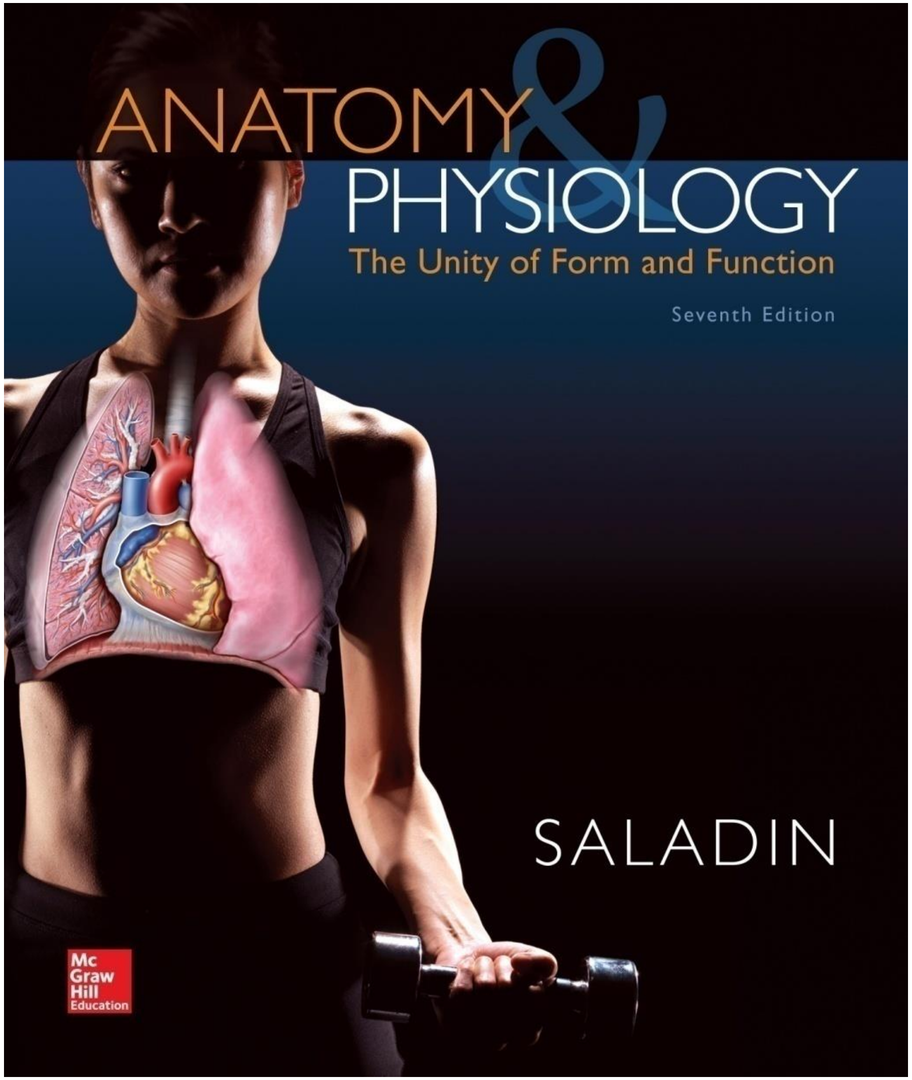
Chapter 26
Lecture Outline

See separate PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes.



Introduction

- **Nutrition** is the starting point and the basis for all human form and function
  - The source of **fuel** that provides energy for all biological work
  - The source of **raw materials** for replacement of worn-out biomolecules and cells

- **Metabolism** is the chemical change that lies at the foundation of form and function

Nutrition

- **Expected Learning Outcomes**
  - Describe some factors that regulate hunger and satiety.
  - Define *nutrient* and list the six major categories of nutrients.
  - State the function of each class of macronutrients, the approximate amounts required in the diet, and some major dietary sources of each.
  - Name the blood lipoproteins, state their functions, and describe how they differ from each other.
  - Name the major vitamins and minerals required by the body and the general functions they serve.

Body Weight and Energy Balance

- **Weight**—determined by the body's energy balance
  - If energy intake and output are equal, **body weight is stable**
  - **Gain weight** if intake exceeds output
  - **Lose weight** if output exceeds intake
  - Weight seems to have a stable, homeostatic set point
    - Varies from person to person
    - Combination of heredity and environmental influences
      - 30% to 50% of variation in human weight is hereditary
      - Environmental factors such as eating and exercise habits account for the rest of the variation

Appetite

- **Control of weight involves several peptide hormones and regulatory pathways that control short- and long-term appetite**
  - **Gut–brain peptides:** act as chemical signals from the gastrointestinal tract to the brain

- **Short-term regulators of appetite**
  - Mechanisms work over periods of minutes to hours
  - Makes one feel hungry and begin eating
  - Makes one feel satiated and end a meal

Appetite

- **Short-term regulators:** include the peptides ghrelin, peptide YY, and cholecystokinin
  - **Ghrelin**
    - Secreted from parietal cells in **fundus of empty stomach**
    - Produces sensation of hunger
    - Stimulates hypothalamus to secrete **growth hormone–releasing hormone**
      - Primes body to take advantage of nutrients about to be absorbed
    - Ghrelin secretion ceases within an hour of eating

Appetite

Short-term regulators (Continued)

- **Peptide YY (PYY)**
  - Secreted by **enteroendocrine cells of ileum and colon** that can sense that food has arrived in stomach
    - Secrete PYY long before chyme reaches ileum
    - Secrete PYY in amounts proportionate to calories consumed
  - Primary effect is to signal satiety and terminate eating
- **Cholecystokinin (CCK)**
  - Secreted by **enteroendocrine cells in duodenum and jejunum**
  - Stimulates secretion of bile and pancreatic enzymes
  - Stimulates brain and sensory fibers of vagus nerve suppressing appetite
  - Along with PYY, CKK acts as a signal to stop eating

Appetite

- **Long-term regulators**—govern caloric intake and energy expenditure over periods of weeks to years
- **Leptin and insulin are peptides that inform the brain of how much adipose the body has, and they activate mechanisms for adding or reducing fat**
  - **Leptin**
    - **Secreted by adipocytes** throughout the body
    - Level proportionate to one's own fat stores
    - Informs brain on how much body fat we have
    - Most obese people have normal levels of leptin, but some have a defective leptin receptor

Appetite

(Continued)

- **Insulin**
  - **Secreted by pancreatic beta cells**
  - Stimulates glucose and amino acid uptake
  - Promotes glycogen and fat synthesis
  - Has receptors in the brain and functions, like leptin, as an index of the body's fat stores
  - Weaker effect on appetite than leptin

Appetite

- **Arcuate nucleus of hypothalamus** has receptors for all five chemical signals just described
  - Has **two neural networks involved in hunger**
  - One group secretes **neuropeptide Y (NPY),** a potent appetite stimulant
    - Gherlin stimulates neuropeptide Y secretion
    - Insulin, PYY, and leptin inhibit it
  - Other group secretes **melanocortin:** inhibits eating
    - Leptin stimulates melanocortin secretion
    - Inhibits secretion of appetite stimulants—**endocannabinoids**
      - Named for their resemblance to the tetrahydrocannabinol (THC) of marijuana

Gut–Brain Peptides in Appetite Regulation

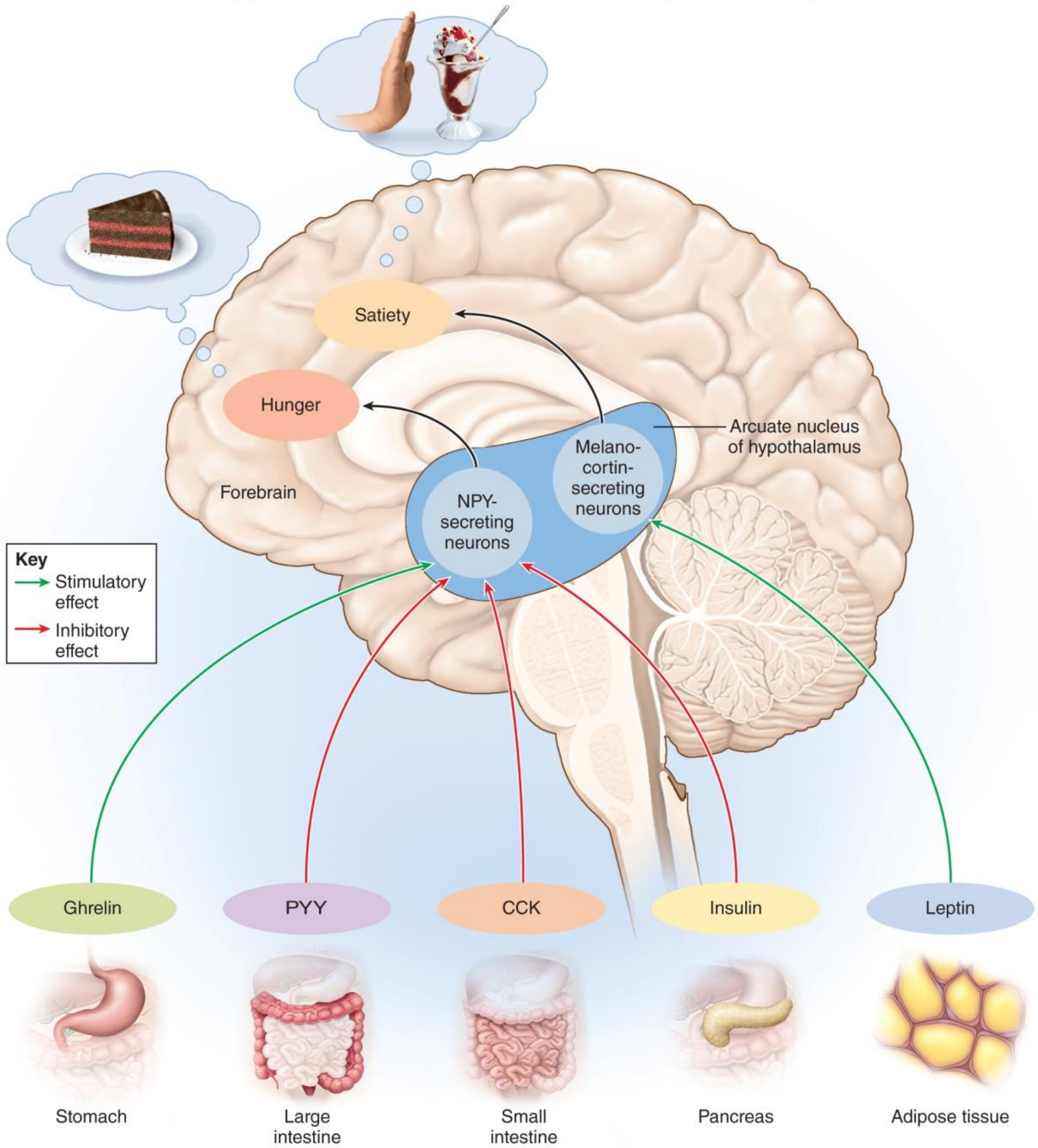


Figure 26.1

Appetite

- Hunger is stimulated partly by **gastric peristalsis**
  - Mild **hunger contractions** begin soon after stomach is empty
  - Increase in intensity over a period of hours
  - Do not affect the amount of food consumed

Appetite

- **Appetite is briefly satisfied by:**
  - Chewing and swallowing
  - Stomach filling
  - Lasting satiation depends upon nutrients entering blood

- **Neurotransmitters stimulate desire for different types of food**
  - Norepinephrine: carbohydrates
  - Galanin: fats
  - Endorphins: protein

Obesity

- **Obesity**—weight more than 20% above recommended norm for one's age, sex, and height
  - U.S. rates
    - 30% obese; another 35% overweight

- **Body mass index (BMI)**—indication of overweight or obese
  - BMI = W/H^2 (W = weight in kg; H = height in meters)
    - 20 to 25 is optimal for most people
    - Over 27: overweight
    - Above 30: obese

Obesity

- **Shortens life expectancy**
  - Increased risk of atherosclerosis, hypertension, diabetes mellitus, joint pain, kidney stones and gallstones, cancer of uterus, breast, and prostate, and sleep apnea
- **Causes are diverse**
  - Heredity, overfeeding in infancy and childhood
  - Evolution resulted in adaptations to store nutrients to cope with times of scarcity
- **Pharmaceutical companies are researching drugs that act on appetite pathways**

