Chapter 25: Metabolism and Nutrition
Metabolism

- Metabolism – refers to all chemical reaction occurring in body
  - Catabolism – break down complex molecules
    - Exergonic – produce more energy than they consume
  - Anabolism – combine simple molecules into complex ones
    - Endergonic – consume more energy than they produce

- Adenosine triphosphate (ATP)
  - “energy currency”
  - ADP + P + energy ↔ ATP
Role of ATP in linking anabolic and catabolic reactions

- Catabolic reactions transfer energy from complex molecules to ATP
- Anabolic reactions transfer energy from ATP to complex molecules
- ATP
- ADP + P

Simple molecules such as glucose, amino acids, glycerol, and fatty acids

Complex molecules such as glycogen, proteins, and triglycerides

Heat released
Energy transfer

- Oxidation-reduction or redox reactions
  - Oxidation – removal of electrons
    - Decrease in potential energy
    - Dehydrogenation – removal of hydrogens
    - Liberated hydrogen transferred by coenzymes
      - Nicotinamide adenine dinucleotide (NAD)
      - Flavin adenine dinucleotide (FAD)
  - Glucose is oxidized
  - Reduction – addition of electrons
    - Increase in potential energy
3 Mechanisms of ATP generation

1. Substrate-level phosphorylation
   - Transferring high-energy phosphate group from an intermediate directly to ADP

2. Oxidative phosphorylation
   - Remove electrons and pass them through electron transport chain to oxygen

3. Photophosphorylation
   - Only in chlorophyll-containing plant cells
Carbohydrate metabolism

- Fate of glucose depends on needs of body cells
  - ATP production or synthesis of amino acids, glycogen, or triglycerides
- GluT transporters bring glucose into the cell via facilitated diffusion
  - Insulin causes insertion of more of these transporters, increasing rate of entry into cells
  - Glucose trapped in cells after being phosphorylated
Glucose catabolism / cellular respiration

1. Glycolysis
   - Anaerobic respiration – does not require oxygen
2. Formation of acetyl coenzyme A
3. Krebs cycle reactions
4. Electron transport chain reactions
   - Aerobic respiration – requires oxygen
Overview of cellular respiration
GLYCOLYSIS

1 Glucose

2 Pyruvic acid

FORMATION OF ACETYL COENZYME A

2 Pyruvic acid

2 Acetyl coenzyme A

KREBS CYCLE

Electrons

ELECTRON TRANSPORT CHAIN

32 or 34 ATP

O₂

H₂O

2 ATP

2 NADH + 2 H⁺

2 CO₂

2 NADH + 2 H⁺

2 ATP

4 CO₂

6 NADH + 6 H⁺

2 FADH₂
Glycolysis

1. Glycolysis
   - Splits 6-carbon glucose into 2 3-carbon molecules of pyruvic acid
   - Consumes 2 ATP but generates 4
   - 10 reactions
   - Fate of pyruvic acid depends on oxygen availability
     - If oxygen is scarce (anaerobic), reduced to lactic acid
       - Hepatocytes can convert it back to pyruvic acid
     - If oxygen is plentiful (aerobic), converted to acetyl coenzyme A
Cellular respiration begins with glycolysis
The 10 reactions of glycolysis
Formation of Acetyl coenzyme A

2. Formation of Acetyl coenzyme A
   - Each pyruvic acid converted to 2-carbon acetyl group
     - Remove one molecule of CO₂ as a waste product
   - Each pyruvic acid also loses 2 hydrogen atoms
     - NAD⁺ reduced to NADH + H⁺
   - Acetyl group attached to coenzyme A to form acetyl coenzyme A (acetyl CoA)
Fate of pyruvic acid

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3. The Krebs cycle
   - Also known as citric acid cycle
   - Occurs in matrix of mitochondria
   - Series of redox reactions
   - 2 decarboxylation reactions release CO$_2$
   - Reduced coenzymes (NADH and FADH$_2$) are the most important outcome
   - One molecule of ATP generated by substrate-level phosphorylation
The Krebs Cycle

(a) Cellular respiration

(b) Overview of the Krebs cycle

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The Eight reactions of the Krebs cycle
4. **Electron transport chain**

