerides are stored in adipose tissue, mostly in the subcutaneous layer.
2. Adipose cells contain lipases that catalyze the deposition of fats from chylomicrons and hydrolyze neutral fats into fatty acids and glycerol.
3. Fats in adipose tissue are not inert. They are catabolized and mobilized constantly throughout the body.

D. Lipid Catabolism: Lipolysis

1. Triglycerides are split into fatty acids and glycerol (a process called lipolysis) under the influence of hormones such as epinephrine, norepinephrine, and glucocorticoids and released from fat deposits. Glycerol and fatty acids are then catabolized separately (Figure 25.14).

2. Glycerol can be converted into glucose by conversion into glyceraldehyde-3-phosphate.
3. In beta oxidation, carbon atoms are removed in pairs from fatty acid chains. The resulting molecules of acetyl coenzyme A enter the Krebs cycle.
 - a. As a part of normal fatty acid catabolism two acetyl CoA molecules can form acetoacetic acid which can then be converted to beta-hydroxybutyric acid and acetone.
 - b. These three substances are known as ketone bodies and their formation is called ketogenesis (Figure 25.14).

E. Lipid Anabolism: Lipogenesis

1. The conversion of glucose or amino acids into lipids is called lipogenesis. The process is stimulated by insulin (Figure 25.14).
2. The intermediary links in lipogenesis are glyceraldehyde-3-phosphate and acetyl coenzyme A.
3. An excess of ketone bodies, called ketosis, may cause acidosis or abnormally low blood pH (Clinical Connection).

VI. PROTEIN METABOLISM

A. During digestion, proteins are hydrolyzed into amino acids. Amino acids are absorbed by the capillaries of villi and enter the liver via the hepatic portal vein.

B. Fate of Proteins

1. Amino acids, under the influence of human growth hormone and insulin, enter body cells by active transport.
2. Inside cells, amino acids are synthesized into proteins that function as enzymes, transport molecules, antibodies, clotting chemicals, hormones, contractile elements in muscle fibers, and structural elements. They may also be stored as fat or glycogen or used for energy. (Table 2.8)

C. Protein Catabolism

1. Before amino acids can be catabolized, they must be converted to substances that can enter the Krebs cycle. These conversions involve deamination, decarboxylation, and hydrogenation (Figure 25.14).
2. Amino acids can be converted into glucose, fatty acids, and ketone bodies.

D. Protein Anabolism

1. Protein anabolism involves the formation of peptide bonds between amino acids to produce new proteins.
2. Protein synthesis is stimulated by human growth hormone, thyroxine, and insulin.
3. Protein synthesis is carried out on the ribosomes of almost every cell in the body, directed by the cells' DNA and RNA.
4. Of the 20 amino acids in your body, 10 are referred to as essential amino acids. These amino acids cannot be synthesized by the human body from molecules present within the body. They are synthesized by plants or bacteria. Food containing these amino acids are "essential" for human growth and must be a part of the diet.
5. Nonessential amino acids can be synthesized by body cells by a process called transamination. Once the appropriate essential and nonessential amino acids are present in cells, protein synthesis occurs rapidly.
6. Phenylketonuria (PKU) is a genetic error of protein metabolism characterized by elevated blood levels of the amino acid phenylalanine. It is caused by a mutation in the gene that codes for the enzyme phenylalanine hydroxylase. This enzyme is needed to convert phenylalanine to tyrosine (Clinical Connection).

VII. KEY MOLECULES AT METABOLIC CROSSROADS

- A. Although there are thousands of different chemicals in your cells, three molecules play key roles in metabolism: glucose-6-phosphate, pyruvic acid, and acetyl CoA (Figure 25.16).
- B. Role of Glucose-6-phosphate
 1. Glucose-6-phosphate can be used to synthesize glycogen or glucose, make ribose-5-phosphate for the synthesis of RNA and DNA, and be converted to pyruvate via glycolysis.
- C. Role of Pyruvic acid
 1. Production of lactic acid
 2. Production of alanine
 3. Gluconeogenesis
- D. Role of Acetyl coenzyme A

1. When ATP is low and oxygen is plentiful, pyruvic acid is converted to acetyl coenzyme A. When oxygen supply is low, pyruvic acid is converted to lactic acid. One link between carbohydrate and protein metabolism is via pyruvic acid.
 2. Acetyl coenzyme A is the gateway into the Krebs cycle and is also used to synthesize fatty acids, ketone bodies, and cholesterol.
- E. Table 25.2 summarizes carbohydrate, lipid, and protein metabolism

