Do not salivate on your self

NUTRITION, METABOLISM,

D.HAMMOUDI.MD
Nutrition

- Nutrient: a substance in food that promotes normal growth, maintenance, and repair
- Major nutrients
  - Carbohydrates, lipids, and proteins
- Other nutrients
  - Vitamins and minerals (and, technically speaking, water)
(a) USDA food guide pyramid
Fats, Oils & Sweets
USE SPARINGLY

Milk, Yogurt & Cheese Group
2-3 SERVINGS

Vegetable Group
3-5 SERVINGS

Meat, Poultry, Fish, Dry Beans, Eggs & Nuts Group
2-3 SERVINGS

Fruit Group
2-4 SERVINGS

Bread, Cereal, Rice & Pasta Group
6-11 SERVINGS

KEY
- Fat (naturally occurring and added)
- Sugar (added)

These symbols show fats and added sugars in foods.
Digestion

• Carbohydrate digestion starts in the mouth

• Protein digestion starts in the stomach

• Nucleic acids & fats start in the small intestine

• Everything completely digested and absorbed by the end of the small intestine
Carbohydrates
General characteristics

- The term carbohydrate is derived from the French: hydrate de carbone.
- Compounds composed of C, H, and O.
- \((\text{CH}_2\text{O})_n\) when \(n = 5\) then \(\text{C}_5\text{H}_{10}\text{O}_5\).
- Not all carbohydrates have this empirical formula: deoxysugars, aminosugars.
- Carbohydrates are the most abundant compounds found in nature (cellulose: 100 billion tons annually).
General characteristics

- Most carbohydrates are found naturally in bound form rather than as simple sugars
  - Polysaccharides (starch, cellulose, inulin, gums)
  - Glycoproteins and proteoglycans (hormones, blood group substances, antibodies)
  - Glycolipids (cerebrosides, gangliosides)
  - Glycosides
  - Mucopolysaccharides (hyaluronic acid)
  - Nucleic acids
Carbohydrates = 4 cal

**Dietary sources**

- Starch (complex carbohydrates) in grains and vegetables
- Sugars in fruits, sugarcane, sugar beets, honey and milk
- Insoluble fiber: cellulose in vegetables; provides roughage
- Soluble fiber: pectin in apples and citrus fruits; reduces blood cholesterol levels
Carbohydrates

- Uses
  - Glucose is the fuel used by cells to make ATP
    - Neurons and RBCs rely almost entirely upon glucose
    - Excess glucose is converted to glycogen or fat and stored
Carbohydrates

- **Dietary requirements**
  - Minimum 100 g/day to maintain adequate blood glucose levels
  - Recommended minimum 130 g/day
  - Recommended intake: 45–65% of total calorie intake; mostly complex carbohydrates
Functions

- Sources of energy
- Intermediates in the biosynthesis of other basic biochemical entities (fats and proteins)
- Associated with other entities such as glycosides, vitamins and antibiotics
- Form structural tissues in plants and in microorganisms (cellulose, lignin, murein)
- Participate in biological transport, cell-cell recognition, activation of growth factors, modulation of the immune system
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<tr>
<td>Fructose</td>
<td>1.73</td>
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</table>
Classification of carbohydrates

- Monosaccharides (monoses or glycoses)
  - Trioses, tetroses, pentoses, hexoses

- Oligosaccharides
  - Di, tri, tetra, penta, up to 9 or 10
  - Most important are the disaccharides

- Polysaccharides or glycans
  - Homopolysaccharides
  - Heteropolysaccharides
  - Complex carbohydrates
Monosaccharides

- also known as simple sugars
- classified by 1. the number of carbons and 2. whether aldoses or ketoses
- most (99%) are straight chain compounds
- D-glyceraldehyde is the simplest of the aldoses (aldotriose)
- all other sugars have the ending *ose* (glucose, galactose, ribose, lactose, etc...)
Sugar cane

Sugar beet
The good news is that you don't have mad cow's disease. The bad news is you're lactose intolerant.
Lipids
Lipids = 9 cal

- **Dietary sources**
  - **Triglycerides**
    - Saturated fats in meat, dairy foods, and tropical oils
    - Unsaturated fats in seeds, nuts, olive oil, and most vegetable oils
  - **Cholesterol** in egg yolk, meats, organ meats, shellfish, and milk products
Lipids

- Essential fatty acids
  - Linoleic and linolenic acid, found in most vegetable oils
  - Must be ingested
Lipids

- **Essential uses of lipids in the body**
  - Help absorb fat-soluble vitamins
  - Major fuel of hepatocytes and skeletal muscle
  - Phospholipids are essential in myelin sheaths and all cell membranes
Lipids

- Functions of fatty deposits (adipose tissue)
  - Protective cushions around body organs
  - Insulating layer beneath the skin
  - Concentrated source of energy
Lipids

- Regulatory functions of prostaglandins
  - Smooth muscle contraction
  - Control of blood pressure
  - Inflammation

- Functions of cholesterol
  - Stabilizes membranes
  - Precursor of bile salts and steroid hormones
Lipids

- Dietary requirements suggested by the American Heart Association
  - Fats should represent 30% or less of total caloric intake
  - Saturated fats should be limited to 10% or less of total fat intake
  - Daily cholesterol intake should be no more than 300 mg
Lipid storage diseases

