Chapter 7: Metabolism: From Food to Life
Metabolism

- **Metabolism** is the sum of all chemical and physical processes by which the body breaks down and builds up molecules
  - **Calorimeter** measures a food's caloric content
  - Chemical reactions in the body require or release energy
Anabolism

- **Anabolism** is the process of making larger, chemically complex molecules from smaller ones
  - Critical for growth, repair, maintenance, and synthesis of chemical products essential for human functioning
  - Requires energy
Anabolic reactions: Glucose $\rightarrow$ Glycogen $\rightarrow$ Triglyceride $\rightarrow$ Protein

Catabolic reactions: Glycogen $\rightarrow$ Glucose $\rightarrow$ Glycerol + Fatty acids $\rightarrow$ Amino acids

Intracellular catabolism: Glucose $\rightarrow$ Glycerol + Fatty acids $\rightarrow$ Amino acids
Catabolism

- **Catabolism**: breakdown of larger, complex molecules to smaller, more basic ones
  - Begins with digestion—chemical reactions break down proteins, lipids, carbohydrates
  - Old cells or tissues are broken down for repair or replacement
  - Releases energy
Adenosine Triphosphate (ATP)

- ATP is an organic compound used by cells as a source of metabolic energy
  - Potential energy is stored in the high-energy phosphate bonds
  - When bonds are broken, energy is released
  - This energy is used to keep cells functioning
  - A small amount of ATP is stored in every cell for immediate use
Adenosine monophosphate (AMP)

Adenosine diphosphate (ADP)

Adenosine triphosphate (ATP)

(a) Structure of ATP

(b) Conversion of ATP to ADP and AMP

(c) Regeneration of ATP
Metabolic Pathways

- *Metabolic pathways* are clusters of chemical reactions that occur sequentially to achieve a particular goal
  - Occur in a specific part of a cell
  - May be limited to specific organs or tissues
- *Mitochondria* are the primary site of chemical energy (ATP) production
- "Networking" of metabolic pathways
Dehydration Synthesis and Hydrolysis

- **Dehydration synthesis** (also called *condensation*) is an anabolic process
  - Simple units combine to form a larger, more complex molecule
  - Water is released as a by-product
- **Hydrolysis** is usually a catabolic process
  - A large molecule is broken apart with the addition of water
(a) Dehydration synthesis of glucose and fructose

(b) Hydrolysis of sucrose
Phosphorylation

- **Phosphorylation**: addition of a phosphate group to a compound
- When the high-energy phosphate bonds in ATP are broken
  - Energy is released
  - Phosphate is transferred to other molecules
- When glucose is phosphorylated, it can be oxidized for energy or stored as glycogen
Oxidation–Reduction Reactions

- Molecules exchange electrons (hydrogen)
- Exchange reactions occur together
- Molecule donating an electron is *oxidized*
  - Its electron is removed by oxygen
- Molecule acquiring an electron is *reduced*
  - In gaining an electron, it becomes more negatively charged

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Metabolic Enzymes

• Enzymes mediate chemical reactions

• **Coenzymes** are non-protein substances that enhance or are necessary for enzyme activity
  • FAD, FADH$_2$, and vitamins function as coenzymes

• **Cofactors** are typically minerals required for enzyme activity
  • Iron, magnesium, and zinc function as cofactors
Energy from Carbohydrates

- When glucose is transported to the liver, it is:
  - Phosphorylated and metabolized for energy or stored as glycogen
  - Released into circulation for other cells to use as fuel or stored as glycogen (muscle tissue)
- If glucose exceeds energy needs, it can be converted to fatty acids and stored as triglycerides in adipose tissue
- Fructose and galactose are converted to glucose in the liver and follow the same process
Glycolysis

• Occurs in the cytosol of cells
• Anaerobic reaction
• Final step is pyruvate production
• Net of 2 ATP to be used as energy for the cell
**Gluconeogenesis**

1. **Glucose** → **ATP** → **ADP** → **Glucose 6-phosphate**
   - Energy investment (2 ATP used)

2. **2 Glyceraldehyde 3-phosphate** → **2 NAD^+** → **2 NADH + H^+** → **2 ADP** → **2 ATP**
   - Energy generation (4 ATP gained)

3. **2 ATP** → **2 ADP** → **2 pyruvate**

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(a) Anaerobic conversion of pyruvate to lactate

(b) Interconversion of lactate and glucose
The diagram shows the conversion of pyruvate to acetyl CoA. Two molecules of pyruvate react to produce two molecules of acetyl CoA, releasing two molecules of carbon dioxide (CO₂), two molecules of NADH and two molecules of hydrogen ions (H⁺), and two molecules of CoA.
Energy from Fat