Calories

- **One calorie**—amount of heat required to raise temperature of 1 g of water 1°C
  - 1,000 calories is a **kilocalorie (kcal)** in physiology or a Calorie in dietetics
  - A measure of the capacity to do biological work
- **Carbohydrates** and **proteins** yield about 4 kcal/g
  - Sugar and alcohol (7.1 kcal/g) are "empty" calories
    - Provide few nutrients and suppress appetite
- **Fats** yield about 9 kcal/g

Calories

- **Good nutrition requires complex foods that meet the body's needs for protein, lipids, vitamins, and other nutrients**

- **Fuel**—substance solely or primarily oxidized to extract energy from it
  - Extracted energy used to make **adenosine triphosphate (ATP)**

Nutrients

- **Nutrient**—any ingested chemical used for growth, repair, or maintenance of the body
- **Six classes of nutrients**
  - **Water, carbohydrates, lipids,** and **proteins**
    - **Macronutrients**—must be consumed in relatively large quantities
  - **Vitamins** and **minerals**
    - **Micronutrients**—only small quantities are required

Nutrients

- **Recommended daily allowances (RDA)**
  - Safe estimate of daily intake that would meet the nutritional needs of most healthy people
- **Essential nutrients** cannot be synthesized in body
  - Minerals, most vitamins, eight amino acids, and one to three of the fatty acids must be consumed in diet

Carbohydrates

- **Well-nourished adult body has 440 g of carbohydrates**
  – 325 g of **muscle glycogen**
  – 90 to 100 g of **liver glycogen**
  – 15 to 20 g of **blood glucose**

Carbohydrates

- **Sugars function as:**
  - **Structural components** of other molecules including nucleic acids, glycoproteins, glycolipids, ATP, and related nucleotides (GTP, cAMP)
  - Most serve as **fuel:** easily oxidized source of chemical energy
    - Most cells meet energy needs by a combination of carbohydrates and fats
    - Neurons and erythrocytes depend solely on carbohydrates
    - **Hypoglycemia—**deficiency of blood glucose
      - Causes nervous system disturbances such as weakness and dizziness

Carbohydrates

- **Blood glucose concentration** carefully regulated
  - Interplay of **insulin** and **glucagon**
  - Regulate balance between glycogen and free glucose
- **Carbohydrate intake influences metabolism of other nutrients**
  - Fats used as fuel when glucose and glycogen levels are low
  - Excess carbohydrates are converted to fat

Carbohydrates

- **Requirements**
  - Since carbohydrates are oxidized so rapidly, they are required in greater amounts than any other nutrient
  - RDA is 125 to 175 g
  - Brain alone consumes about 120 g of glucose per day
- **Consumption**
  - A century ago, Americans consumed an average of 4 lb of sugar a year
  - Now, the consumption averages 60 lb of sugar and 46 lb of corn syrup per year
  - 8 teaspoons of sugar in a 12 oz non-diet soft drink

Carbohydrates

- **Dietary carbohydrates** come in three principal **forms**
  - **Monosaccharides: glucose, galactose, fructose**
    - Arise mainly from digestion of starch and disaccharides
    - Small intestine and liver convert galactose and fructose to glucose
      - Ultimately, all carbohydrate digestion generates glucose
      - Normal blood sugar (glucose) concentration: 70 to 110 mg/dL
  - **Disaccharides:** sucrose (table sugar), maltose, lactose
  - **Polysaccharides** (complex carbohydrates): starch, glycogen, and cellulose (not a nutrient because it is not digested, but important as dietary fiber)

Dietary Sources

- **Glycemic index (GI)—**effect of a dietary carbohydrate on blood glucose level
  - High-GI carbohydrates stimulate a high insulin demand and raise the risk of obesity and type 2 diabetes mellitus
- **Nearly all dietary carbohydrates come from plants**
  - **Sucrose** is refined from sugarcane and sugar beets
  - **Fructose** is present in fruits and corn syrup
  - **Maltose** is present in germinating cereal grains
  - **Lactose** is found in cow's milk

Fiber

- **Dietary fiber**—all fibrous material of plant and animal origin that resists digestion
  - Cellulose, pectin, gums, and lignins
- **Fiber is important to diet—RDA is 30 g/day**
- **Water-soluble fiber (e.g., pectin)**
  - Found in oats, beans, peas, brown rice, and fruits
  - Decreases blood cholesterol and LDL levels

Fiber

- **Water-insoluble fiber (cellulose, hemicellulose, lignin)**
  - No effect on cholesterol and LDL levels
  - Absorbs water in intestines, softens stool and increases its bulk, stretches colon, and stimulates peristalsis thereby quickening passage of feces
  - No clear effect on incidence of colorectal cancer
  - Excessive intake can interfere with absorption of some elements such as iron, calcium, magnesium, phosphorus, and others

Lipids

- **Average male 15% body fat; female 25% body fat**
- **Well-nourished adult meets 80% to 90% of resting energy needs from fat**
  - **Fat is superior to carbohydrates** for energy storage for two reasons
    - Carbohydrates are hydrophilic, absorb water, and expand and occupy more space, whereas fat is hydrophobic, and is a **more compact energy storage substance**
    - Fat is less oxidized than carbohydrates and **contains over twice as much energy:** 9 kcal/g for fat; 4 kcal/g for carbohydrates

Lipids

- Fat has **glucose-sparing** and **protein-sparing** effects when used for energy needs
  - Glucose is spared for consumption by cells that cannot use fat, like neurons
  - Protein not catabolized for fuel
- **Fat-soluble vitamins (A, D, E, K) absorbed with dietary fat**
  - Ingestion of less than 20 g of fat per day risks vitamin deficiency

Lipids

- **Diverse functions besides energy source**
  - **Structural**
    - **Phospholipids** and **cholesterol** are components of plasma membranes and myelin
  - **Chemical precursors**
    - **Cholesterol**—a precursor of steroids, bile salts, vitamin D
    - **Thromboplastin,** an essential blood-clotting factor, is a lipoprotein
    - **Fatty acids**—arachidonic acid and linoleic acid: precursors of prostaglandins and other eicosanoids
  - Important **protective and insulating functions**

Lipids

- **Requirements: fat should be less than 30% of daily calorie intake**
  - Typical American gets 40% to 50% from fat
  - Saturated fat and cholesterol should be limited
- **Most fatty acids synthesized by body**
  - Essential fatty acids must be consumed

Lipids

- **Sources**
  - **Saturated fats**
    - **Animal origin**—meat, egg yolks, dairy products
    - Some in coconut and palm oils
  - **Unsaturated fats**
    - Found in nuts, seeds, and most vegetable oils
  - **Cholesterol**
    - Found in egg yolks, cream, shellfish, organ meats, and other meats
    - Only in tiny, trace amounts in foods of plant origin

Cholesterol and Serum Lipoproteins

- **Lipids are an important part of the diet**
  - Must be transported to all cells of the body
  - Are hydrophobic and do not dissolve in blood plasma
- **Lipoprotein complexes** transport lipids in plasma
  - Tiny droplets with core of cholesterol and triglycerides
  - Coated with protein and phospholipids
    - Coating allows lipid to be suspended in blood
    - Also serves as a recognition marker for cells that absorb them

Cholesterol and Serum Lipoproteins

- Serum lipoproteins are classified into **four major categories** by their density (higher density have higher lipid content)
  - **Chylomicrons:** 75–1,200 nm in diameter
  - **Very low–density lipoproteins (VLDLs):** 30–80 nm
  - **Low-density lipoproteins (LDL):** 18–25 nm
  - **High-density lipoproteins (HDL):** 5–12 nm

- **These differ in composition and function**

Lipoprotein Processing

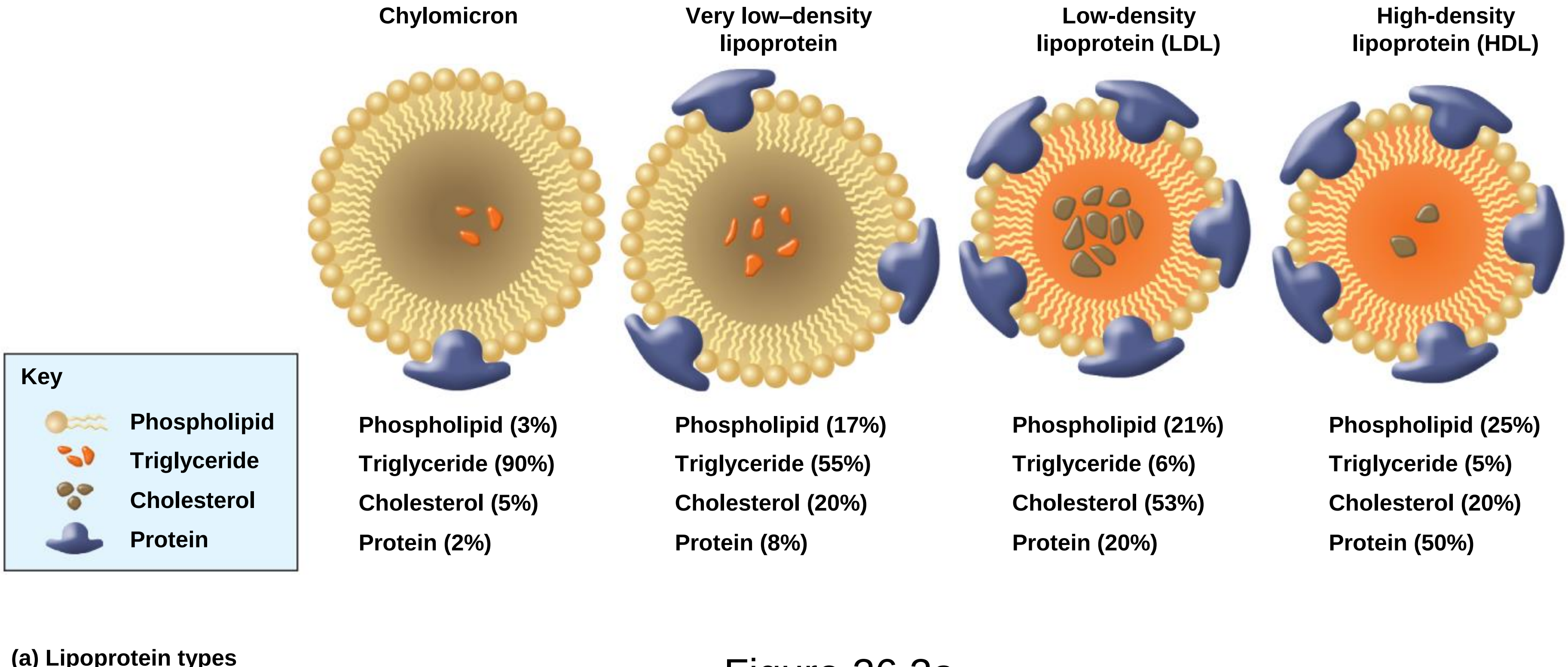


Figure 26.2a

Cholesterol and Serum Lipoproteins

- **Chylomicrons** form in absorptive cells of small intestine
- **Enter lymphatic system, then bloodstream**
- Blood capillary endothelial cells have **lipoprotein lipase** to hydrolyze triglycerides into monoglycerides and free fatty acids
- **Resulting free fatty acids (FFAs) and glycerol enter adipocytes to be made into triglycerides for storage**
- **Chylomicron remnant**—the remainder of a chylomicron after the triglycerides have been extracted and degraded by liver

Cholesterol and Serum Lipoproteins

- **VLDL**
  - Produced by liver to transport lipids to adipose tissue for storage
  - When triglycerides are removed in adipose tissue, VLDLs become LDLs and contain mostly cholesterol
- **LDL**
  - Absorbed by receptor-mediated endocytosis by cells in need of cholesterol
  - Digested by lysosomal enzymes to release the cholesterol for intracellular use