- also known as sphingolipidoses
- genetically acquired
- due to the deficiency or absence of a catabolic enzyme
- examples:
  - Tay Sachs disease
  - Gaucher’s disease
  - Niemann-Pick disease
  - Fabry’s disease
Proteins
Proteins

- **Dietary sources**
  - Eggs, milk, fish, and most meats contain complete proteins
  - Legumes, nuts, and cereals contain incomplete proteins (lack some essential amino acids)
  - Legumes and cereals together contain all essential amino acids
Proteins

- **Uses**
  - Structural materials: keratin, collagen, elastin, muscle proteins
  - Most functional molecules: enzymes, some hormones
Proteins

- Use of amino acids in the body
  1. All-or-none rule
     - All amino acids needed must be present for protein synthesis to occur
  2. Adequacy of caloric intake
     - Protein will be used as fuel if there is insufficient carbohydrate or fat available
Proteins

3. Nitrogen balance
   - State where the rate of protein synthesis equals the rate of breakdown and loss
   - Positive if synthesis exceeds breakdown (normal in children and tissue repair)
   - Negative if breakdown exceeds synthesis (e.g., stress, burns, infection, or injury)
4. **Hormonal controls**

- Anabolic hormones (GH, sex hormones) accelerate protein synthesis
Vegetarian diets providing the eight essential amino acids for humans.
Proteins

- Dietary requirements
  - Rule of thumb: daily intake of 0.8 g per kg body weight
Vitamins

- Organic compounds
- Crucial in helping the body use nutrients
- Most function as coenzymes
- Vitamins D, some B, and K are synthesized in the body
Vitamins

- Two types, based on solubility
  1. Water-soluble vitamins
    - B complex and C are absorbed with water
    - B$_{12}$ absorption requires intrinsic factor
    - Not stored in the body
2. Fat-soluble vitamins
   - A, D, E, and K are absorbed with lipid digestion products
   - Stored in the body, except for vitamin K
   - Vitamins A, C, and E act as antioxidants
Minerals

- Seven required in moderate amounts:
  - Calcium, phosphorus, potassium, sulfur, sodium, chloride, and magnesium

- Others required in trace amounts

- Work with nutrients to ensure proper body functioning

- Uptake and excretion must be balanced to prevent toxic overload
Minerals

- Examples
  - Calcium, phosphorus, and magnesium salts harden bone
  - Iron is essential for oxygen binding to hemoglobin
  - Iodine is necessary for thyroid hormone synthesis
  - Sodium and chloride are major electrolytes in the blood
Metabolism

- Metabolism: biochemical reactions inside cells involving nutrients
- Two types of reactions
  - Anabolism: synthesis of large molecules from small ones
  - Catabolism: hydrolysis of complex structures to simpler ones
Metabolism

- Cellular respiration: catabolism of food fuels and capture of energy to form ATP in cells
- Enzymes shift high-energy phosphate groups of ATP to other molecules (phosphorylation)
- Phosphorylated molecules are activated to perform cellular functions
Stages of Metabolism

- Processing of nutrients
  1. Digestion, absorption and transport to tissues
  2. Cellular processing (in cytoplasm)
     - Synthesis of lipids, proteins, and glycogen, or
     - Catabolism (glycolysis) into intermediates
  3. Oxidative (mitochondrial) breakdown of intermediates into \( \mathrm{CO}_2 \), water, and ATP
**Stage 1** Digestion in GI tract lumen to absorbable forms. Transport via blood to tissue cells.

**Stage 2** Anabolism (incorporation into molecules) and catabolism of nutrients to form intermediates within tissue cells.

**Stage 3** Oxidative breakdown of products of stage 2 in mitochondria of tissue cells. CO₂ is liberated, and H atoms removed are ultimately delivered to molecular oxygen, forming water. Some energy released is used to form ATP. Catabolic reactions

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**Anabolic reactions**

**Catabolic reactions**

**Figure 24.3**
Oxidation-Reduction (Redox) Reactions

- Oxidation; gain of oxygen or loss of hydrogen
- Oxidation-reduction (redox) reactions
  - Oxidized substances lose electrons and energy
  - Reduced substances gain electrons and energy
Oxidation-Reduction (Redox) Reactions

- Coenzymes act as hydrogen (or electron) acceptors
  - Nicotinamide adenine dinucleotide (NAD⁺)
  - Flavin adenine dinucleotide (FAD)
ATP Synthesis

- Two mechanisms
  1. Substrate-level phosphorylation
  2. Oxidative phosphorylation
Substrate-Level Phosphorylation

- High-energy phosphate groups directly transferred from phosphorylated substrates to ADP
- Occurs in glycolysis and the Krebs cycle
(a) Substrate-level phosphorylation
Oxidative Phosphorylation

- Chemiosmotic process
  - Couples the movement of substances across a membrane to chemical reactions
Oxidative Phosphorylation

- In the mitochondria
  - Carried out by electron transport proteins
  - Nutrient energy is used to create $H^+$ gradient across mitochondrial membrane
  - $H^+$ flows through ATP synthase
  - Energy is captured and attaches phosphate groups to ADP
High $H^+$ concentration in intermembrane space

Low $H^+$ concentration in mitochondrial matrix

(b) Oxidative phosphorylation

Energy from food

Proton pumps (electron transport chain)