- **Lipolysis**: dietary and adipose triglycerides are broken down by lipases to yield glycerol and three free fatty acids.
- Glycerol is converted to pyruvate, then to acetyl CoA for entry into the TCA cycle.
- **β-oxidation (fatty acid oxidation)**: metabolic reactions that oxidize free fatty acids, producing water, carbon dioxide and ATP.
Triglyceride

Lipase

Glycerol

Fatty acids (released into bloodstream)

In liver

Pyruvate

Acetyl CoA

Glucose
β-oxidation of Fatty Acids

- Attached to albumin, fatty acids are transported to working cells in need of energy (muscle or liver cells)
- Fatty acids must be activated by coenzyme A before being shuttled across the mitochondrial membrane by carnitine
- Long-chain fatty acids are broken down into two-carbon segments to form acetyl CoA
Fatty Acids Cannot Form Glucose

- There is no metabolic pathway to convert acetyl CoA into pyruvate
  - Cells cannot convert acetyl CoA to glucose
  - Impossible for fatty acids to feed into glucose production
Ketone Synthesis

- *Ketones* are by-products of fat catabolism
- *Ketosis* occurs when ketones (acidic) inappropriately lower blood pH
- *Ketoacidosis* occurs when blood pH falls, further resulting in severe dehydration
- Production of energy from ketones is metabolically inefficient
- Ketone production is a back-up source of energy for carbohydrate-deprived cells
Energy from Protein

• The body preferentially uses fat and carbohydrate as fuel sources
• Protein is saved for metabolic functions that cannot be performed by other compounds
• Protein is used for fuel primarily when total energy or carbohydrate intake is low
Energy from Protein (cont.)

- **Proteolysis**: dietary proteins are digested into amino acids or small peptides
- Amino acids are transported to the liver
  - Made into proteins
  - Released into the blood for uptake by other cells for building and repair functions
- Excess dietary protein
  - Used for energy or stored as triglycerides
Deamination is the process of removing an amine group (NH₂) from an amino acid, resulting in a keto acid.
Energy from Protein (cont.)

- During *starvation*, the body turns to its own tissues for energy
- *Deamination*: amine group is removed from amino acid; end products are carbon skeleton and ammonia
- Ammonia is used as nitrogen source for synthesis of nonessential amino acids
  - High levels are toxic
  - Liver converts ammonia to less toxic urea
ABC News Video: Could Chocolate Milk be the Perfect Post-Workout Drink?

saw in the "New York Times,"
Alcohol Oxidation

• Alcohol is oxidized primarily in the liver by enzymes:
  • Alcohol dehydrogenase (ADH)
  • Aldehyde dehydrogenase (ALDH)
  • Microsomal ethanol oxidizing system (MEOS)
Ammonia is converted to urea in the liver. Urea is transported to the kidneys via the bloodstream. Urea is excreted in the urine by the kidneys.
Alcohol Oxidation (cont.)

- *First-pass metabolism*: small amount of alcohol is oxidized in the stomach, before being absorbed into the bloodstream
- Gastric **alcohol dehydrogenase (ADH)** activity
  - Reduces alcohol absorption
  - Genetic differences in amount of activity
<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Yields Energy as ATP?</th>
<th>Oxidative End Products?</th>
<th>Feeds into Glucose Production?</th>
<th>Feeds into Nonessential Amino Acid Production?</th>
<th>Feeds into Fatty Acid Production and Storage as Triglycerides?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate (glucose)</td>
<td>Yes</td>
<td>CO₂, H₂O</td>
<td>Yes</td>
<td>Yes, if source of nitrogen is available</td>
<td>Yes, although process is inefficient</td>
</tr>
<tr>
<td>Triglycerides: fatty acids</td>
<td>Yes</td>
<td>CO₂, H₂O</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Triglycerides: glycerol</td>
<td>Yes</td>
<td>CO₂, H₂O</td>
<td>Yes, if carbohydrate is unavailable to cells</td>
<td>Yes, if source of nitrogen is available</td>
<td>Yes</td>
</tr>
<tr>
<td>Protein (amino acids)</td>
<td>Yes</td>
<td>CO₂, H₂O, N as urea</td>
<td>Yes, if carbohydrate is unavailable to cells</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Yes</td>
<td>CO₂, H₂O</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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</tbody>
</table>
Alcohol Absorption