Cholesterol and Serum Lipoproteins

- **HDL production begins in the liver**
  - Produces an empty, **collapsed protein shell**
  - Shell travels through blood and picks up cholesterol and phospholipids from other organs
  - When passes through liver again, cholesterol is removed and eliminated in bile as cholesterol or bile acids
  - HDLs are vehicles for removing excess cholesterol from the body
- Desirable to maintain total plasma cholesterol concentration of **less than 200 mg/dL**
  - 200 to 239 mg/dL is considered borderline high
  - Levels above 240 mg/dL are pathological

Cholesterol and Serum Lipoproteins

- Most of the body’s cholesterol is **endogenous**—internally synthesized rather than dietary
  - Body compensates for variation in intake
  - High dietary intake lowers liver cholesterol production
  - Low dietary intake raises liver production
  - Lowering dietary cholesterol lowers level by no more than 5%
  - Certain saturated fatty acids (SFAs) raise serum cholesterol level
    - Moderate reduction in SFAs can lower blood cholesterol by 15% to 20%

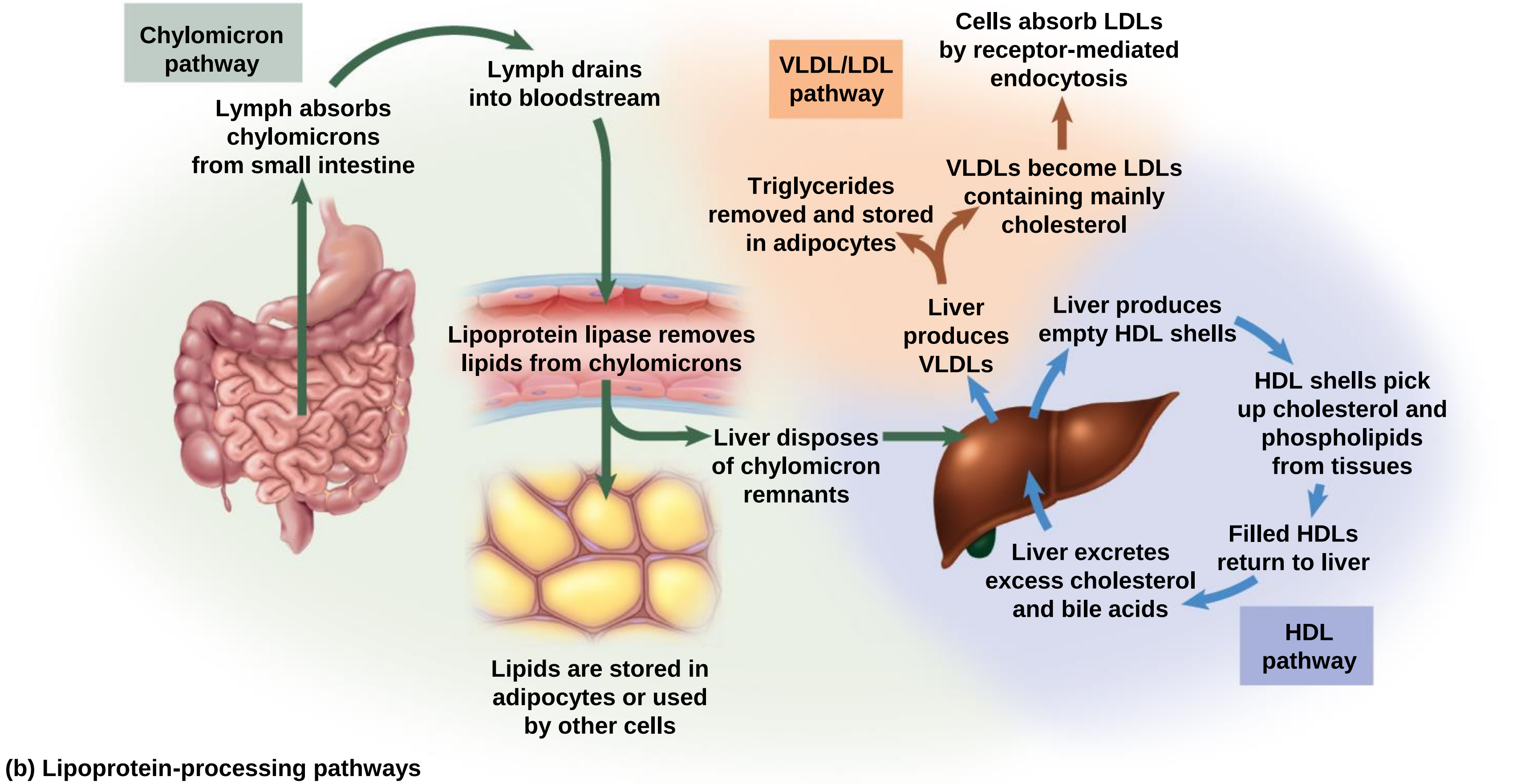
Cholesterol and Serum Lipoproteins

- **Vigorous exercise lowers blood cholesterol**
  - Sensitivity of right atrium to blood pressure is reduced
  - Heart secretes less **atrial natriuretic peptide** and thus kidneys excrete less sodium and water
  - Raises blood volume
  - Dilution of blood lipoproteins causes adipocytes to produce more **lipoprotein lipase**
  - Adipocytes consume more blood triglycerides
  - VLDL particles shed some cholesterol which is picked up by HDL and removed by the liver

Cholesterol and Serum Lipoproteins

- **Levels of LDL**
  - High LDL is a warning sign that correlates with cholesterol deposition in arteries
  - Elevated by saturated fat intake, cigarette smoking, coffee, and stress
- **Levels of HDL**
  - High level of HDL is beneficial
  - Indicates that cholesterol is being removed from arteries and transported to the liver for disposal
- **Recommendation: increase the ratio of HDL to LDL**
  - Regular aerobic exercise
  - Avoid smoking, saturated fats, coffee, stress

Lipoprotein Processing



(b) Lipoprotein-processing pathways

Figure 26.2b

Proteins

- **Protein constitutes 12% to 15% of total body mass**
  - 65% of it is in skeletal muscle
- **Proteins have a wide variety of functions**
  - **Muscle contraction**
  - **Motility of cilia and flagella**
  - **Structural components**
    - **All cellular membranes**
      - Receptors, pumps, ion channels, and cell-identity markers
    - **Fibrous proteins**
      - Collagen, elastin, and keratin make up much of the structure of bone, cartilage, tendons, ligaments, skin, hair, and nails

Proteins

Protein functions (Continued)

- **Globular proteins**
  - Antibodies, hormones, myoglobin, neuromodulators, hemoglobin, and about 2,000 enzymes that control nearly every aspect of cellular metabolism
- **Plasma proteins**
  - Albumins and other plasma proteins that maintain blood viscosity and osmolarity and transport lipids and some other plasma solutes

– **Buffer pH of body fluids**

– **Contribute to resting membrane potential of all cells**

Proteins

- **Protein RDA is 44 to 60 g/day**
  - Weight in pounds x 0.37 = estimate of RDA of protein in grams
  - Higher intake recommended under conditions of stress, infection, injury, and pregnancy
  - Excessive intake overloads the kidneys with nitrogenous waste and can cause kidney damage

Proteins

- **Nutritional value of a protein depends on proportions of amino acids needed for human proteins**
  - 8 **essential amino acids** cannot be synthesized by the body
    - Isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine
  - 12 **inessential amino acids** synthesized by the body if the diet does not supply them
- **Cells do not store surplus amino acids for later use**
  - When a protein is synthesized, all amino acids must be present at once
  - If one is missing, the protein cannot be synthesized

Proteins

- **Complete proteins**—high-quality dietary proteins that provide all essential amino acids in the necessary proportions for human tissue growth, maintenance, and nitrogen balance
- **Incomplete proteins**—lower quality because they lack one or more essential amino acids

Proteins

- **Net protein utilization**—the percentage of amino acids in a protein that the human body uses
  - 70% to 90% of animal proteins
  - 40% to 70% of plant proteins
    - 14 oz of rice and beans provides same amount of usable protein as 4 oz hamburger
  - Advantages of decreasing meat intake and increasing plant intake
    - More vitamins, minerals, and fiber
    - Less saturated fat
    - No cholesterol
    - Less pesticide

Dietary Sources

- **Animal proteins of meat, eggs, and dairy products are complete proteins**
  - Closely match human proteins in amino acid composition
- **Plant sources are incomplete proteins and must be combined in the right proportions**
  - Beans and rice are a complementary choice

Nitrogen Balance

- **Nitrogen balance**—rate of nitrogen ingested equals rate of nitrogen excreted
  - Proteins are chief dietary source of nitrogen

- **Positive nitrogen balance**
  - Nitrogen ingestion exceeds its excretion
  - Occurs in children because they retain protein for tissue growth
  - Pregnant women and athletes in resistance training show positive nitrogen balance
  - **Growth hormone** and **sex steroids** promote protein synthesis and positive nitrogen balance

Nitrogen Balance

- **Negative nitrogen balance**
  - Excretion exceeds ingestion
  - Body proteins being broken down for fuel; muscle atrophy
    - Muscles and liver proteins are more easily broken down than others
    - Carbohydrate and fat intake is insufficient to meet body's energy needs
  - Glucocorticoids promote protein catabolism in states of stress

Minerals and Vitamins

- **Minerals**—inorganic elements that plants extract from soil or water and introduce into the food web
- **Vitamins**—small dietary organic compounds that are necessary for metabolism
- **Neither is used as fuel**
- **Both are essential to our ability to use other nutrients**

Minerals

- **Minerals** constitute about 4% of the body mass
  - Three-quarters being **calcium** and **phosphorus** in bones and teeth
  - **Phosphorus**
    - Key structural component of phospholipids, ATP, cAMP, GTP, and creatine phosphate
    - Basis for the phosphate buffer system
  - **Calcium, iron, magnesium, and manganese** function as cofactors for enzymes

Minerals

Minerals (Continued)

- **Iron** is essential for the oxygen-carrying capacity of hemoglobin and myoglobin
- **Chlorine:** component of stomach acid
- Many **mineral salts** function as **electrolytes** and govern functions of nerve and muscle cells, osmotically regulate the content and distribution of water in the body, and maintain blood volume
- Best sources of minerals are vegetables, legumes, milk, eggs, fish, shellfish, and some other meats

Minerals

- **Animal tissues contain large amounts of salt**
  - Carnivores rarely lack salt in their diets
  - Herbivores often supplement by ingesting salt from soil
- Recommended sodium intake is **1.1 g/day**
- Typical American diet contains 4.5 g/day
- **Hypertension** can be caused by elevated salt intake

Vitamins

- **Most vitamins must be obtained from the diet**
- Body synthesizes some vitamins from precursors called **provitamins**
  - Niacin from amino acid tryptophan
  - Vitamin A from carotene
  - Vitamin D from cholesterol
  - Vitamin K, pantothenic acid, biotin, and folic acid are produced by bacteria of the large intestine

Vitamins

- **Water-soluble vitamins**
  - Absorbed with water in small intestine and quickly excreted by kidneys, not stored
  - **Vitamin C (ascorbic acid)**
    - Promotes hemoglobin synthesis, collagen synthesis, and sound connective tissue structure
    - An antioxidant that scavenges free radicals and possibly reduces the risk of cancer
  - **B vitamins**
    - Function as coenzymes or parts of coenzyme molecules
    - Assist enzymes by transferring electrons from one metabolic reaction to another
    - Make it possible for enzymes to catalyze these reactions

Vitamins

- **Fat-soluble vitamins**
  - Incorporated into lipid micelles in the small intestine and absorbed with dietary lipids
  - **Vitamin A**
    - Component of visual pigments
    - Promotes proteoglycan synthesis and epithelial maintenance
  - **Vitamin D**
    - Promotes calcium absorption and bone mineralization
  - **Vitamin K**
    - Essential for prothrombin synthesis and blood clotting
  - **Vitamins A and E**
    - Antioxidants like ascorbic acid

Vitamins

- **Disorders of excess or insufficiency**
  - **Hypervitaminosis**—excess of (fat-soluble) vitamin
    - **Vitamin A excess**—may cause anorexia, nausea and vomiting, headache, pain and fragility in the bones, hair loss, an enlarged liver and spleen, and birth defects
    - Can be caused by taking megavitamins
  - Deficiencies
    - **Vitamin A deficiency**—night blindness; dry skin, hair, and conjunctiva; cloudy cornea; and increased incidence of infections
      - World's most common vitamin deficiency

Carbohydrate Metabolism

- **Expected Learning Outcomes**
  - Describe the principal reactants and products of each major step of glucose oxidation.
  - Contrast the functions and products of anaerobic fermentation and aerobic respiration.
  - Explain where and how cells produce ATP.
  - Describe the production, function, and use of glycogen.