ATP synthase

ADP + $P_i$ → ATP

Figure 24.4b
Carbohydrate Metabolism

- Oxidation of glucose
  \[ C_6H_{12}O_6 + 6O_2 \rightarrow 6H_2O + 6CO_2 + 36 \text{ ATP} + \text{heat} \]
- Glucose is catabolized in three pathways
  - Glycolysis
  - Krebs cycle
  - Electron transport chain and oxidative phosphorylation
During glycolysis, each glucose molecule is broken down into two molecules of pyruvic acid in the cytosol. The pyruvic acid then enters the mitochondrial matrix, where the Krebs cycle decomposes it to CO₂. During glycolysis and the Krebs cycle, small amounts of ATP are formed by substrate-level phosphorylation. Energy-rich electrons picked up by coenzymes are transferred to the electron transport chain, built into the cristae membrane. The electron transport chain carries out oxidative phosphorylation, which accounts for most of the ATP generated by cellular respiration. Figure 24.5
Glycolysis

- 10-step pathway
- Anaerobic
- Occurs in the cytosol
- Glucose → 2 pyruvic acid molecules
- Three major phases
  1. Sugar activation
  2. Sugar cleavage
  3. Sugar oxidation and ATP formation
Phases of Glycolysis

1. Sugar activation
   - Glucose is phosphorylated by 2 ATP to form fructose-1,6-bisphosphate
Phases of Glycolysis

2. Sugar deavage
   - Fructose-1,6-bisphosphate is split into 3-carbon sugars
     - Dihydroxyacetone phosphate
     - Glyceraldehyde 3-phosphate
Phases of Glycolysis

3. Sugar oxidation and ATP formation
   - 3-carbon sugars are oxidized (reducing NAD\(^+\))
   - Inorganic phosphate groups (P\(_i\)) are attached to each oxidized fragment
   - 4 ATP are formed by substrate-level phosphorylation
Glucose is activated by phosphorylation and converted to fructose-1,6-bisphosphate.

Phase 1
Sugar Activation
Glucose is activated by phosphorylation and converted to fructose-1,6-bisphosphate.
Phase 2  
Sugar Cleavage  
Fructose-1,6-bisphosphate is cleaved into two 3-carbon fragments

Fructose-1,6-bisphosphate

Dihydroxyacetone phosphate  \(\rightleftharpoons\) Glyceraldehyde 3-phosphate

Figure 24.6 (2 of 3)
Phase 3
Sugar oxidation and formation of ATP
The 3-carbon fragments are oxidized (by removal of hydrogen) and 4 ATP molecules are formed.

Glycolysis

Krebs cycle

Electron transport chain and oxidative phosphorylation

Dihydroxyacetone $\rightleftharpoons$ Glyceraldehyde 3-phosphate

To Krebs cycle (aerobic pathway)
Glycolysis

- Final products of glycolysis
  - 2 pyruvic acid
    - Converted to lactic acid if $O_2$ not readily available
    - Enter aerobic pathways if $O_2$ is readily available
  - 2 NADH + H$^+$ (reduced NAD$^+$)
  - Net gain of 2 ATP
Krebs Cycle

- Occurs in mitochondrial matrix
- Fueled by pyruvic acid and fatty acids
Krebs Cycle

- Transitional phase
  - Each pyruvic acid is converted to acetyl CoA
    1. Decarboxylation: removal of 1 C to produce acetic acid and CO₂
    2. Oxidation: H⁺ is removed from acetic acid and picked up by NAD⁺
    3. Acetic acid + coenzyme A forms acetyl CoA
Krebs Cycle

- Coenzyme A shuttles acetic acid to an enzyme of the Krebs cycle
- Each acetic acid is decarboxylated and oxidized, generating:
  - 3 NADH + H⁺
  - 1 FADH₂
  - 2 CO₂
  - 1 ATP
Krebs Cycle

- Does not directly use $O_2$
- Breakdown products of fats and proteins can also enter the cycle
- Cycle intermediates may be used as building materials for anabolic reactions
Electron Transport Chain and Oxidative Phosphorylation

- The part of metabolism that directly uses oxygen
- Chain of proteins bound to metal atoms (cofactors) on inner mitochondrial membrane
- Substrates NADH + H⁺ and FADH₂ deliver hydrogen atoms
Electron Transport Chain and Oxidative Phosphorylation

- Hydrogen atoms are split into $H^+$ and electrons
- Electrons are shuttled along the inner mitochondrial membrane, losing energy at each step
- Released energy is used to pump $H^+$ into the intermembrane space
Electron Transport Chain and Oxidative Phosphorylation

- Respiratory enzyme complexes I, III, and IV pump $H^+$ into the intermembrane space
- $H^+$ diffuses back to the matrix via ATP synthase
- ATP synthase uses released energy to make ATP

Animation: Electron Transport
Electron transport chain and oxidative phosphorylation

**Electron Transport Chain**
Electrons are transferred from complex to complex and some of their energy is used to pump protons (H+) into the intermembrane space, creating a proton gradient.

**Chemiosmosis**
ATP synthesis is powered by the flow of H+ back across the inner mitochondrial membrane through ATP synthase.