- Most is absorbed into the blood and transported to be oxidized by the liver
- Liver typically oxidizes alcohol at a constant rate (about 1 drink per hour)
- This rate varies with the individual's genetic profile, state of health, body size, use of medication, and nutritional status
- Excess alcohol goes back into the blood
# ALCOHOL IMPAIRMENT CHART

## FEMALE

<table>
<thead>
<tr>
<th>Drinks</th>
<th>Body Weight in Pounds</th>
<th>Approximate blood alcohol concentration</th>
</tr>
</thead>
<tbody>
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<td>90  100  120  140  160  180  200  220  240</td>
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<td>9</td>
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<tr>
<td>10</td>
<td>.51 .45 .38 .32 .28 .25 .23 .21 .19† .17</td>
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</tr>
</tbody>
</table>

*Legally Intoxicated Criminal Penalties*

*Driving Skills Affected Possible Criminal Penalties*

*Impairment Begins*

*ONLY SAFE DRIVING LIMIT*

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## MALE

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<td>1</td>
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<td>.11 .09 .08 .07 .06 .06 .05 .05 .05</td>
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</tbody>
</table>

*Legally Intoxicated Criminal Penalties*

*Driving Skills Affected Possible Criminal Penalties*

*Impairment Begins*

*ONLY SAFE DRIVING LIMIT*

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Your body can get rid of one drink per hour. Each 1.5 oz of 80 proof liquor, 12 oz of beer or 5 oz of table wine = 1 drink.
Stored Energy

- Stored energy can be used during times of sleep, fasting, or exercise
- Extra energy is stored as
  - Carbohydrate in *limited* amounts as liver and muscle glycogen
  - Fat (triglycerides) in *unlimited* amounts
- The body has no mechanism for storing amino acids or nitrogen
<table>
<thead>
<tr>
<th></th>
<th>Triglycerides</th>
<th>Glycogen</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>15 kg</td>
<td>0.2 kg</td>
<td>6 kg</td>
</tr>
<tr>
<td>Kilocalories</td>
<td>135,000</td>
<td>800</td>
<td>24,000</td>
</tr>
</tbody>
</table>

*70 kg equals about 154 lb.*
Synthesizing Macronutrients

- **Gluconeogenesis**: making new glucose from noncarbohydrate precursors
  - Primarily from glucogenic amino acids
  - Small amount from glycerol (triglyceride)
  - Maintains blood glucose during sleep, fasting, trauma, and exercise
- **Protein catabolism** for glucose production can draw on vital tissue proteins (skeletal and heart muscles and organ proteins)
Proteins

- Ketogenic amino acids
- Glucogenic amino acids

Triglycerides

- Glycerol
- Fatty acids

Glucose
Synthesizing Macronutrients (cont.)

- **Lipogenesis (de novo synthesis):** production of fat from nonfat substances such as carbohydrates, ketogenic amino acids, and alcohol
  - When consuming excess calories, acetyl CoA units form fatty acid chains
  - Fatty acids combine with glycerol to form triglycerides
  - Mostly occurs in liver cells
Glucose \xrightarrow{\text{Glycolysis}} \text{Pyruvate} \xrightarrow{\text{Acetyl CoA}} \text{Fatty acid synthesis} \xrightarrow{\text{Fatty acids}} \text{Glycerol} \xrightarrow{\text{Triglycerides}}

Alcohol

Proteins \xrightarrow{\text{Ketogenic amino acids}} \text{Glucogenic amino acids}
Synthesizing Macronutrients

• Amino acid synthesis
  • The body makes the carbon skeleton of nonessential amino acids (NEAA)
  • Amine group comes from *transamination*
  • Synthesis of NEAA occurs only when the body has enough energy and nitrogen
  • Since essential amino acids cannot be synthesized, they must be consumed
(a) Amino acid A

(b) Keto acid A

Amino acid B

Keto acid B
Hormones Regulate Metabolism

- Insulin is the primary *anabolic* hormone
  - Increases in the blood after a meal
  - Activates storage enzymes
  - Signals cellular uptake of glucose, fatty acids, and amino acids
- Glucagon, epinephrine, and cortisol are *catabolic* hormones
  - Trigger the breakdown of stored triglycerides, glycogen, and body protein for energy
### TABLE 7.3 Hormonal Regulation of Metabolism