Carbohydrate Metabolism

- **Most dietary carbohydrates burned as fuel within hours of absorption**

- Oxidative carbohydrate metabolism is **glucose catabolism**

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$$

- **Function of this reaction is to transfer energy from glucose to ATP**

Glucose Catabolism

- **Glucose catabolism**—a series of small steps, each controlled by a separate enzyme, in which energy is released in small manageable amounts, and as much as possible, is transferred to ATP and the rest is released as heat

Glucose Catabolism

- **Three major pathways of glucose catabolism**
  - **Glycolysis**
    - Glucose (6 C) split into two *pyruvic acid* molecules (3 C)
  - **Anaerobic fermentation**
    - Occurs in the absence of oxygen
    - Reduces *pyruvic acid* to lactic acid
  - **Aerobic respiration**
    - Occurs in the presence of oxygen
    - Oxidizes *pyruvic acid* to CO_2 and H_2O

Glycolysis and Anaerobic Fermentation

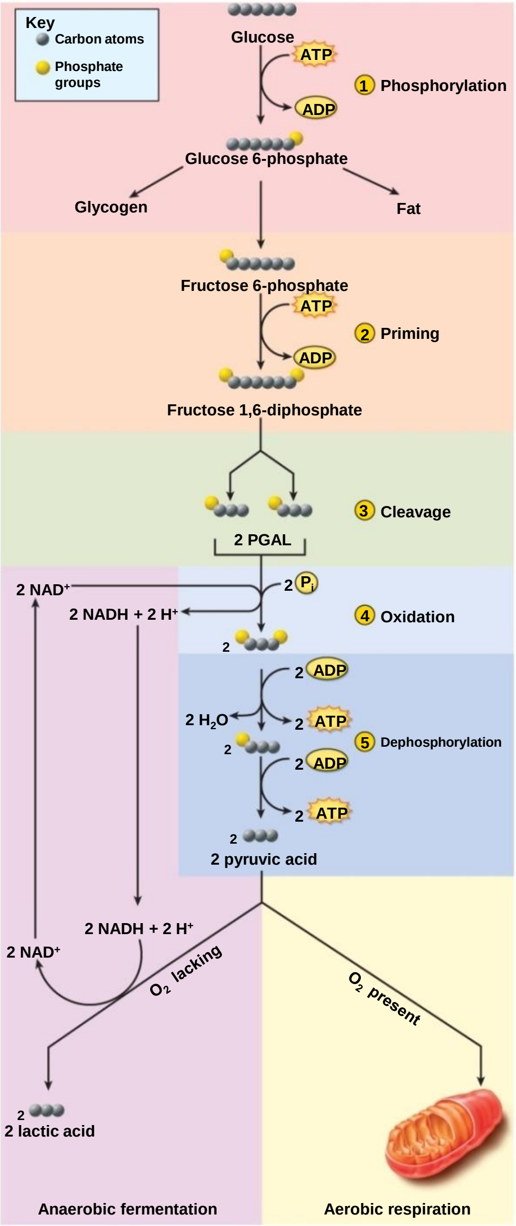


Figure 26.3

Glucose Catabolism

- **Enzymes** remove **electrons** (as hydrogen atoms) from intermediate compounds of these pathways
- Enzymes transfer the hydrogen atoms to **coenzymes**
- **Coenzymes** donate them to other compounds later in the reaction pathways
- **Enzymes of glucose catabolism cannot function without their coenzymes**

Glucose Catabolism

- **Two coenzymes** of special importance
  - **NAD^+** (nicotinamide adenine dinucleotide)
    - Derived from niacin (B vitamin)
    - $NAD^+ + 2\ H \rightarrow NADH + H^+$
  - **FAD** (flavin adenine dinucleotide)
    - Derived from riboflavin
    - $FAD + 2\ H \rightarrow FADH_2$

Glucose Catabolism

- **Hydrogen atoms are removed from metabolic intermediates in pairs**
  - Two protons and two electrons (2 H^+ and 2 e^-) at a time
  - Transferred to a coenzyme
- **This produces a reduced coenzyme with a higher free energy content than before the reaction**
- **Coenzymes** become temporary carriers of the energy extracted from the glucose metabolites

Glucose Catabolism

- **FAD** binds two protons and two electrons to become **$FADH_2$**
- NAD^+ binds two electrons but only one of the protons to become **NADH,** and the other proton remains a free hydrogen ion, **H^+**

Glycolysis

- **Glycolysis**—series of conversions that occur when glucose enters the cell
- **Phosphorylation**
  - **Hexokinase** enzyme transfers an inorganic phosphate group from ATP to glucose
  - Produces **glucose 6-phosphate (G6P)**
    - Keeps intracellular concentration of glucose low, favoring continued diffusion of glucose into the cell
    - Prevents sugar from leaving the cell, since phosphorylated compounds cannot pass through the membrane
    - **G6P** can be converted to fat or amino acids, polymerized to form glycogen, or oxidized to extract its energy

Glycolysis

- **Priming**
  - G6P is rearranged **(isomerized)** to form **fructose 6-phosphate**
  - **Phosphorylated again** to form **fructose 1,6-diphosphate**
  - “Primes” the process by providing **activation energy**
    - Two ATPs have been consumed
- **Cleavage**
  - Fructose 1,6-diphosphate **lyses** or splits into two three-carbon molecules
    - Small changes results in two molecules of **PGAL (phosphoglyceraldehyde)**

Glycolysis

- **Oxidation**
  - Each **PGAL** molecule is **oxidized** by removing a pair of hydrogen atoms
  - The **electrons** and **one proton** are picked up by **NAD^+** yielding NADH and H^+
  - **Phosphate group is added** to each C_3 fragment from cell's pool of free phosphate ions

- **Dephosphorylation**
  - Phosphate groups are taken from glycolysis intermediates and added to ADP making ATP
  - C_3 compound becomes **pyruvic acid**

Glycolysis

- **4 ATP produced but 2 ATP consumed to initiate glycolysis, so net gain is 2 ATP per glucose**
- **Some of glucose's original energy is in the ATP, some in NADH, some lost as heat, but most of the energy remains in the pyruvic acid**
- **End products of glycolysis**
  - 2 pyruvic acid + 2 NADH + 2 ATP + 2 H^+

Anaerobic Fermentation

- Fate of pyruvic acid **depends on oxygen availability**
- **In the absence of oxygen (or mitochondria) cells can only generate ATP through glycolysis**
  - Glycolysis cannot continue without supply of NAD^+
    - Anaerobic fermentation: NADH donates electrons to pyruvic acid reducing it to lactic acid and regenerating NAD^+

Anaerobic Fermentation

- **Lactic acid leaves the cells that generate it and travel to the liver via the blood**
  - When oxygen becomes available the liver oxidizes it back to pyruvic acid
    - Oxygen required for this is part of the reason we breathe more vigorously after exercising (**postexercise oxygen consumption)**

Anaerobic Fermentation

- **Liver can also convert lactic acid back to G6P and:**
  – Polymerize it to form glycogen for storage
  – Remove phosphate group and release free glucose into the blood
- **Drawbacks of anaerobic fermentation**
  – Wasteful, because most of the energy of glucose is still in the lactic acid and has contributed no useful work
  – Lactic acid is toxic
- **Skeletal muscle is relatively tolerant of anaerobic fermentation, cardiac muscle less so**
  – The brain employs no anaerobic fermentation

Aerobic Respiration

- Most ATP generated in mitochondria, which requires **oxygen** as final electron acceptor
- In the presence of oxygen, **pyruvic acid** enters the mitochondria and is oxidized by aerobic respiration
- Occurs in **two principal steps**
  - **Matrix reactions:** their controlling enzymes are in the fluid of the mitochondrial matrix
  - **Membrane reactions:** their controlling enzymes are bound to the membranes of the mitochondrial cristae

The Matrix Reactions

- Three steps prepare **pyruvic acid** to enter **citric acid cycle**
  - **Decarboxylation—CO_2** removed from pyruvic acid to make a C_2 compound
  - Convert C_2 compound to an acetyl group (acetic acid)
    - NAD^+ removes hydrogen atoms from the C_2 compound
  - Acetyl group binds to coenzyme A
    - Results in **acetyl-coenzyme A (acetyl-CoA)**

The Mitochondrial Matrix Reactions

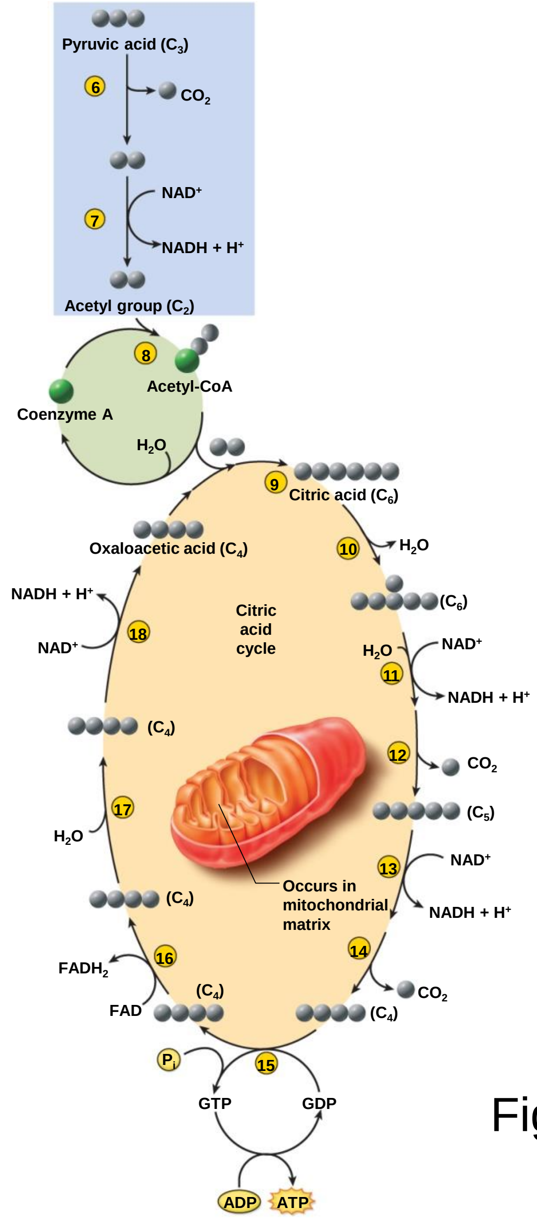


Figure 26.4

The Matrix Reactions

- **Citric acid cycle**
  - **Acetyl-CoA** (a C_2 compound) combines with a C_4 to form a C_6 compound **(citric acid)**—start of cycle
  - Water is removed and citric acid molecules rearranged
  - Hydrogen atoms are removed and accepted by NAD^+
  - Another CO_2 is removed and the substrate becomes a five-carbon chain
  - Previous step repeated removing another free CO_2 leaving a four-carbon chain

The Matrix Reactions

Citric acid cycle (Continued)

- Some of the energy in the C_4 substrate goes to phosphorylate guanosine diphosphate (GDP) and converts it to guanosine triphosphate (GTP)
  - Molecule similar to ATP
  - Quickly transfers P_i group to ADP to make ATP
- Two hydrogen atoms are removed and accepted by the coenzyme FAD
- Water is added
- Two final hydrogen atoms are removed and transferred to NAD+
- Reaction generates oxaloacetic acid, which is available to start the cycle again

The Matrix Reactions

$$2 \text{ pyruvate} + 6\ H_2O \rightarrow 6\ CO_2$$
$$+ 2\ ADP + 2\ P_i \rightarrow 2\ ATP$$
$$+ 8\ NAD^+ + 8\ H_2 \rightarrow 8\ NADH + 8\ H^+$$
$$+ 2\ FAD + 2\ H_2 \rightarrow 2\ FADH_2$$