- Series of electron carriers in inner mitochondrial membrane reduced and oxidized
- As electrons pass through chain, exergonic reactions release energy used to form ATP
  - Chemiosmosis
- Final electron acceptor is oxygen to form water
Chemiosmosis

- Carriers act as proton pumps to expel H^+ from mitochondrial matrix
- Creates H^+ electrochemical gradient – concentration gradient and electrical gradient
- Gradient has potential energy – proton motive force
- As H^+ flows back into matrix through membrane, generates ATP using ATP synthase
Energy from NADH + H⁺

Low H⁺ concentration in matrix of mitochondrion

High H⁺ concentration between inner and outer mitochondrial membranes

Inner mitochondrial membrane

Electron transport chain (includes proton pumps)

1 Energy from NADH + H⁺

2 H⁺

3 ATP synthase

ADP + P → ATP

Low H⁺ concentration in matrix of mitochondrion

Outer membrane

Inner membrane

Matrix
The actions of the three proton pumps and ATP synthase in the inner membrane of mitochondria

1. NADH dehydrogenase complex: FMN and five Fe-S centers
2. Cytochrome b-c₁ complex: cyt b, cyt c₁, and an Fe-S center
3. Cytochrome oxidase complex: cyt a, cyt a₃, and two Cu
Summary of cellular respiration

<table>
<thead>
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<th>TABLE 25.1</th>
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<tr>
<td>Summary of ATP Produced in Cellular Respiration</td>
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<table>
<thead>
<tr>
<th>SOURCE</th>
<th>ATP YIELD PER GLUCOSE MOLECULE (PROCESS)</th>
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<tr>
<td><strong>GLYCOLYSIS</strong></td>
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<tr>
<td>Oxidation of one glucose molecule to two pyruvic acid molecules</td>
<td>2 ATPs (substrate-level phosphorylation)</td>
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<tr>
<td>Production of 2 NADH + H⁺</td>
<td>4 or 6 ATPs (oxidative phosphorylation in electron transport chain)</td>
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<td></td>
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<td>2 NADH + 2 H⁺</td>
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</tr>
<tr>
<td><strong>KREBS CYCLE AND ELECTRON TRANSPORT CHAIN</strong></td>
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<tr>
<td>Oxidation of succinyl CoA to succinic acid</td>
<td>2 GTPs that are converted to 2 ATPs (substrate-level phosphorylation)</td>
</tr>
<tr>
<td>Production of 6 NADH + 6 H⁺</td>
<td>18 ATPs (oxidative phosphorylation in electron transport chain)</td>
</tr>
<tr>
<td>Production of 2 FADH₂</td>
<td>4 ATPs (oxidative phosphorylation in electron transport chain)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>36 or 38 ATPs per glucose molecule (theoretical maximum)</td>
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Glucose anabolism

- **Glucose storage: glycogenesis**
  - Polysaccharide that is the only stored carbohydrate in humans
  - Insulin stimulates hepatocytes and skeletal muscle cells to synthesize glycogen

- **Glucose release: glycogenolysis**
  - Glycogen stored in hepatocytes broken down into glucose and release into blood
Glycogenesis and glycogenolysis

Key:
- **Glycogenesis** (stimulated by insulin)
- **Glycogenolysis** (stimulated by glucagon and epinephrine)
Formation of glucose from proteins and fats: gluconeogenesis

- Glycerol part of triglycerides, lactic acid, and certain amino acids can be converted by the liver into glucose
- Glucose formed from noncarbohydrate sources
- Stimulated by cortisol and glucagon
Lipid metabolism

- Transport by lipoproteins
  - Most lipids nonpolar and hydrophobic
  - Made more water-soluble by combining them with proteins to form lipoproteins
  - Proteins in outer shell called apoproteins (apo)
    - Each has specific functions
    - All essentially are transport vehicles
Apoproteins