Figure 24.8
Electron Transport Chain and Oxidative Phosphorylation

- Electrons are delivered to O, forming O⁻
- O⁻ attracts H⁺ to form H₂O
Figure 24.9

Glycolysis

Krebs cycle

Electron transport chain and oxidative phosphorylation

Free energy relative to O₂ (kcal/mol)

NADH+H⁺

FADH₂

Enzyme Complex II

Enzyme Complex I

Enzyme Complex III

Enzyme Complex IV

FMN

Fe•S

Q

Cyt b

Fe•S

Cyt c₁

Cyt c

Cyt a

Cyt a₃

½ O₂
Electronic Energy Gradient

- Transfer of energy from NADH + H⁺ and FADH₂ to oxygen releases large amounts of energy.
- This energy is released in a stepwise manner through the electron transport chain.
ATP Synthase

- Two major parts connected by a rod
  1. Rotor in the inner mitochondrial membrane
  2. Knob in the matrix
- Works like an ion pump in reverse
A rotor in the membrane spins clockwise when $H^+$ flows through it down the $H^+$ gradient.

A stator anchored in the membrane holds the knob stationary.

As the rotor spins, a rod connecting the cylindrical rotor and knob also spins.

The protruding, stationary knob contains three catalytic sites that join inorganic phosphate to ADP to make ATP when the rod is spinning.
Figure 24.12

Mitochondrion

Cytosol

Glucose → Glycolysis → Pyruvic acid → Net +2 ATP
by substrate-level phosphorylation

Electron shuttle across mitochondrial membrane

2 NADH + H⁺ → 2 NAD⁺ + H⁺

Acetyl CoA

Krebs cycle (4 ATP–2 ATP used for activation energy)

2 NADH + H⁺ → 6 NAD⁺ + H⁺

2 FADH₂

Electron transport chain and oxidative phosphorylation

Krebs cycle

2 NADH + H⁺ + 2 NADH + H⁺ + 6 NADH + H⁺ + 2 FADH₂

Electron transport chain and oxidative phosphorylation

10 NADH + H⁺ × 2.5 ATP
2 FADH₂ × 1.5 ATP

Maximum ATP yield per glucose

About 32 ATP

About 32 ATP

Maximum ATP yield per glucose

About 32 ATP

Maximum ATP yield per glucose

Figure 24.12
Glycogenesis and Glycogenolysis

- **Glycogenesis**
  - Glycogen formation when glucose supplies exceed need for ATP synthesis
  - Mostly in liver and skeletal muscle

- **Glycogenolysis**
  - Glycogen breakdown in response to low blood glucose
Figure 24.13

Cell exterior

Blood glucose

Cell interior

Glucose-6-phosphate
Hexokinase (all tissue cells)
ADP

Glycogenolysis
Mutase

Glycogen

Glycogenesis
Mutase

Glucose-6-phosphate

Glucose-1-phosphate

Pyrophosphorylase

Uridine diphosphate glucose

Glycogen phosphorylase

Glycogen synthase

2

Glycogen
Gluconeogenesis

- Glucose formation from noncarbohydrate (glycerol and amino acid) molecules
- Mainly in the liver
- Protects against damaging effects of hypoglycemia
Lipid Metabolism

- Fat catabolism yields 9 kcal per gram (vs 4 kcal per gram of carbohydrate or protein)
- Most products of fat digestion are transported as chylomicrons and are hydrolyzed by endothelial enzymes into fatty acids and glycerol
Lipid Metabolism

- Only triglycerides are routinely oxidized for energy
- The two building blocks are oxidized separately
  - Glycerol pathway
  - Fatty acid pathway
Lipid Metabolism

- Glycerol is converted to glyceraldehyde phosphate
  - Enters the Krebs cycle
  - Equivalent to $\frac{1}{2}$ glucose
Lipid Metabolism

- Fatty acids undergo beta oxidation, which produces
  - Two-carbon acetic acid fragments, which enter the Krebs cycle
  - Reduced coenzymes, which enter the electron transport chain
Figure 24.14

Krebs cycle

Glycerol

Fatty acids

Coenzyme A

Lipase

Glycolysis

Glyceraldehyde phosphate (a glycolysis intermediate)

Pyruvic acid

Acetyl CoA

Krebs cycle

Lipids

Oxidation in the mitochondria

Cleavage enzyme snips off 2C fragments

H₂O

Coenzyme A

NAD⁺

NADH + H⁺

FAD

FADH₂

ATP
Lipogenesis

- Triglyceride synthesis occurs when cellular ATP and glucose levels are high.
- Glucose is easily converted into fat because acetyl CoA is:
  - An intermediate in glucose catabolism
  - A starting point for fatty acid synthesis
Lipolysis

- The reverse of lipogenesis
- Oxaloacetic acid is necessary for complete oxidation of fat
  - Without it, acetyl CoA is converted by ketogenesis in the liver into ketone bodies (ketones)
Figure 24.15

Electron transport

Cholesterol

Stored fats in adipose tissue

Dietary fats

Glycerol

Glycolysis

Glucose

Glyceraldehyde phosphate

Pyruvic acid

Acetyl CoA

CO₂ + H₂O

Certain amino acids

Ketogenesis (in liver)

Acetyl CoA

Ketogenesis (in liver)

Krebs cycle

Electron transport

ATP

Catabolic reactions

Anabolic reactions

Triglycerides (neutral fats)

Lipolysis

Fatty acids

β-Oxidation

Ketone bodies

Lipolysis

Glycerol

Lipogenesis

Steroids

Bile salts

Cholesterol

Krebs cycle
Synthesis of Structural Materials

- Phospholipids for cell membranes and myelin
- Cholesterol for cell membranes and steroid hormone synthesis
- In the liver
  - Synthesis of transport lipoproteins for cholesterol and fats
  - Synthesis of cholesterol from acetyl CoA
  - Use of cholesterol to form bile salts
Protein Metabolism

- When dietary protein is in excess, amino acids are
  - Oxidized for energy
  - Converted into fat for storage
Oxidation of Amino Acids

- First deaminated; then converted into
  - Pyruvic acid
  - A keto acid intermediate of the Krebs cycle
- Events include transamination, oxidative deamination, and keto acid modification
Figure 24.16

During transamination, an amine group is switched from an amino acid to a keto acid.