- **Carbon atoms of glucose are carried away as CO_2 and exhaled**
- **Most of the energy from the glucose molecule is in the 8 NADH and 2 $FADH_2$ molecules made in the matrix reactions**
- **Some of glucose's energy is lost as heat, stored in 2 ATP, and 2 NADH from glycolysis**
- **Citric acid cycle not only oxidizes glucose metabolites, it is also a source of substances for synthesis of fats and nonessential amino acids**

The Membrane Reactions

- **Membrane reactions have two purposes**
  - To further oxidize NADH and $FADH_2$ and transfer their energy to ATP
  - To regenerate NAD^+ and FAD and make them available again to earlier reaction steps

- **Mitochondrial electron-transport chain**—series of compounds that carry out this series of membrane reactions
  - Most bound to the inner mitochondrial membrane
  - Arranged in a precise order that enables each one to receive a pair of electrons from the member on one side of it
  - Pass electrons to member on the other side

The Membrane Reactions

- **Flavin mononucleotide (FMN)**—derivative of riboflavin similar to FAD
  - Bound to a membrane protein
  - FMN accepts electrons from NADH
- **Iron–sulfur (Fe-S) centers**—complexes of iron and sulfur atoms bound to membrane proteins
- **Coenzyme Q (CoQ)**—accepts electrons from $FADH_2$
  - Small molecule that moves around in membrane

The Membrane Reactions

- **Copper (Cu) ions**—bound to two membrane proteins
- **Cytochromes**—five enzymes with iron cofactors
  - Brightly colored in pure form
  - In order of participation in the chain, b, c_1, c, a, a_3

Electron Transport

- **Hydrogen atoms are split apart as they transfer from coenzymes to the chain**
- **Protons pumped into the intermembrane space**
- **Electrons travel in pairs (2 e^-) along the transport chain**
- Each electron carrier becomes **reduced** when it receives an electron pair and **oxidized** again when it passes the electrons along to the next carrier

Electron Transport

- **Oxygen is the final electron acceptor**
  - Each oxygen atom accepts two electrons from cytochrome a_3 and two protons from the mitochondrial matrix forming water
    - Body's primary source of **metabolic water**—water synthesized in the body
  - This reaction explains the body's oxygen requirement
  - No oxygen, cell produces too little ATP to sustain life

The Mitochondrial Electron-Transport Chain

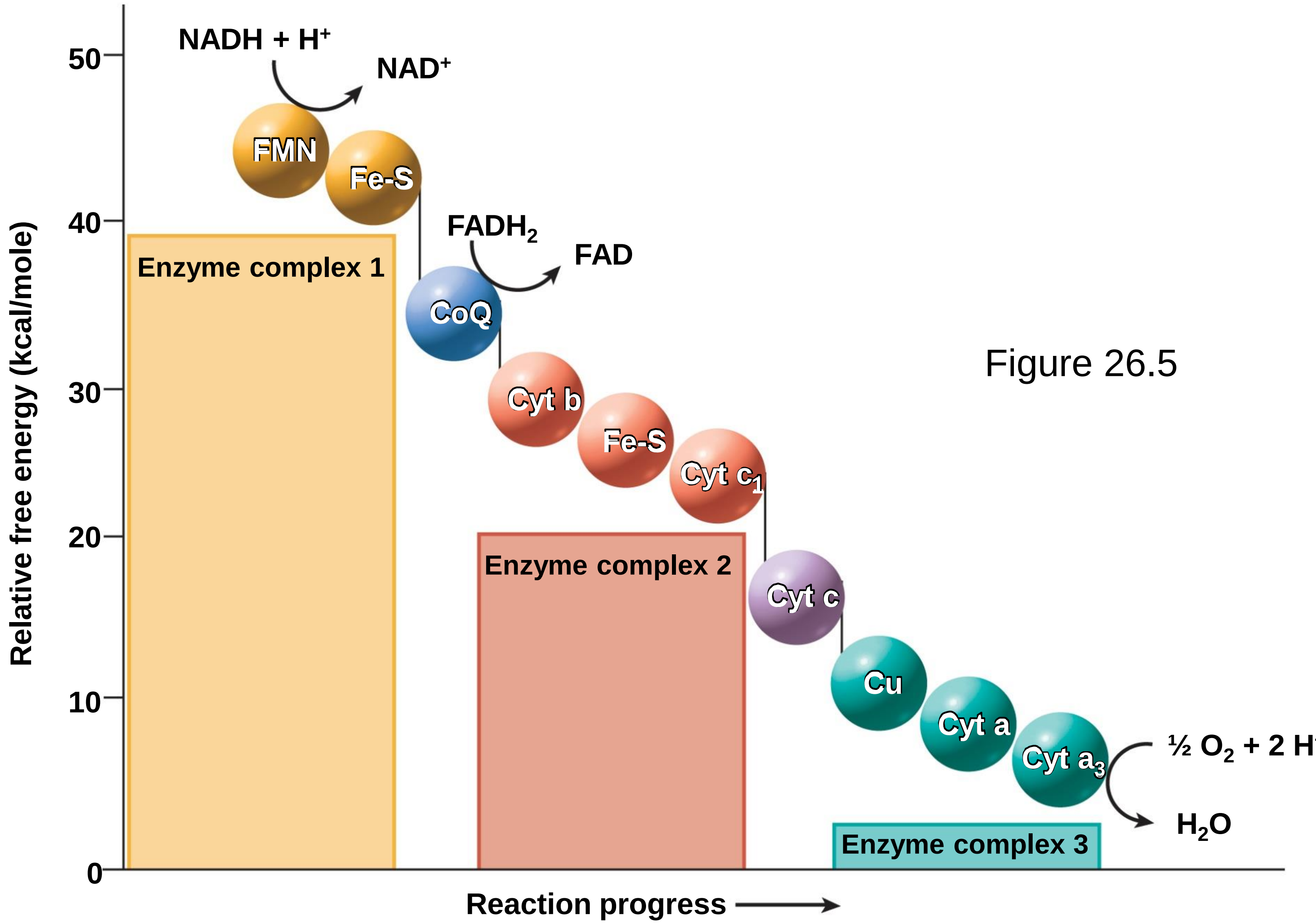


Figure 26.5

The Chemiosmotic Mechanism

- Electron-transport chain energy fuels **respiratory enzyme complexes**
  - Pump protons from matrix into space between inner and outer mitochondrial membranes
  - Creates steep electrochemical gradient for H^+ across inner mitochondrial membrane
- Inner membrane is permeable to H^+ only at channel proteins called **ATP synthase**
- **Chemiosmotic mechanism**—H^+ current rushing back through ATP synthase channels drives ATP synthesis

Chemiosmotic Mechanisms of ATP Synthesis

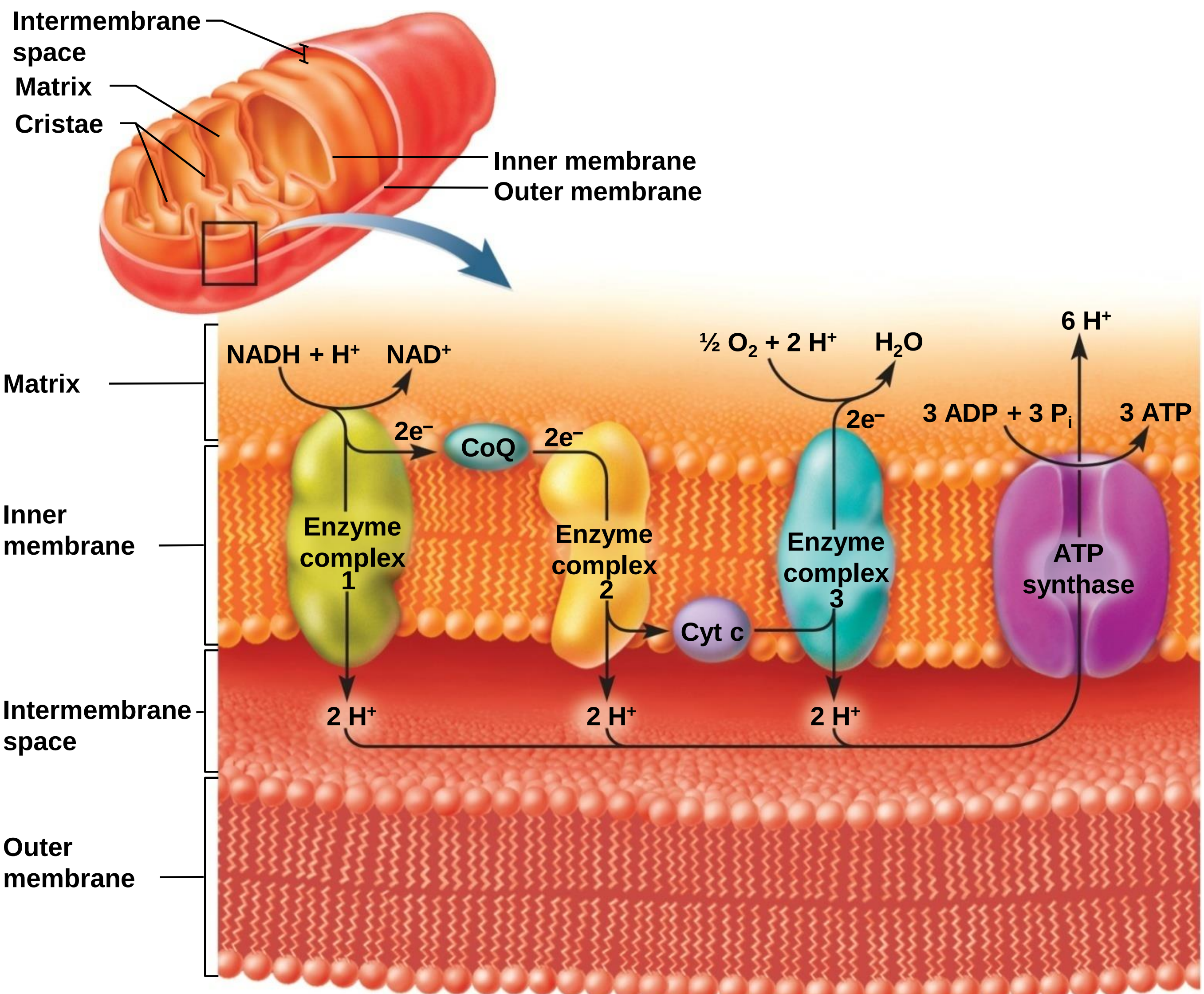


Figure 26.6

Overview of ATP Production

- **NADH releases electron pairs to FMN in proton pump of electron transport chain**
  - Enough energy to synthesize 2.5 ATP
- **$FADH_2$ releases its electron pairs further along electron-transport system**
  - Enough energy to synthesize 1.5 ATP
- Complete aerobic oxidation of glucose to CO_2 and H_2O produces **32 ATP**
  - Efficiency rating of 34% (the rest lost as heat)