- Apoproteins categorized and named according to density (ratio of lipids to proteins)
  - Chylomicrons
    - Form in small intestine mucosal epithelial cells
    - Transport dietary lipids to adipose tissue
  - Very low-density lipoproteins (VLDLs)
    - Form in hepatocytes
    - Transport endogenous lipids to adipocytes
  - Low-density lipoproteins (LDLs) – “bad” cholesterol
    - Carry 75% of total cholesterol in blood
    - Deliver to body cells for repair and synthesis
    - Can deposit cholesterol in fatty plaques
  - High-density lipoproteins (HDLs) – “good” cholesterol
    - Remove excess cholesterol from body cells and blood
    - Deliver to liver for elimination
Lipid Metabolism

- 2 sources of cholesterol in the body
  - Present in foods
  - Synthesized by hepatocytes
- As total blood cholesterol increases, risk of coronary artery disease begins to rise
  - Treated with exercise, diet, and drugs
- Lipids can be oxidized to provide ATP
  - Stored in adipose tissue if not needed for ATP
- Major function of adipose tissue to remove triglycerides from chylomicrons and VLDLs and store it until needed
  - 98% of all body energy reserves
Lipid Metabolism

- Lipid catabolism: lipolysis
  - Triglycerides split into glycerol and fatty acids
  - Must be done for muscle, liver, and adipose tissue to oxidize fatty acids
  - Enhanced by epinephrine and norepinephrine

- Lipid anabolism: lipogenesis
  - Liver cells and adipose cells synthesize lipids from glucose or amino acids
  - Occurs when more calories are consumed than needed for ATP production
Protein metabolism

- Amino acids are either oxidized to produce ATP or used to synthesize new proteins.
- Excess dietary amino acids are not excreted but converted into glucose (gluconeogenesis) or triglycerides (lipogenesis).

Protein catabolism

- Proteins from worn out cells broken down into amino acids.
- Before entering Krebs cycle amino group must be removed – deamination.
  - Produces ammonia, liver cells convert to urea, excreted in urine.
Various points at which amino acids enter the Krebs cycle for oxidation
Protein anabolism

- Carried out in ribosomes of almost every cell in the body
- 10 essential amino acids in the human
  - Must be present in the diet because they cannot be synthesized
  - Complete protein – contains sufficient amounts of all essential amino acids – beef, fish, poultry, eggs
  - Incomplete protein – does not – leafy green vegetables, legumes, grains
- 10 other nonessential amino acids can be synthesized by body cells using transamination
Key molecules at metabolic crossroads

- 3 molecules play pivotal roles in metabolism
- Stand at metabolic crossroads – reactions that occur or not depend on nutritional or activity status of individual

1. Glucose 6-phosphate
   - Made shortly after glucose enters body cell
   - 4 fates – synthesis of glycogen, release of glucose into blood stream, synthesis of nucleic acids, glycolysis
Key molecules at metabolic crossroads

2. Pyruvic acid
   - If there is enough oxygen, aerobic cellular respiration occurs
   - If there is not enough oxygen, anaerobic reactions can produce lactic acid, produce alanine or gluconeogenesis

3. Acetyl Coenzyme A
   - When ATP is low and oxygen plentiful, most pyruvic acid goes to ATP production via Acetyl CoA
   - Acetyl CoA is the entry into the Krebs cycle
   - Can also be used for synthesis of certain lipids
Metabolic adaptations

- During the absorptive state ingested nutrients are entering the blood stream
  - Glucose readily available for ATP production

- During postabsorptive state absorption of nutrients from GI tract complete
  - Energy needs must be met by fuels in the body
  - Nervous system and red blood cells depend on glucose so maintaining steady blood glucose critical
  - Effects of insulin dominate
Metabolism during absorptive state

- Soon after a meal nutrients enter blood
  - Glucose, amino acids, and triglycerides in chylomicrons
- 2 metabolic hallmarks
  - Oxidation of glucose for ATP production in all body cells
  - Storage of excess fuel molecules in hepatocytes, adipocytes, and skeletal muscle cells
- Pancreatic beta cells release insulin
  - Promotes entry of glucose and amino acids into cells
Principal metabolic pathways during the absorptive state
Metabolism during postabsorptive state

- About 4 hours after the last meal absorption in small intestine nearly complete
- Blood glucose levels start to fall
- Main metabolic challenge to maintain normal blood glucose levels
- Glucose production
  - Breakdown of liver glycogen, lipolysis, gluconeogenesis using lactic acid and/or amino acids
- Glucose conservation
  - Oxidation of fatty acids, lactic acid, amino acids, ketone bodies and breakdown of muscle glycogen
Principal metabolic pathways during the postabsorptive state
Hormones and autonomic nervous system regulate metabolism during postabsorptive state