During keto acid modification, the keto acids formed during transamination are altered so they can easily enter the Krebs cycle pathways.

In oxidative deamination, the amine group of glutamic acid is removed as ammonia and combined with CO$_2$ to form urea.

During keto acid modification, the keto acids formed during transamination are altered so they can easily enter the Krebs cycle pathways.

In oxidative deamination, the amine group of glutamic acid is removed as ammonia and combined with CO$_2$ to form urea.

Excreted in urine
Protein Synthesis

- Is hormonally controlled
- Requires a complete set of amino acids
  - Essential amino acids must be provided in the diet
Catabolic-Anabolic Steady State

- A dynamic state in which
  - Organic molecules (except DNA) are continuously broken down and rebuilt
  - Organs have different fuel preferences
Nutrient Pools

- Three interconvertible pools
  - Amino acids
  - Carbohydrates
  - Fats
Amino Acid Pool

- Body’s total supply of free amino acids
- Source for
  - Resynthesizing body proteins
  - Forming amino acid derivatives
  - Gluconeogenesis
Food intake

Dietary proteins and amino acids

Dietary carbohydrates and lipids

Pool of free amino acids

Components of structural and functional proteins

Nitrogen-containing derivatives (e.g., hormones, neurotransmitters)

Some lost via cell sloughing, hair loss

Excreted in urine

Structural components of cells (membranes, etc.)

Some lost via surface secretion, cell sloughing

Urea

Specialized derivatives (e.g., steroids, acetylcholine); bile salts

Catabolized for energy

Storage forms

CO₂

Excreted via lungs

Pool of carbohydrates and fats (carbohydrates fats)

Dietary carbohydrates and lipids

Components of structural and functional proteins

Nitrogen-containing derivatives (e.g., hormones, neurotransmitters)

Some lost via cell sloughing, hair loss

Excreted in urine

Structural components of cells (membranes, etc.)

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Urea

Specialized derivatives (e.g., steroids, acetylcholine); bile salts

Catabolized for energy

Storage forms

CO₂

Excreted via lungs

Figure 24.17
Carbohydrate and Fat Pools

- Easily interconverted through key intermediates
- Differ from the amino acid pool in that:
  - Fats and carbohydrates are oxidized directly to produce energy
  - Excess carbohydrate and fat can be stored
Proteins

- Proteins
  - Amino acids
    - Keto acids
      - NH₃
        - Urea
          - Excreted in urine

Carbohydrates

- Glycogen
  - Glucose
    - Glucose-6-phosphate
      - Glyceraldehyde phosphate
        - Pyruvic acid
          - Acetyl CoA
            - Krebs cycle
              - Urea

Fats

- Triglycerides (neutral fats)
  - Glycerol and fatty acids
    - Lactic acid
      - Ketone bodies
Absorptive and Postabsorptive States

- **Absorptive (fed) state**
  - During and shortly after eating
  - Absorption of nutrients is occurring

- **Postabsorptive (fasting) state**
  - When the GI tract is empty
  - Energy sources are supplied by breakdown of reserves
Absorptive State

- Anabolism exceeds catabolism
- Carbohydrates
  - Glucose is the major energy fuel
  - Glucose is converted to glycogen or fat
Absorptive State

- Fats
  - Lipoprotein lipase hydrolyzes lipids of chylomicrons in muscle and fat tissues
  - Most glycerol and fatty acids are converted to triglycerides for storage
  - Triglycerides are used by adipose tissue, liver, and skeletal and cardiac muscle as a primary energy source
Absorptive State

- Proteins
  - Excess amino acids are deaminated and used for ATP synthesis or stored as fat in the liver
  - Most amino acids are used in protein synthesis
Figure 24.19a

(a) Major events of the absorptive state

**Major metabolic thrust:** anabolism and energy storage
- Amino acids
  - Proteins
- Glucose
- Glycerol and fatty acids
  - Triglycerides

**Major energy fuel:** glucose (dietary)
- Glucose
  - $\text{CO}_2 + \text{H}_2\text{O} + \text{ATP}$

**Liver metabolism:** amino acids deaminated and used for energy or stored as fat
- Amino acids
  - Keto acids
  - Triglycerides
  - Glycogen
  - Fats
  - $\text{CO}_2 + \text{H}_2\text{O} + \text{ATP}$
(b) Principal pathways of the absorptive state
Absorptive State: Hormonal Control

- Insulin secretion is stimulated by
  - Elevated blood levels of glucose and amino acids
  - GIP and parasympathetic stimulation
Insulin Effects on Metabolism

- Insulin, a hypoglycemic hormone, enhances
  - Facilitated diffusion of glucose into muscle and adipose cells
  - Glucose oxidation
  - Glycogen and triglyceride formation
  - Active transport of amino acids into tissue cells
  - Protein synthesis
Figure 24.20