ATP Generated by Oxidation of Glucose

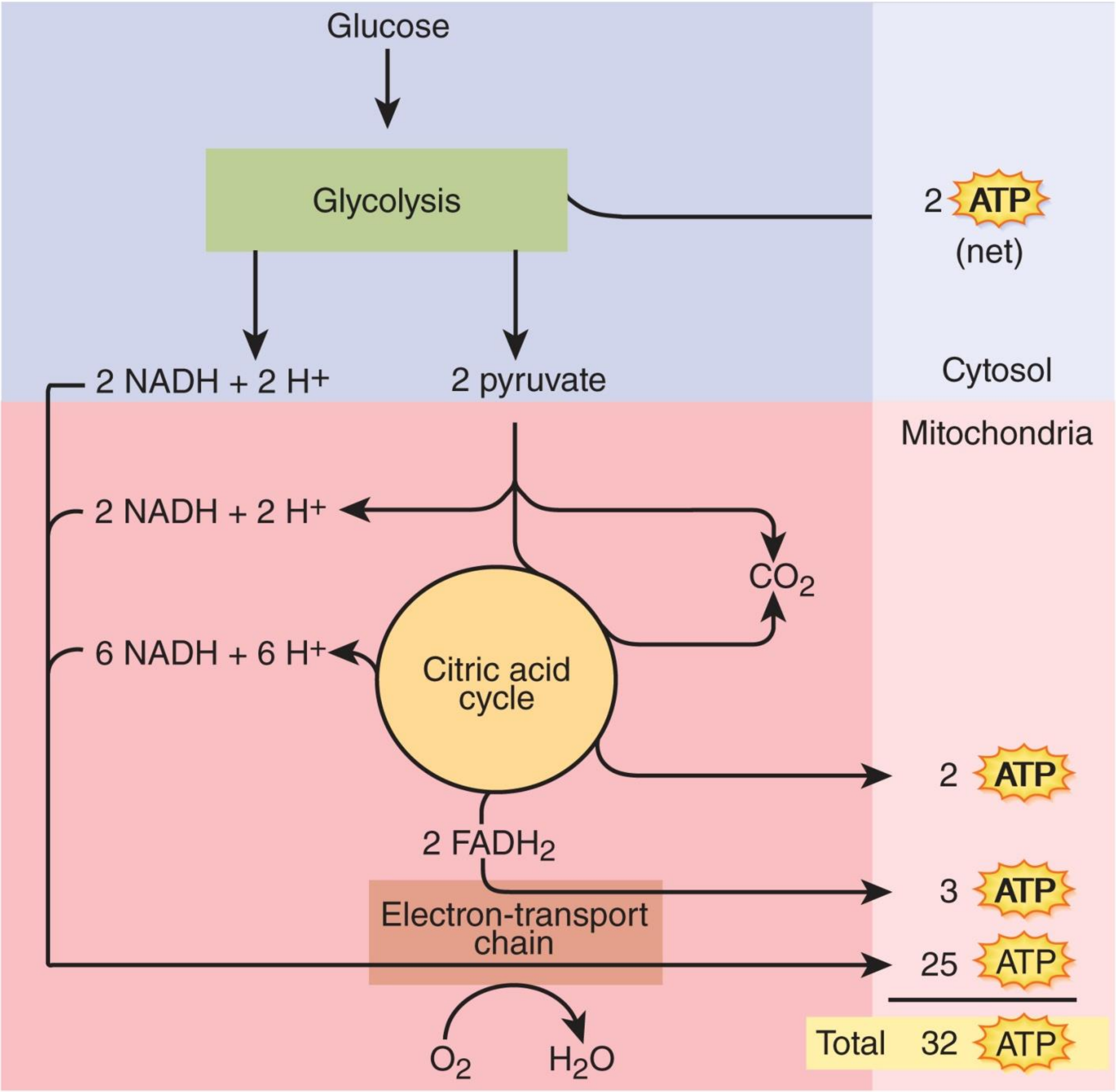


Figure 26.7

Glycogen Metabolism

- **ATP is quickly used after it is formed**
  - It is an **energy transfer molecule,** not an energy storage molecule
  - Body converts extra glucose to other compounds better suited for energy storage (glycogen and fat)
- **Glycogenesis**—synthesis of glycogen
  - Stimulated by insulin
  - Chains glucose monomers together

Glycogen Metabolism

- **Glycogenolysis**—hydrolysis of glycogen
  - Releases glucose between meals
  - Stimulated by glucagon and epinephrine
  - Liver cells can release glucose back into blood

- **Gluconeogenesis**—synthesis of glucose from noncarbohydrates, such as glycerol and amino acids
  - Occurs chiefly in the liver and later, kidneys if necessary

Glycogen Metabolism

TABLE 26.5	Some Terminology Related to Glucose and Glycogen Metabolism
Anabolic (synthesis) reactions	
Glycogenesis	The synthesis of glycogen by polymerizing glucose
Gluconeogenesis	The synthesis of glucose from noncarbohydrates such as glycerol and amino acids
Catabolic (breakdown) reactions	
Glycolysis	The splitting of glucose into two molecules of pyruvic acid in preparation for anaerobic fermentation or aerobic respiration
Glycogenolysis	The hydrolysis of glycogen to release free glucose or glucose 1-phosphate

Major Pathways of Glucose Storage and Use

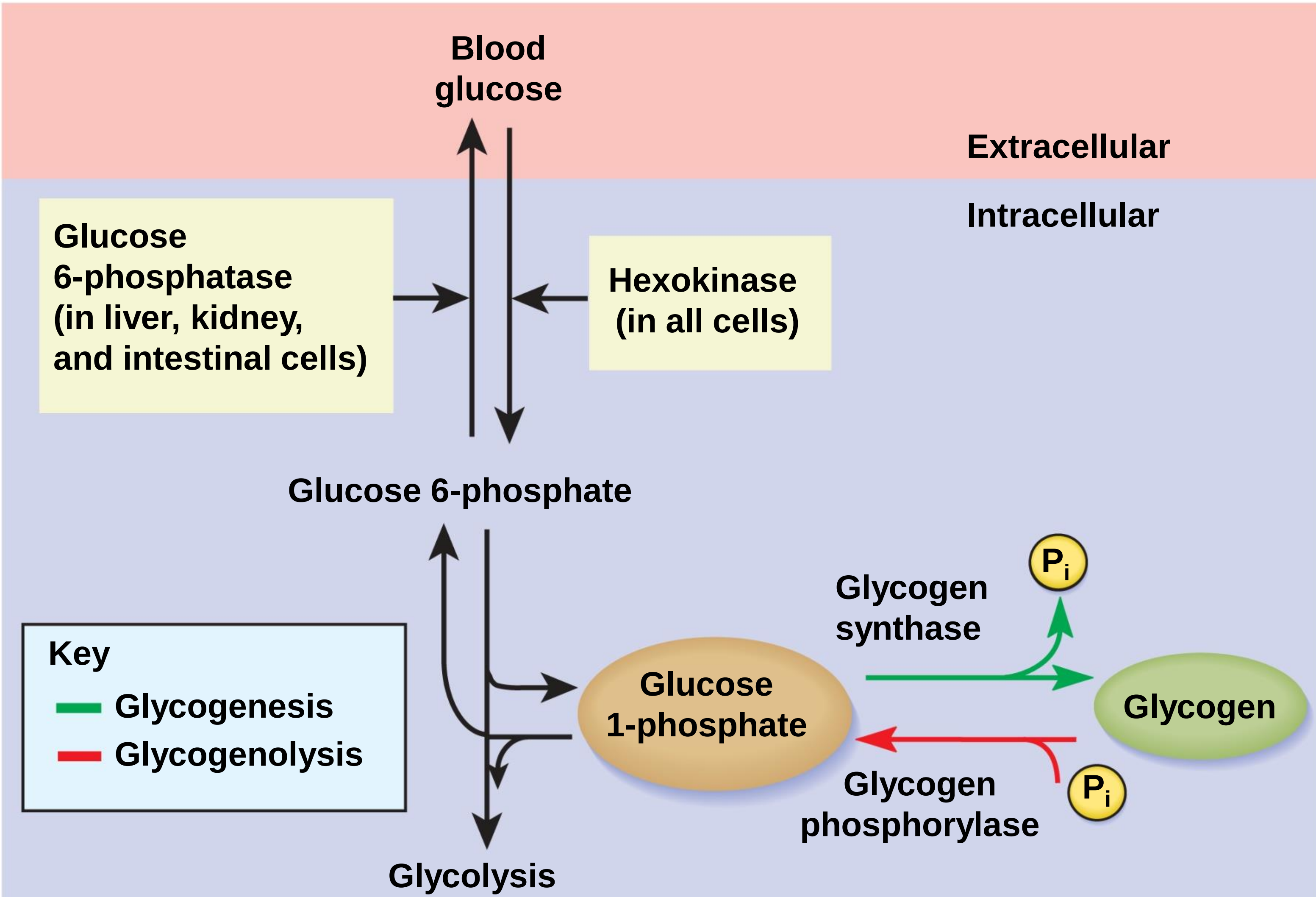


Figure 26.8

Lipid and Protein Metabolism

- **Expected Learning Outcomes**
  - Describe the processes of lipid catabolism and anabolism.
  - Describe the processes of protein catabolism and anabolism.
  - Explain the metabolic source of ammonia and how the body disposes of it.

Lipids

- **Triglycerides are stored in body's adipocytes**
  - Turnover of lipid molecules every 2 to 3 weeks
    - Released into blood, transported and either oxidized or redeposited in other fat cells

- **Lipogenesis**—synthesis of fat from other types of molecules
  - Amino acids and sugars used to make fatty acids and glycerol
  - PGAL can be converted to glycerol
  - Acetyl-CoA used to make fatty acids

Lipogenesis and Lipolysis Pathways

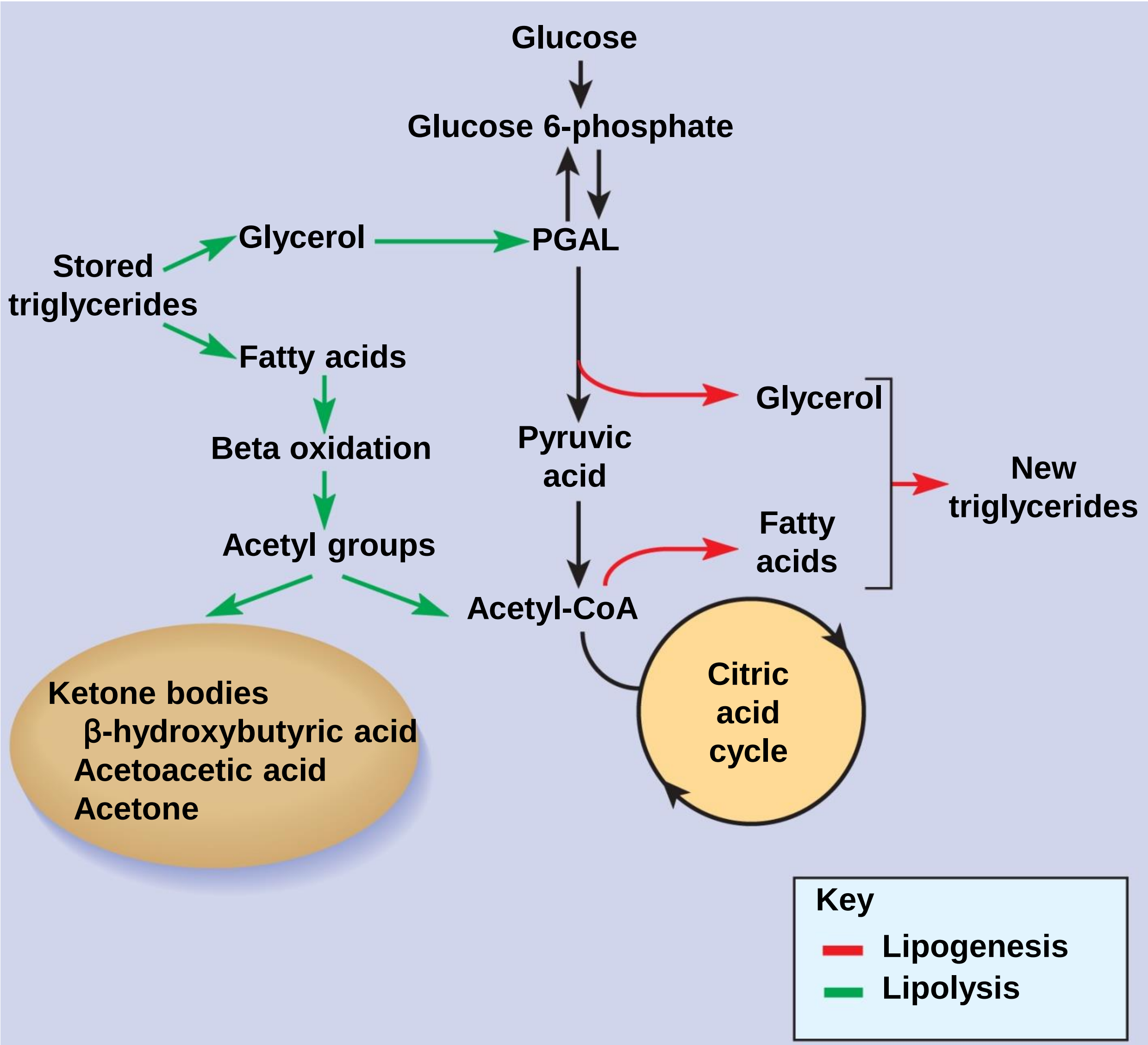


Figure 26.9

Lipids

- **Lipolysis**—breaking down fat for fuel
  - Begins with the hydrolysis of a triglyceride to **glycerol and fatty acids**
  - Stimulated by epinephrine, norepinephrine, glucocorticoids, thyroid hormone, and growth hormone
  - **Glycerol** easily converted to PGAL and enters the pathway of glycolysis
    - Generates only half as much ATP as glucose