- As blood glucose decline, insulin secretion falls
  - Glucagon – increases release of glucose into blood via gluconeogenesis and glycogenolysis
- Sympathetic nerve endings of ANS release norepinephrine and adrenal medulla releases epinephrine and norepinephrine
  - Stimulate lipolysis, glycogen breakdown
Heat and energy balance

- Heat – form of energy that can be measured as temperature and can be expressed in calories
  - calorie (cal) – amount of heat required to raise 1 gram of water 1°C
  - Kilocalorie (kcal) or Calorie (Cal) is 1000 calories

- Metabolic rate – overall rate at which metabolic reactions use energy
  - Some energy used to make ATP, some lost as heat
  - Basal metabolic rate (BMR) – measurement with body in quiet, resting, fasting condition
Body temperature homeostasis

- Despite wide fluctuations in environmental temperatures, homeostatic mechanisms maintain normal range for internal body temperature.
- Core temperature (37°C or 98.6°F) versus shell temperature (1-6°C lower).
- Heat produced by exercise, some hormones, sympathetic nervous system, fever, ingestion of food, younger age, etc.
Heat and energy balance

- Heat can be lost through:
  - Conduction to solid materials in contact with body
  - Convection – transfer of heat by movement of a gas or liquid
  - Radiation – transfer of heat in form of infrared rays
  - Evaporation of exhaled air and skin surface (insensible water loss)

- Hypothalamic thermostat in preoptic area
  - Heat-losing center and heat-promoting center
Thermoregulation

- If core temperature declines
  - Skin blood vessels constrict
  - Release of thyroid hormones, epinephrine and norepinephrine increases cellular metabolism
  - Shivering

- If core body temperature too high
  - Dilation of skin blood vessels
  - Decrease metabolic rate
  - Stimulate sweat glands
Negative feedback mechanisms that conserve heat and increase production

Some stimulus disrupts homeostasis by decreasing body temperature.

- **Receptors**: Thermoreceptors in skin and hypothalamus
- **Input**: Nerve impulses
- **Control centers**: Preoptic area, heat promoting center, and neurosecretory cells in hypothalamus and thyrotopins in anterior pituitary gland
- **Output**: Nerve impulses and TSH

**Effectors**
- Vasoconstriction decreases heat loss through the skin
- Adrenal medulla releases hormones that increase cellular metabolism
- Skeletal muscles contract in a repetitive cycle called shivering
- Thyroid gland releases thyroid hormones, which increase metabolic rate

Return to homeostasis when response brings body temperature back to normal.

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Nutrition

- Nutrients are chemical substances in food that body cells use for growth, maintenance, and repair

- 6 main types
  1. Water – needed in largest amount
  2. Carbohydrates
  3. Lipids
  4. Proteins
  5. Minerals
  6. Vitamins

- Essential nutrients must be obtained from the diet
Guidelines for healthy eating

- We do not know with certainty what levels and types of carbohydrates, fat and protein are optimal
- Different populations around the world eat radically different diets adapted to their particular lifestyle
- Basic guidelines
  - Eat a variety of foods
  - Maintain a healthy weight
  - Choose foods low in fat, saturated fat and cholesterol
  - Eat plenty of vegetables, fruits and grain products
  - Use sugars in moderation only
MyPyramid
Minerals

- Inorganic elements that occur naturally in Earth’s crust
- Eat foods that contain enough calcium, phosphorus, iron and iodine
- Excess amounts of most minerals are excreted in urine and feces
- Major role of minerals to help regulate enzymatic reactions
Vitamins

- Organic nutrients required in small amounts to maintain growth and normal metabolism
- Do not provide energy or serve as body’s building materials
- Most are coenzymes
- Most cannot be synthesized by the body
- Vitamin K produced by bacteria in GI tract
- Some can be assembled from provitamins
- No single food contains all the required vitamins
- 2 groups
  - Fat-soluble – A, D, E, K
  - Water-soluble – several B vitamins and vitamin C
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