VIII. METABOLIC ADAPTATIONS

- A. Your metabolic reactions depends on how recently you have eaten. During the absorptive state, which alternates with the postabsorptive state, ingested nutrients enter the blood and lymph from the GI tract, and glucose is readily available for ATP production.
1. An average meal requires about 4 hours for complete absorption, and given three meals a day, the body spends about 12 hours of each day in the absorptive state. (The other 12 hours, during late morning, late afternoon, and most of the evening, are spent in the postabsorptive state.)
 2. Hormones are the major regulators of reactions during each state.
- B. Metabolism During the Absorptive State
1. Several things typically happen during the absorptive state (Figure 25.17).
 - a. Most body cells produce ATP by oxidizing glucose to carbon dioxide and water.
 - b. Glucose transported to the liver is converted to glycogen or triglycerides. Little is oxidized for energy.
 - c. Most dietary lipids are stored in adipose tissue.
 - d. Amino acids in liver cells are converted to carbohydrates, fats, and proteins.
 2. Regulation of Metabolism During the Absorptive State
 - a. Soon after eating, gastric inhibitory peptide and the rise in blood glucose concentration stimulate insulin release from pancreatic beta cells. In several ways, insulin stimulates absorptive state metabolism.
 - b. Table 25.3 summarizes the hormonal regulation of metabolism in the absorptive state.
- C. Metabolism During the Postabsorptive State
1. During the postabsorptive state, absorption is complete, and the energy needs of the body must be satisfied by nutrients already present in the body

- a. The major concern of the body during the postabsorptive state is to maintain normal blood glucose level (70 to 110 mg/100 ml of blood).
 - b. Homeostasis of blood glucose concentration is especially important for the nervous system and red blood cells.
 - 1) The dominant fuel molecule for ATP production in the nervous system is glucose because fatty acids are unable to pass the blood-brain barrier.
 - 2) Red blood cells derive all of their ATP from glycolysis of glucose because they lack mitochondria and thus lack the Krebs cycle and electron transport chain.
2. Postabsorptive State Reactions
- a. Reactions that produce glucose are the breakdown of liver glycogen, gluconeogenesis using lactic acid, and gluconeogenesis using amino acids (Figure 25.18).
 - b. Reactions that produce ATP without using glucose are oxidation of fatty acids, oxidation of lactic acid, oxidation of amino acids, oxidation of ketone bodies, and breakdown of muscle glycogen.
3. Regulation of Metabolism During the Postabsorptive State
- a. The hormones that stimulate metabolism in the postabsorptive state sometimes are called anti-insulin hormones because they counter the insulin effects that dominate the absorptive state. The most important anti-insulin hormone is glucagon.
 - b. A low blood glucose level also activates the sympathetic branch of the ANS.
 - c. Table 25.4 summarizes hormonal regulation of metabolism in the postabsorptive state.

D. Metabolism During Fasting and Starvation

1. Fasting means going without food for many hours or a few days whereas starvation implies weeks or months of food deprivation or inadequate food intake.
 - a. Catabolism of stored triglycerides and structural proteins can provide energy for several weeks.
 - b. The amount of adipose tissue determines the lifespan possible without food.

2. During fasting and starvation, nervous tissue and red blood cells continue to use glucose for ATP production.
3. During prolonged fasting, large amounts of amino acids from tissue protein breakdown (primarily from skeletal muscle) are released to be converted to glucose in the liver by gluconeogenesis.
4. The most dramatic metabolic change that occurs with fasting and starvation is the increase in formation of ketone bodies by hepatocytes.
 - a. Ketogenesis increases as catabolism of fatty acids rises.
 - b. The presence of ketones actually reduces the use of glucose for ATP production, which in turn decreases the demand for gluconeogenesis and slows the catabolism of muscle proteins.

IX. HEAT AND ENERGY BALANCE

- A. A normal body temperature is maintained by a delicate balance between heat-producing and heat-losing mechanisms.
- B. Metabolic Rate
 1. The overall rate at which heat is produced is termed the metabolic rate.
 - a. Measurement of the metabolic rate under basal conditions is called the basal metabolic rate (BMR).
 - b. BMR is a measure of the rate at which the quiet, resting, fasting body breaks down nutrients to liberate energy.
 - c. BMR is also a measure of how much thyroxine the thyroid gland is producing, since thyroxine regulates the rate of ATP use and is not a controllable factor under basal conditions.
 2. Heat is a form of kinetic energy that can be measured as temperature and expressed in units called calories.
 - a. A calorie, spelled with a little c, is the amount of heat energy required to raise the temperature of 1 gram of water from 14°C to 15°C.
 - b. A kilocalorie or Calorie, spelled with a capital C, is equal to 1000 calories.
- C. Body Temperature Homeostasis
 1. If the amount of heat production equals the amount of heat loss, one maintains a constant core temperature near 37°C (98.6°F).