Lipids

(Continued)

- **Beta oxidation** in the mitochondrial matrix catabolizes the fatty acid components
  - Removes 2 carbon atoms at a time which bonds to coenzyme A
  - Forms acetyl-CoA, the entry point for the citric acid cycle
- A fatty acid with 16 carbons can yield 129 molecules of ATP
  - Richer source of energy than the glucose molecule

Lipids

- Fatty acids catabolized into acetyl groups (by **beta oxidation** in mitochondrial matrix) may:
  - Enter citric acid cycle as acetyl-CoA
  - Undergo ketogenesis
    - Metabolized by liver to produce ketone bodies
      - Acetoacetic acid
      - β-hydroxybutyric acid
      - Acetone
    - Rapid or incomplete oxidization of fats raises blood ketone levels (ketosis) and may lead to a pH imbalance (ketoacidosis)

Proteins

- **Amino acid pool**—dietary amino acids plus 100 g of tissue protein broken down each day into free amino acids
- **May be used to synthesize new proteins**
  - Fastest rate of protein turnover is in intestinal lining—epithelial cells are frequently replaced
- **Of all the amino acids absorbed by the small intestine:**
  - 50% come from the diet
  - 25% from dead epithelial cells
  - 25% from enzymes that have digested each other

Proteins

- **Some amino acids in the pool can be converted to others**
- **Free amino acids also can be converted to glucose and fat or directly used as fuel**
- **Conversions involve three processes**
  - **Deamination:** removal of an amino group ($-NH_2$)
  - **Amination:** addition of $-NH_2$
  - **Transamination:** transfer of $-NH_2$ from one molecule to another

Use as Fuel

- **As fuel, amino acids first must be deaminated (removal of $-NH_2$)**
  - What remains is **keto acid** and may be converted to pyruvic acid, acetyl-CoA, or one of the acids of the citric acid cycle
    - These reactions are reversible in case there is a deficiency of amino acids
  - In gluconeogenesis, keto acids are used to synthesis glucose

Transamination, Ammonia, and Urea

- When an amino acid is **deaminated**
  - Its amino group is transferred to a citric acid cycle intermediate, **α-ketoglutaric acid,** converting it to **glutamic acid**
  - **Glutamic acid** can travel to the **liver**
    - $-NH_2$ is removed converting it back α-ketoglutaric acid
    - **$-NH_2$** becomes **ammonia** (NH_3) which is toxic and cannot be allowed to accumulate
    - **Urea cycle**—pathway by which liver combines ammonia with carbon dioxide to produce less toxic waste, **urea**
    - Urea excreted in the urine as one of the body’s nitrogenous wastes

Protein Synthesis

- **Protein synthesis**—process involving DNA, mRNA, tRNA, and ribosomes
- Stimulated by **growth hormone, thyroid hormone,** and **insulin**
- **Requires an ample supply of all amino acids**
  - **Nonessential amino acids** can be made by the **liver** from other amino acids or citric acid cycle intermediates
  - **Essential amino acids** must be obtained from the diet

Pathways of Amino Acid Metabolism

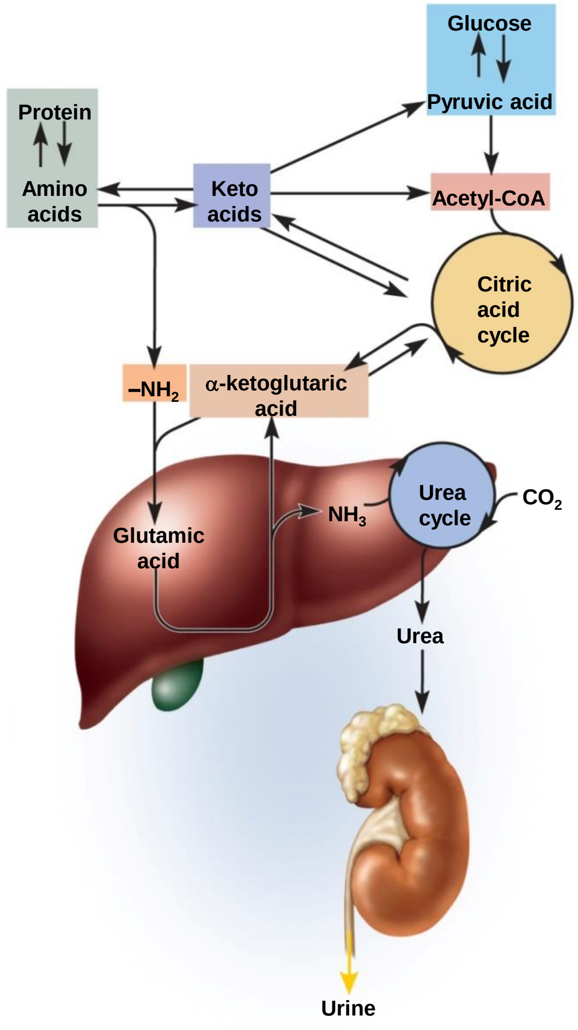


Figure 26.10

Liver Functions in Metabolism

- Liver plays a wide variety of roles in **carbohydrate, lipid,** and **protein metabolism**
  - Most of its functions are nondigestive
  - **Hepatocytes** perform all functions, except **phagocytosis**
- **Degenerative liver diseases** such as hepatitis, cirrhosis, and liver cancer are especially life-threatening

Hepatitis and Cirrhosis

- **Hepatitis** or inflammation of the liver is caused by one of five strains of hepatitis viruses
  - Hepatitis A is common and mild
    - Causes up to 6 months of illness, but most recover
  - Hepatitis B and C are more serious
    - Transmitted sexually and through blood and other body fluids
    - Often lead to cirrhosis or liver cancer
- **Cirrhosis—**irreversible inflammatory liver disease
  - Scar tissue starts to dominate, vessels rupture, and necrosis occurs
  - Results from alcohol abuse

Metabolic States and Metabolic Rate

- **Expected Learning Outcomes**
  - Define the *absorptive* and *postabsorptive states.*
  - Explain what happens to carbohydrates, fats, and proteins in each of these states.
  - Describe the hormonal and nervous regulation of each state.
  - Define *metabolic rate* and *basal metabolic rate.*
  - Describe some factors that alter the metabolic rate.

Metabolic States and Metabolic Rate

- **Your metabolism changes from hour to hour**
  – Depending on how long since your last meal
- **Absorptive (fed) state**
  – About 4 hours during and after a meal
  – Nutrients are being absorbed
  – Nutrients may be used immediately to meet energy and other needs
- **Postabsorptive (fasting) state**
  – Prevails in the late morning, late afternoon, and overnight
  – Stomach and intestines are empty
  – Body's energy needs are met from stored fuels

The Absorptive State

- **Glucose is readily available for ATP synthesis**
  – Serves as the primary fuel and spares use of stored fuels
- **Carbohydrates**
  – Absorbed sugars transported to liver by hepatic portal system
  – Most glucose passes through the liver and becomes available to cells everywhere
  – Glucose excess absorbed by liver which forms glycogen or fat
  – Most fat synthesized by the liver is released into the circulation

The Absorptive State

- **Fats**
  - Enter the lymph as chylomicrons
  - Initially bypass the liver
  - **Lipoprotein lipase** removes fats from chylomicrons for uptake by tissues
  - Liver disposes of **chylomicron remnants**
  - Fats are primary energy substrates for hepatocytes, adipocytes, and muscle cells
- **Amino acids**
  - Most pass through the liver and go on to other cells for protein synthesis
  - In liver cells, may be used for protein synthesis, fuel for ATP synthesis, or fatty acid synthesis

Regulation of the Absorptive State

- Regulated by **insulin** secreted in response to elevated blood glucose and amino acid levels, and the **intestinal hormones** gastrin, secretin, cholecystokinin, and glucose-dependent insulinotropic peptide (GIP)

- **Insulin**
  - Regulates glucose uptake by nearly all cells, except neurons, kidney cells, and erythrocytes
    - Have independent rates of uptake

Regulation of the Absorptive State

- **Insulin effects on target cell**
  - Increases the cellular uptake of glucose, causing blood glucose concentration to fall
  - Stimulates glucose oxidation, glycogenesis, and lipogenesis
  - Inhibits gluconeogenesis
  - Stimulates active transport of amino acids into cells and promotes protein synthesis
  - Acts on the brain as an adiposity signal (index of fat stores)
- High amino acid levels stimulate release of both insulin and glucagon supporting adequate levels of glucose to meet the needs of the brain

The Postabsorptive State

- Postabsorptive state regulates blood glucose concentration to be between about **90 to 100 mg/dL**
  - Especially **critical to the brain**
  - Uses stored fuels as needed

- **Postabsorptive status of major nutrients**
  - **Carbohydrates**
    - Glucose is drawn from glycogen reserves or synthesized from other compounds **(gluconeogenesis)**
    - Liver usually stores enough glycogen to support 4 hours of postabsorptive metabolism before gluconeogenesis occurs

The Postabsorptive State

(Continued)

- **Fats**
  - Adipocytes and hepatocytes hydrolyze fat and convert glycerol to glucose
  - Free fatty acids cannot be converted to glucose, but they can favorably affect blood glucose concentration by having a glucose-sparing effect
    - Free fatty acids are oxidized by liver to **ketone bodies** which other cells absorb and use as their source of energy (leaving glucose for the brain)

The Postabsorptive State

(Continued)

- **Proteins**
  - Used as fuel when glycogen and fat reserves are depleted
  - Collagen is almost never broken down for fuel, but muscle protein goes quickly
  - **Cachexia**—the extreme wasting away seen in cancer and some other chronic diseases, resulting from loss of appetite **(anorexia)** as well as altered metabolism

Regulation of the Postabsorptive State

- Regulated mainly by the **sympathetic nervous system** and **glucagon**
- **As blood glucose levels drop, insulin secretion declines**
- The **pancreatic alpha cells** secrete **glucagon**
  - Promotes **glycogenolysis** and **gluconeogenesis**
    - Raising blood glucose level
  - Promotes **lipolysis** and rise in FFA levels
  - Makes both glucose and lipid available for fuel

Regulation of the Postabsorptive State

- **Sympathoadrenal system** also promotes **glycogenolysis** and **lipolysis**
  - Especially under the conditions of injury, fear, anger, and other forms of stress
  - Adipose tissue richly innervated by **sympathetic nervous system**
  - Adipocytes, hepatocytes, and muscle cells also respond to **epinephrine from the adrenal medulla**
  - Mobilizes stored energy reserves and makes them available to meet the demands of tissue repair

Regulation of the Postabsorptive State

- **Cortisol** released in response to stress which promotes fat and protein catabolism and gluconeogenesis

- **Growth hormone** is secreted in response to a rapid drop in glucose levels
  - Opposes insulin and raises blood glucose concentrations

Metabolic Rate

- **Metabolic rate**—the amount of energy liberated in the body in a given period of time (kcal/hr or kcal/day)
  – Measured directly with a **calorimeter:** a closed chamber with water-filled walls that absorb the heat given off by the body
  – Measured indirectly with a **spirometer** by measuring the amount of oxygen a person consumes
- **Metabolic rate depends on physical activity, mental state, absorptive or postabsorptive status, thyroid hormone, and other hormones**

Metabolic Rate

- **Basal metabolic rate (BMR)**
  - A baseline or standard of comparison that minimizes the effects of activity, feeding, and hormone levels
  - Relaxed, awake, fasting, comfortable room temperature
  - Adult male BMR is 2,000 kcal/day; slightly less for a female

Metabolic Rate

- **Total metabolic rate (TMR)**—the sum of the BMR and energy expenditures for voluntary activities
- **Factors raising TMR**
  - Physical activity, pregnancy, anxiety, fever, eating, catecholamines and thyroid hormones
  - High in children and decreases with age
- **Factors lowering TMR**
  - Apathy, depression, and prolonged starvation
  - As one reduces food intake, the body reduces its metabolic rate to conserve body mass, making weight loss more difficult

Body Heat and Thermoregulation

- **Expected Learning Outcomes**
  - Identify the principal sources of body heat.
  - Describe some factors that cause variations in body temperature.
  - Define and contrast the different forms of heat loss.
  - Describe how the hypothalamus monitors and controls body temperature.
  - Describe conditions in which the body temperature is excessively high or low.