Stimulates targets tissue cells
Beta cells of pancreatic islets

Blood glucose

Blood insulin

Targets tissue cells

Active transport of amino acids into tissue cells

Facilitated diffusion of glucose into tissue cells

Protein synthesis

Enhances glucose conversion to:

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

Fatty acids + glycerol + glycogen

Initial stimulus
Physiological response
Result
**Postabsorptive State**

- Catabolism of fat, glycogen, and proteins exceeds anabolism
- Goal is to maintain blood glucose between meals
  - Makes glucose available to the blood
  - Promotes use of fats for energy (glucose sparing)
Sources of Blood Glucose

1. Glycogenolysis in the liver
2. Glycogenolysis in skeletal muscle
3. Lipolysis in adipose tissues and the liver
   - Glycerol is used for gluconeogenesis in the liver
Sources of Blood Glucose

4. Catabolism of cellular protein during prolonged fasting
   - Amino acids are deaminated and used for gluconeogenesis in the liver and (later) in the kidneys
(a) Major events of the postabsorptive state

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<th>Major metabolic thrust: catabolism and replacement of fuels in blood</th>
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<td>Proteins</td>
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<td>Amino acids</td>
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<th>Major energy fuels: glucose provided by glycogenolysis and gluconeogenesis, fatty acids, and ketones</th>
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<tr>
<td>Glucose</td>
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<td>CO₂ + H₂O + ATP</td>
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<th>Liver metabolism: amino acids converted to glucose</th>
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<tr>
<td>Amino acids</td>
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<tr>
<td>Keto acids</td>
</tr>
<tr>
<td>Glucose</td>
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</table>
(b) Principal pathways of the postabsorptive state

Figure 24.21b
Postabsorptive State: Hormonal Controls

- Glucagon release is stimulated by
  - Declining blood glucose
  - Rising amino acid levels
Effects of Glucagon

- Glucagon, a hyperglycemic hormone, promotes:
  - Glycogenolysis and gluconeogenesis in the liver
  - Lipolysis in adipose tissue
  - Modulation of glucose effects after a high-protein, low-carbohydrate meal
Plasma glucose (and rising amino acid levels) stimulates Plasma glucagon, which stimulates glycogenolysis and gluconeogenesis.

Negative feedback: rising glucose levels shut off initial stimulus. Plasma glucagon stimulates fat breakdown.

Liver and adipose tissue respond with increased plasma fatty acids and increased plasma glucose (and insulin).

Fat used by tissue cells = glucose sparing.

Figure 24.22
Postabsorptive State: Neural Controls

- In response to low plasma glucose, or during fight-or-flight or exercise, the sympathetic nervous system and epinephrine from the adrenal medulla promote
  - Fat mobilization
  - Glycogenolysis
Metabolic Role of the Liver

- Hepatocytes
  - Process nearly every class of nutrient
  - Play a major role in regulating plasma cholesterol levels
  - Store vitamins and minerals
  - Metabolize alcohol, drugs, hormones, and bilirubin
Cholesterol

- Structural basis of bile salts, steroid hormones, and vitamin D
- Major component of plasma membranes
- Makes up part of the hedgehog signaling molecule that directs embryonic development
- Transported in lipoprotein complexes containing triglycerides, phospholipids, cholesterol, and protein
Lipoproteins

- Types of lipoproteins
  - HDLs (high-density lipoproteins)
    - The highest protein content
  - LDLs (low-density lipoproteins)
    - Cholesterol-rich
  - VLDLs (very low density lipoproteins)
    - Mostly triglycerides
  - Chylomicrons
Figure 24.23

- **Triglyceride**
  - From intestine: 80–95%
  - Made by liver: 55–65%
  - Returned to liver: 45–50%

- **Cholesterol**
  - From intestine: 1–2%
  - Made by liver: 10%
  - Returned to liver: 5%

- **Protein**
  - From intestine: 2–7%
  - Made by liver: 20%
  - Returned to liver: 30%

- **Phospholipid**
  - From intestine: 3–6%
  - Made by liver: 20%
  - Returned to liver: 20%

- **VLDL**
  - From intestine: 15–20%
  - Made by liver: 25%
  - Returned to liver: 45–50%

- **LDL**
  - Made by liver: 10%
  - Returned to liver: 30%

- **HDL**
  - Made by liver: 5%
  - Returned to liver: 45–50%

Legend:
- Yellow: Triglyceride
- Gray: Phospholipid
- Orange: Cholesterol
- Purple: Protein

From intestine, Made by liver, Returned to liver
Lipoproteins

- VLDLs
  - Transport triglycerides to peripheral tissues (mostly adipose)

- LDLs
  - Transport cholesterol to peripheral tissues for membranes, storage, or hormone synthesis

- HDLs
  - Transport excess cholesterol from peripheral tissues to the liver to be broken down and secreted into bile
  - Also provide cholesterol to steroid-producing organs
Lipoproteins

- High levels of HDL are thought to protect against heart attack
- High levels of LDL, especially lipoprotein (a), increase the risk of heart attack
Plasma Cholesterol Levels

- The liver produces cholesterol
  - At a basal level regardless of dietary cholesterol intake
  - In response to saturated fatty acids
Plasma Cholesterol Levels