<table>
<thead>
<tr>
<th>Metabolic State</th>
<th>Hormone</th>
<th>Site of Secretion</th>
<th>Role in Carbohydrate Metabolism</th>
<th>Role in Lipid Metabolism</th>
<th>Role in Protein Metabolism</th>
<th>Overall Metabolic Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fed</td>
<td>Insulin</td>
<td>Pancreatic beta cells</td>
<td>Increases cell uptake of glucose</td>
<td>Increases synthesis and storage of triglycerides</td>
<td>Increases cell uptake of amino acids and protein synthesis</td>
<td>Anabolic</td>
</tr>
<tr>
<td>Fasted</td>
<td>Glucagon</td>
<td>Pancreatic alpha cells</td>
<td>Increases glycogen degradation</td>
<td>Increases lipolysis</td>
<td>Increases degradation of proteins</td>
<td>Catabolic</td>
</tr>
<tr>
<td>Exercise</td>
<td>Epinephrine</td>
<td>Adrenal medulla</td>
<td>Increases glycogen degradation</td>
<td>Increases lipolysis</td>
<td>No significant effect</td>
<td>Catabolic</td>
</tr>
<tr>
<td>Stress</td>
<td>Cortisol</td>
<td>Adrenal cortex</td>
<td>Decreases cell uptake of glucose</td>
<td>Increases lipolysis</td>
<td>Decreases cell uptake of amino acids Increases degradation of proteins</td>
<td>Catabolic</td>
</tr>
</tbody>
</table>
Metabolic Responses to Feeding

• *Anabolic state*: bloodstream is enriched with glucose, fatty acids, and amino acids
  - Glucose is stored as glycogen
  - When glycogen stores are saturated, remaining glucose is stored as triglycerides
  - Fatty acids are stored as triglycerides mostly in adipose tissues
  - Amino acids are deaminated and carbon skeletons are converted to fatty acids for storage as triglycerides
The fed state is generally an anabolic state: After digestion, absorption, and transport in the body, the end products of digestion can be synthesized into important biological compounds, used for energy, or converted to storage forms of energy.

- **Proteins** → Amino acids
  - Amino acids are used to synthesize body proteins for tissues such as muscle.
  - Excess amino acids can be used for energy or converted to fatty acids, which can be stored as triglycerides.

- **Carbohydrates** → Glucose
  - Glucose is the primary fuel source for all tissues.
  - Excess glucose is stored as glycogen in the liver and muscle. Additional excess glucose can be converted to fatty acids and eventually stored in the adipose tissue as triglycerides. Glucose can also be converted to glycerol.

- **Triglycerides** → Fatty acids and glycerol
  - Fatty acids and glycerol are fuel sources for some tissues.
  - Excess fatty acids are stored.

- **Fatty acids and glycerol** → Triglycerides
  - Triglycerides
  - Adipose tissue
Metabolic Responses to Short-Term Fasting

• Liver glycogen is broken down, releasing glucose into the blood
• Most cells can switch to using fatty acids as fuel to conserve glucose for brain and other cells that rely on glucose as fuel
• Ketones form as acetyl CoA units are blocked from entering TCA cycle
• Glucose synthesis from glucogenic amino acids and glycerol
The fasting state is generally a catabolic state: After a period of fasting, when the body glycogen stores are reduced, the body increases its use of stored fatty acids.

**SHORT-TERM FASTING**
- Muscle glycogen → Glucose → Fuel source for muscle cells
- Liver glycogen → Glucose → Fuel source for red blood cells, brain cells, and other tissues
- Adipose tissue triglycerides → Fatty acids and glycerol → Fuel source for all cells and tissues except red blood cells and the brain

**LONG-TERM FASTING**
- Muscle protein → Amino acids → Glycerol → Fuel source for all cells and tissues, especially the brain, CNS, and red blood cells
- Liver → Amino acids → Glucose → Fuel source for all cells and tissues except red blood cells and the brain
- Adipose tissue triglycerides → Glycerol → Fatty acids → Ketone bodies → Alternative fuel source for all cells and tissues except red blood cells
Metabolic Responses to Starvation

• The body shifts to survival mode
• Blood glucose is maintained to support brain and red blood cells
• Decline in activity, body temperature, and resting metabolic rate
• Fatty acids become the primary fuel
• Brain cells start to use ketone bodies
• Muscle (skeletal, cardiac) and organ proteins supplies glucose
LONG-TERM FASTING

Muscle protein → Liver → Amino acids → Glycerol → Adipose tissue triglycerides → Liver fatty acids

Amino acids → Glucose

Glycerol → Fatty acids

Ketone bodies

Fuel source for all cells and tissues, especially the brain, CNS, and red blood cells
Fuel source for all cells and tissues except red blood cells and the brain
Alternative fuel source for all cells and tissues except red blood cells