Body Heat and Thermoregulation

- **Enzymes** that control our metabolism depend on an optimal, **stable working temperature**
  - To maintain this, heat loss must match heat generation
  - **Low body temperature (hypothermia)** can slow metabolism and cause death
  - **High body temperature (hyperthermia)** can disrupt coordination of metabolic pathways and cause death

- **Thermoregulation**—the balance between heat production and loss

Body Temperature

- **“Normal” body temperature** varies about 1.8°F in a 24-hour cycle
  - Low in morning and high in late afternoon
- **Core body temperature—**temperature of organs in cranial, thoracic, and abdominal cavities
  - Rectal temperature is an estimate of core temperature
  - Adult varies normally from 99.0° to 99.7°F

Body Temperature

- **Shell temperature**—temperature closer to the surface (oral cavity and skin)
  - Slightly lower than rectal temperature
  - Adult varies normally from 97.9° to 98.6°F
  - As high as 104°F during hard exercise
  - Fluctuates in response to processes that maintain stable core temperature

Heat Production and Loss

- Most of body's heat comes from **exergonic** (energy-releasing) **chemical reactions** such as nutrient oxidation and ATP use
  - A little heat is generated by joint friction, blood flow, and other movements
  - **At rest,** most heat is generated by the brain, heart, liver, and endocrine glands
    - Skeletal muscle contributes 20% to 30% of total resting heat
  - **During vigorous exercise** the muscles produce 30 to 40 times as much heat as the rest of the body

Heat Production and Loss

- **The body loses heat in three ways**
  - **Radiation:** the emission of infrared (IR) rays by moving molecules
    - Heat means molecular motion
    - All molecular motion produces IR rays
    - When IR rays are absorbed by an object, they increase its molecular motion and raise its temperature
    - IR radiation removes heat from its source and adds heat to anything that absorbs it
    - Since we are usually warmer than the objects around us, we usually lose more heat this way than we gain

Heat Production and Loss

(Continued)

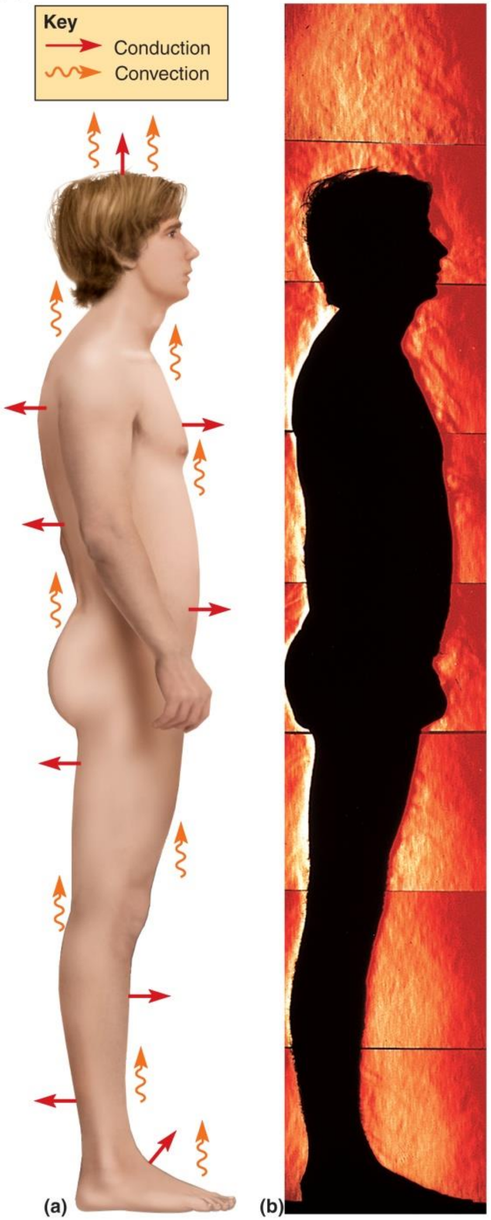
- **Conduction—**transfer of kinetic energy between molecules as they collide
  - Body heat is conducted through tissues to body surface and then lost to anything next to skin that is cooler than it
  - Body heat can also be gained by conduction if skin is contacting something warmer than the body

Heat Production and Loss

(Continued)

- **Convection—**transfer of heat to a moving fluid (blood, air, or water)
  - Heat from metabolism is carried in blood to body surface
  - Body heat warms the air at skin surface, so the air rises and is replaced by cooler air from below
  - Natural convection occurs when fluid movement is caused only by its temperature change
  - Forced convection occurs when fluid movement is caused by some other force (wind, for example)

Conduction and Convection



Heat Production and Loss

(Continued)

- **Evaporation:** change from a liquid to a gaseous state
  - Cohesion of water molecules hampers their vibratory movements in response to heat input
  - If the temperature of the water is raised sufficiently, its molecular motion becomes great enough for molecules to break free and evaporate
  - Carries a substantial amount of heat with it (0.58 kcal/g)
  - Sweat evaporation carries heat away
    - Forced convection increases evaporative heat loss, such as when you are sweaty and stand in front of a fan
  - In extreme conditions, the body can lose 2 L or more of sweat per hour

Heat Production and Loss

- **A nude body at air temperature of 70°F loses:**
  - **60% of its heat by radiation**
  - **18% by conduction**
  - **22% by evaporation**
- If air temperature is higher than skin temperature**, evaporation** becomes the only means of heat loss
  - Radiation and conduction add more heat to the body than they remove from it
- **Hot, humid weather** hinders even evaporation because there is less of a humidity gradient from the skin to the air

Thermoregulation

- **Thermoregulation** is achieved through several negative feedback loops

- **Hypothalamic thermostat**—the **preoptic area** of the hypothalamus functions as the body's thermostat
  - Monitors temperature of the blood
  - Receives signals from peripheral thermoreceptors in the skin
  - Sends appropriate signals to nearby centers:
    - **Heat-loss center:** a nucleus in the anterior hypothalamus
    - **Heat-promoting center:** a nucleus near the mammillary bodies of the brain

Thermoregulation

- When heat-loss center senses that **blood temperature is too high** it activates **heat-losing mechanisms:**
  - **Cutaneous vasodilation:** increases blood flow close to the body’s surface and promotes heat loss
    - If necessary, triggers sweating
    - Inhibits heat-promoting center

Thermoregulation

- When **heat-promoting center** senses **blood temperature** is **too low** it activates mechanisms to **conserve or generate heat**
  - **Cutaneous vasoconstriction**
    - By way of the sympathetic nervous system
    - Warm blood is retained deeper in the body and less heat is lost through the skin
  - If not enough to restore core temperature, the body resorts to **shivering thermogenesis**
    - **Shivering**—involves a spinal reflex that causes tiny alternating contractions of antagonistic muscle pairs
    - Muscle contractions release heat from ATP consumption
    - Shivering can increase body's heat production fourfold

Thermoregulation

(Continued)

- **Nonshivering thermogenesis:** a more long-term mechanism for generating heat
  - Sympathetic nervous system and thyroid hormone **increase metabolic rate**
  - More nutrients burned as fuel, increased heat production, and we consume more calories
- **Behavioral thermoregulation:** behaviors that raise or lower the body’s heat gains and losses—adding or removing clothing

Disturbances of Thermoregulation

- **Fever**
  - Normal protective mechanism that should be allowed to run its course if it is not excessively high
  - Above 108° to 110°F can be very dangerous
    - Elevates metabolic rate
    - Body generates heat faster than heat-losing mechanisms can disperse it
    - Causes dangerous **positive feedback loop**
    - Core temperatures of 111° to 113°F promote metabolic dysfunction, neurological damage, and death

Disturbances of Thermoregulation

- **Exposure to excessive heat**
  - **Heat cramps:** painful muscle spasms due to electrolyte imbalance from excessive sweating
    - Occur especially when a person begins to relax after strenuous exertion and heavy sweating
  - **Heat exhaustion:** from severe water and electrolyte loss
    - Hypotension, dizziness, vomiting, and sometimes fainting

Disturbances of Thermoregulation

(Continued)

- **Heat stroke (sunstroke):** state in which the core body temperature is over 104°F
  - Brought about by prolonged heat wave with high humidity
  - Skin is hot and dry
  - Nervous system dysfunctions—delirium, convulsions, or coma
  - Tachycardia, hyperventilation, inflammation and multiorgan dysfunction, death

Disturbances of Thermoregulation

- **Exposure to excessive cold**
  - **Hypothermia** can cause life-threatening positive feedback loops
  - If core temperature drops below 91°F
    - Metabolic rate drops so low that heat production cannot keep pace with heat loss
    - Temperature falls even more
    - Death from cardiac fibrillation may occur below 90°F
    - Below 75°F is usually fatal
    - Dangerous to give alcohol to someone in hypothermia, as it accelerates heat loss by dilating cutaneous vessels

Alcohol and Alcoholism

- **Alcohol**—mind-altering drug, empty calories, addictive drug, and a toxin
- Rapidly **absorbed** from GI tract
  - 10% in stomach and 90% in small intestine
  - Carbonation increases rate of absorption
  - Food reduces absorption
  - Easily crosses blood–brain barrier to exert intoxicating effects on the brain

Alcohol and Alcoholism

- **Detoxified** by hepatic enzyme **alcohol dehydrogenase** which oxidizes it to acetaldehyde—in citric cycle is oxidized to CO_2 and H_2O
  - **Women** have less alcohol dehydrogenase and clear alcohol from the bloodstream more slowly than men
    - More vulnerable to alcohol-related illnesses such as cirrhosis of the liver

Physiological Effects of Alcohol

- **Nervous system**
  - Depressant because it inhibits the release of norepinephrine and disrupts GABA receptors
    - Low dose provides euphoria and giddiness
    - High dose—nerves less responsive to neurotransmitters
      - Timing and coordination between neurons is impaired
      - Slurred speech, poor coordination, slower reaction time

Physiological Effects of Alcohol

- **Liver**
  - Excessive acetaldehyde produced during metabolism causes inflammation of liver and pancreas
    - Disruption of digestive function
  - Destroys hepatocytes faster than they can regenerate, producing cirrhosis
    - Hepatic coma and jaundice

Physiological Effects of Alcohol

- **Circulatory system**
  - Clotting problems
    - Clotting factors reduced due to liver damage
  - Edema due to inadequate production of albumin
  - Cirrhosis obstructs hepatic portal circulation
  - Portal hypertension and hypoproteinemia
    - Liver and other organs “weep” serous fluid into peritoneal cavity
    - **Ascites**—swelling of abdomen with as much as several liters of serous fluid
    - Hemorrhaging and **hematemesis (vomiting blood)**
    - Destroys myocardial tissue, reduces heart contractility, and causes arrhythmias

Physiological Effects of Alcohol

- **Digestive system and nutrition**
  - Breaks down protective mucous barrier of stomach
    - Gastritis and bleeding
    - Linked to esophageal cancer and peptic ulcers
  - Malnutrition from appetite suppression
  - Acetaldehyde interferes with vitamin absorption and use

Addiction

- **Alcohol is the most widely available addictive drug in America**
  - Similar to barbiturates in toxic effects
- **Alcoholism involves: potential for tolerance, dependence, and risk of overdose**
  - Physiological tolerance of high concentrations
  - Impaired physiological, psychological, and social functionality
  - Withdrawal symptoms when intake is reduced or stopped: **delirium tremens (DT)**
    - Restlessness, insomnia, confusion, irritability, tremors, incoherent speech, hallucinations, convulsions, and coma
    - Has 5% to 15% mortality rate

Addiction

- **Type I** (more common) sets in after age 25—usually associated with life stress or peer pressure
- **Type II** is addicted before 25—partially hereditary
  - Sons of other type II alcoholics

Treatment

- **Behavioral modification**
  - Abstinence, peer support, avoidance or correction of stress that encourages drinking, psychotherapy
- **Disulfiram (Antabuse): drug used to support behavioral modification programs**