- Saturated fatty acids
  - Stimulate liver synthesis of cholesterol
  - Inhibit cholesterol excretion from the body
- Unsaturated fatty acids
  - Enhance excretion of cholesterol
Plasma Cholesterol Levels

- Trans fats
  - Increase LDLs and reduce HDLs
Plasma Cholesterol Levels

- Unsaturated omega-3 fatty acids (found in cold-water fish)
  - Lower the proportions of saturated fats and cholesterol
  - Have antiarrhythmic effects on the heart
  - Help prevent spontaneous clotting
  - Lower blood pressure
Non-Dietary Factors Affecting Cholesterol

- Stress, cigarette smoking, and coffee lower HDL levels
- Aerobic exercise and estrogen increase HDL levels and decrease LDL levels
- Body shape
  - “Apple”: Fat carried on the upper body is correlated with high cholesterol and LDL levels
  - “Pear”: Fat carried on the hips and thighs is correlated with lower cholesterol and LDL levels
Energy Balance

- Bond energy released from food must equal the total energy output
- Energy intake = the energy liberated during food oxidation
- Energy output
  - Immediately lost as heat (~60%)
  - Used to do work (driven by ATP)
  - Stored as fat or glycogen
Energy Balance

- Heat energy
  - Cannot be used to do work
  - Warms the tissues and blood
  - Helps maintain the homeostatic body temperature
  - Allows metabolic reactions to occur efficiently
Obesity

- Body mass index (BMI) = \( \frac{\text{wt (lb)} \times 705}{\text{ht (inches)}^2} \)
- Considered overweight if BMI is 25 to 30
- Considered obese if BMI is greater than 30
  - Higher incidence of atherosclerosis, diabetes mellitus, hypertension, heart disease, and osteoarthritis
Regulation of Food Intake

- Two distinct sets of hypothalamic neurons
  1. LHA neurons promote hunger when stimulated by neuropeptides (e.g., NPY)
  2. VMN neurons cause satiety through release of CRH when stimulated by appetite-suppressing peptides (e.g., POMC and CART peptides)
Regulation of Food Intake

- Factors that affect brain thermoreceptors and chemoreceptors
  - Neural signals from the digestive tract
  - Bloodborne signals related to body energy stores
  - Hormones
  - To a lesser extent, body temperature and psychological factors
Short-Term Regulation of Food Intake

- Neural signals
  - High protein content of meal increases and prolongs afferent vagal signals
  - Distension sends signals along the vagus nerve that suppress the hunger center
Short-Term Regulation of Food Intake

- **Nutrient signals**
  - Increased nutrient levels in the blood depress eating
    - Blood glucose
    - Amino acids
    - Fatty acids
Short-Term Regulation of Food Intake

- **Hormones**
  - Gut hormones (e.g., insulin and CCK) depress hunger
  - Glucagon and epinephrine stimulate hunger
  - Ghrelin (Ghr) from the stomach stimulates appetite just before a meal
Long-Term Regulation of Food Intake

- Leptin
  - Hormone secreted by fat cells in response to increased body fat mass
  - Indicator of total energy stores in fat tissue
  - Protects against weight loss in times of nutritional deprivation
Long-Term Regulation of Food Intake

- Leptin
  - Acts on the ARC neurons in the hypothalamus
  - Suppresses the secretion of NPY, a potent appetite stimulant
  - Stimulates the expression of appetite suppressants (e.g., CART peptides)
Figure 24.24

Long-term controls

- Hunger (appetite enhancement)
- LHA (orexin-releasing neurons)
- Satiety (appetite suppression)

Short-term controls

- Stretch (distension of GI tract)
- Vagal afferents
- Nutrient signals
- Insulin (from pancreas)
- Leptin (from lipid storage)

- Glucose
- Amino acids
- Fatty acids
- Ghrelin
- Glucagon
- Epinephrine

- Inhibits
- Stimulates

Brain stem

- Solitary nucleus
- Gut hormones
- Gut hormones and others
- Insulin
- Leptin

Gut hormones and others

- ARC nucleus
- POMC/CART group
- NPY/AgRP group
- VMN (CRH-releasing neurons)
- LHA (orexin-releasing neurons)
- PYY
- CCK

Insulin

- Hypothalamus
- Brain stem
- Stretch (distension of GI tract)
- Glucose
- Amino acids
- Fatty acids
- Ghrelin
- Glucagon
- Epinephrine
Long-Term Regulation of Food Intake

- Additional factors
  - Temperature
  - Stress
  - Psychological factors
  - Adenovirus infections
  - Sleep deprivation
Metabolic Rate

- Total heat produced by chemical reactions and mechanical work of the body
- Measured directly with a calorimeter or indirectly with a respirometer
Metabolic Rate

- **Basal metabolic rate (BMR)**
  - Reflects the energy the body needs to perform its most essential activities
Factors that Influence BMR

- As the ratio of body surface area to volume increases, BMR increases
- Decreases with age
- Increases with temperature or stress
- Males have a disproportionately higher BMR
- Thyroxine increases oxygen consumption, cellular respiration, and BMR
Metabolic Rate

- **Total metabolic rate (TMR)**
  - Rate of kilocalorie consumption to fuel all ongoing activities
  - Increases with skeletal muscle activity and food ingestion
Regulation of Body Temperature