- a. Core temperature refers to the body's temperature in body structures below the skin and subcutaneous tissue.
 - b. Shell temperature refers to the body's temperature at the surface, that is, the skin and subcutaneous tissue.
 - c. Too high a core temperature kills by denaturing body proteins, while too low a core temperature causes cardiac arrhythmias that can result in death.
2. Heat Production
- a. The production of body heat is influenced by metabolic rate and responses that occur when body temperature starts to fall.
 - b. Factors that affect metabolic rate include exercise, hormones, the nervous system, body temperature, ingestion of food, age, and other factors such as gender, climate, sleep, and malnutrition.
 - c. Heat conservation mechanisms include vasoconstriction, sympathetic stimulation, skeletal muscle contraction (shivering), and thyroid hormone production.
3. Mechanisms of Heat Transfer: Heat is lost from the body by radiation, evaporation, conduction, and convection.
- a. Radiation is the transfer of heat from a warmer object to a cooler object without physical contact.
 - b. Evaporation is the conversion of a liquid to a vapor. Water evaporating from the skin takes with it a great deal of heat. The rate of evaporation is inversely related to relative humidity.
 - c. Conduction is the transfer of body heat to a substance or object in contact with the body, such as chairs, clothing, jewelry, air, or water.
 - d. Convection is the transfer of body heat by a liquid or gas between areas of different temperature.
4. Hypothalamic Thermostat
- a. The hypothalamic thermostat is the preoptic area.
 - b. Nerve impulses from the preoptic area propagate to other parts of the hypothalamus known as the heat-losing center and the heat-promoting center.
5. Several negative feedback loops work to raise body temperature when it drops too low or raises too high (Figure 25.19).

6. Hypothermia refers to a lowering of body temperature to 35°C (95°F) or below. It may be caused by an overwhelming cold stress, metabolic disease, drugs, burns, malnutrition, transection of the cervical spinal cord, and lowering of body temperature for surgery. (Clinical Connection).

D. Energy Homeostasis and Regulation of Food Intake

1. Energy homeostasis occurs when energy intake is matched to energy expenditure
 - a. Energy intake depends on the amount of food consumed
 - b. Energy expenditure depends on basal metabolic rate (BMR), nonexercise thermogenesis (NEAT), and food induced thermogenesis.
2. Two centers in the hypothalamus related to regulation of food intake are the feeding (hunger) center and satiety center. The feeding center is constantly active but may be inhibited by the satiety center (Figure 14.10).
3. The hormone leptin acts on the hypothalamus to inhibit circuits that stimulate eating and to activate circuits that increase energy expenditure.
4. Other stimuli that affect the feeding and satiety centers are glucose, amino acids, lipids, body temperature, distention of the GI tract, and cholecystokinin.
5. Eating in response to emotions is called emotional eating. Problems arise when emotional eating becomes so excessive that it interferes with health (Clinical Connection).

X. NUTRITION

- A. Guidelines for healthy eating include eating a variety of foods; maintaining healthy weight; choosing foods low in fat, saturated fat, and cholesterol; eating plenty of vegetables, fruits, and grain products; using sugar only in moderation; using salt and sodium only in moderation; and drinking alcohol only in moderation or not at all.
 1. The Food Guide Pyramid (Figure 25.20) shows how many servings of the five major food groups to eat each day.
 2. Foods high in complex carbohydrates serve as the base of the pyramid since they should be consumed in largest quantity.
- B. Minerals are inorganic substances that help regulate body processes.
 1. Minerals known to perform essential functions include calcium, phosphorus, sodium, chlorine, potassium, magnesium, iron, sulfur, iodine, manganese, cobalt, copper, zinc, selenium, and chromium.

2. Their functions are summarized in Table 25.5.
- C. Vitamins are organic nutrients that maintain growth and normal metabolism. Many function in enzyme systems as coenzymes.
1. Most vitamins cannot be synthesized by the body. No single food contains all of the required vitamins – one of the best reasons for eating a varied diet.
 2. Based on solubility, vitamins fall into two main groups: fat-soluble and water-soluble.
 - a. Fat-soluble vitamins are emulsified into micelles and absorbed along with ingested dietary fats by the small intestine. They are stored in cells (particularly liver cells) and include vitamins A, D, E, and K.
 - b. Water-soluble vitamins are absorbed along with water in the GI tract and dissolve in the body fluids. Excess quantities of these vitamins are excreted in the urine. The body does not store water-soluble vitamins well. They include the B vitamins and vitamin C.
 - c. Vitamins C, E, and beta-carotene (a provitamin) are termed antioxidant vitamins because they inactivate oxygen free radicals.
 3. The sources, functions, and related deficiency disorders of the principal vitamins are listed in Table 25.6.
 4. Most physicians do not recommend taking vitamin or mineral supplements except in special circumstances, and instead suggest being sure to eat a balanced diet that includes a variety of food. (Clinical Connection)

XI. DISORDERS: HOMEOSTATIC IMBALANCES

- A. Fever is an elevation of body temperature that is due to resetting of the hypothalamic thermostat. The most common cause of fever is a viral or bacterial infection
- B. Obesity is defined as a body weight more than 20% above desirable standard as the result of excessive accumulation of fat.
 1. Even moderate obesity is hazardous to health.
 2. Obesity is implicated as a risk factor in cardiovascular disease, hypertension, pulmonary disease, non-insulin dependent diabetes mellitus (type II), arthritis, certain cancers (breast, uterus, and colon), varicose veins, and gallbladder disease.