- Body temperature reflects the balance between heat production and heat loss.
- At rest, the liver, heart, brain, kidneys, and endocrine organs generate most heat.
- During exercise, heat production from skeletal muscles increases dramatically.
Regulation of Body Temperature

- Normal body temperature $= 37^\circ\text{C} \pm 5^\circ\text{C} (98.6^\circ\text{F})$
- Optimal enzyme activity occurs at this temperature
- Increased temperature denatures proteins and depresses neurons
Heat production
- Basal metabolism
- Muscular activity (shivering)
- Thyroxine and epinephrine (stimulating effects on metabolic rate)
- Temperature effect on cells

Heat loss
- Radiation
- Conduction/convection
- Evaporation
Core and Shell Temperature

- Organs in the core have the highest temperature.
- Blood is the major agent of heat exchange between the core and the shell.
- Core temperature is regulated.
- Core temperature remains relatively constant, while shell temperature fluctuates substantially (20°C–40°C).
Mechanisms of Heat Exchange

- **Four mechanisms**
  1. Radiation is the loss of heat in the form of infrared rays
  2. Conduction is the transfer of heat by direct contact
  3. Convection is the transfer of heat to the surrounding air
  4. Evaporation is the heat loss due to the evaporation of water from body surfaces
Mechanisms of Heat Exchange

- Insensible heat loss accompanies insensible water loss from lungs, oral mucosa, and skin.
- Evaporative heat loss becomes sensible (active) when body temperature rises and sweating increases water vaporization.
Role of the Hypothalamus

- Preoptic region of the hypothalamus contains the two thermoregulatory centers
  - Heat-loss center
  - Heat-promoting center
Role of the Hypothalamus

- The hypothalamus receives afferent input from
  - Peripheral thermoreceptors in the skin
  - Central thermoreceptors (some in the hypothalamus)
- Initiates appropriate heat-loss and heat-promoting activities
Heat-Promoting Mechanisms

- Constriction of cutaneous blood vessels
- Shivering
- Increased metabolic rate via epinephrine and norepinephrine
- Enhanced thyroxine release
Heat-Promoting Mechanisms

- Voluntary measures include
  - Putting on more clothing
  - Drinking hot fluids
  - Changing posture or increasing physical activity
Heat-Loss Mechanisms

- Dilation of cutaneous blood vessels
- Enhanced sweating
- Voluntary measures include
  - Reducing activity and seeking a cooler environment
  - Wearing light-colored and loose-fitting clothing
Figure 24.27, step 1

Activates heat-loss center in hypothalamus

Sweat glands activated: secrete perspiration, which is vaporized by body heat, helping to cool the body

Skin blood vessels dilate: capillaries become flushed with warm blood; heat radiates from skin surface

Body temperature decreases: blood temperature declines and hypothalamus heat-loss center “shuts off”

Stimulus
Increased body temperature; blood warmer than hypothalamic set point

Homeostasis: Normal body temperature (35.8°C–38.2°C)
**Stimulus**
Decreased body temperature; blood cooler than hypothalamic set point

**Homeostasis:** Normal body temperature (35.8°C–38.2°C)

- **Body temperature increases:** blood temperature rises and hypothalamus heat-promoting center “shuts off”
- **Skin blood vessels constrict:** blood is diverted from skin capillaries and withdrawn to deeper tissues; minimizes overall heat loss from skin surface
- **Skeletal muscles activated when more heat must be generated:** shivering begins
- **Activates heat-promoting center in hypothalamus**

Figure 24.27, step 2
Homeostatic Imbalance

- Hyperthermia
  - Elevated body temperature depresses the hypothalamus
  - Positive-feedback mechanism (heat stroke) begins at core temperature of 41°C
  - Can be fatal if not corrected
Homeostatic Imbalance

- Heat exhaustion
  - Heat-associated collapse after vigorous exercise
  - Due to dehydration and low blood pressure
  - Heat-loss mechanisms are still functional
  - May progress to heat stroke
Homeostatic Imbalance

- Hypothermia
  - Low body temperature where vital signs decrease
  - Shivering stops at core temperature of 30 - 32°C
  - Can progress to coma a death by cardiac arrest at ~ 21°C
Fever

- Controlled hyperthermia
- Due to infection (also cancer, allergies, or CNS injuries)
- Macrophages release interleukins ("pyrogens") that cause the release of prostaglandins from the hypothalamus
Fever

- Prostaglandins reset the hypothalamic thermostat higher.
- Natural body defenses or antibiotics reverse the disease process; cryogens (e.g., vasopressin) reset the thermostat to a lower (normal) level.
Developmental Aspects

- Lack of proteins in utero and in the first three years → mental deficits and learning disorders
- Insulin-dependent diabetes mellitus and genetic disorders → metabolic problems in children
- Non-insulin-dependent diabetes mellitus may occur in middle and old age, especially in obese people
- Metabolic rate declines throughout the life span
Developmental Aspects

- Many medications for age-related problems influence nutrition:
  - Diuretics for heart failure and hypertension increase the risk of hypokalemia
  - Some antibiotics interfere with digestion and absorption
  - Mineral oil (laxative) decreases absorption of fat-soluble vitamins
  - Excessive alcohol consumption may lead to malabsorption, vitamin and mineral deficiencies, deranged metabolism, damage to liver and pancreas
Nonenzymatic binding of glucose to proteins increases with age, leading to lens clouding and general tissue stiffening.