Exercise and Physiology – Fuel

Basics

- **Energy**: the capacity for work
- **Exergonic Reactions**: release energy (high energy state $\rightarrow$ low energy state)
- **Endergonic Reactions**: store or absorb energy
  - Endergonic pathway surpasses exergonic pathway when you eat
- **Anabolic**: use extracted chemical energy from ATP to synthesize new compounds
  - Endergonic + Anabolic: small molecules $\rightarrow$ large molecules; biosynthesis
- **Catabolic**: release energy for biological work
  - Exergonic + Catabolic: large molecules $\rightarrow$ small molecules; biodegradation
- Limits of exercise intensity depend on rate that cells extract, conserve, transfer chemical energy in the food nutrients to the contractile filaments of skeletal muscle

Factors Affecting Bioenergetics

- **Enzymes**
  - Highly specific protein catalysts
  - Accelerate the forward and reverse reactions; neither consumed nor changed in the rxn
  - pH and temperature affect enzyme activity
    - Low pH and high temperature denature enzymes
      - **Denature**: causes protein to lose its shape and the function of the enzyme depends on its shape
  - **Reaction Rates**: operation rate of enzymes
  - **Enzyme mode of Action**: how an enzyme reacts with its specific substrate

- **Coenzymes**
- Rates of Endergonic and Exergonic reactions depend on
  - Substrate availability
  - Enzyme availability
  - Metabolic state of cell (ill, exercising, at rest – rxn rate slower at rest than exercising)
  - Cellular conditions (temperature, pH)

ATP and Stored Sources of Energy

- **Adenosine Triphosphate (ATP)**: adenine + ribose + 3 phosphates; carrier molecule of free energy

\[
\text{ATP Hydrolysis} \quad \text{ATP} \quad \text{ADP} + \text{P} \\
\text{Energy}
\]

\[
\text{ADP Phosphorylation} \quad \text{ADP} + \text{P} \quad \text{ATP} \\
\text{Energy}
\]
Cells contain a small amount of stored ATP as it is a heavy molecule
  – Intramuscular ATP used for short bursts of activity; anaerobic hydrolysis to do so

**Phosphocreatine (PCr):** high-energy reservoir within cell
  – Intracellular concentration of PCr is 4-6 times more than that of ATP
  – PCr + ADP → Cr + ATP
  – Hydrolysis reaction of PCr reaches a maximum energy yield in 10 seconds
  – Creatine Kinase (enzyme that catalyzes PCr breakdown) cannot supply long-term energy demands
  – When activity is only sustained for a few seconds, ATP is resynthesized from PCr

**Adenylate Kinase Reaction**
  – Less common in muscle, unless other sources of energy are lacking
  – 2ADP → ATP + AMP
  – This reaction catalyzed by the enzyme Adenylate Kinase

**Resynthesis of ATP through Phosphorylation/Oxidation of Macronutrients**

- The catabolism of glycogen and fat as energy sources are needed to meet further energy demands, as PCr and Adenylate Kinase cannot supply long-term energy demands
- The breakdown of macronutrients to resynthesize ATP occurs at a rate equivalent to ATP’s rate of use and the intensity of the physical activity performed
  - Resynthesis of ATP can be aerobic or anaerobic → glucose metabolism
  - Resynthesis of ATP can be exclusively aerobic → lipid and protein metabolism
- *Most of energy for ATP generation derives from the aerobic phosphorylation/oxidation pathway*
  - Carbohydrates, lipids, proteins are oxidized; oxygen is reduced

**Carbohydrate Metabolism**

- Carbohydrate is the only macronutrient to generate ATP anaerobically; next fastest energy source
- Carbohydrate = intramuscular glycogen
- **Glycolysis:** ATP resynthesis from anaerobic catabolism of glycogen
  - 1) 2 ATP + Glucose → 2 Glyceraldehyde-3-phosphate
  - 2) 2 G3P → 2 Pyruvate + 4 ATP (net gain of 2 ATP through substrate-level phosphorylation; also get 2NADH)
- **Phosphofructokinase (PFK):** rate-limiting enzyme in glycolysis

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<tr>
<th>PFK Rate Increases</th>
<th>PFK Rate Decreases</th>
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<td>Increase in ADP</td>
<td>Increase in Pyruvate</td>
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<tr>
<td>Increase in Phosphate</td>
<td>Increase in ATP</td>
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<tr>
<td>Decrease in O2</td>
<td>Increase in H+</td>
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<tr>
<td>ATP levels low</td>
<td>Increase in Citrate</td>
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Fast-twitch muscle fibers contain large quantities of PFK

- **Anaerobic Conditions**
  - Pyruvate reduced into lactate by enzyme lactate dehydrogenase
  - Anaerobic oxidation of NADH → NAD+ for continuation of glycolysis and limited ATP resynthesis
  - Results in lactate accumulation in muscle → muscle fatigue
    - Decreased pH (acidic environment)
    - Slows muscle contraction
    - Slows enzymatic reactions
  - If O₂ becomes available or exercise pace slows
    - NAD+ takes back 2H+ from lactate → pyruvate
    - Pyruvate (oxidized) → energy
    - Pyruvate (via Cori Cycle) → Glucose
      - Cori Cycle sustains Glucose levels
    - Fast twitch muscle fibers shuttle lactate for its conversion to pyruvate
    - Slow twitch fibers take up lactate and convert it pyruvate for re-entry into Citric acid cycle

- **Aerobic Conditions**
  - 2 Pyruvate + 2 NADH⁺ + 2 CoA → 2 AcetylCoA + 2 CO₂ + 2 NADH⁺ + 2H⁺
  - Citric Acid cycle in mitochondria
    - 2 AcetylCoA (oxidized) → 4CO₂ + 6H₂O + 2GTP + 6NADH + 2FADH₂
    - ETC
      - Final electron acceptor = Oxygen → water
      - Oxidative Phosphorylation: process that synthesizes ATP as energy released from redox reactions move electrons from high energy state to low energy state
        - Each NADH + H⁺ → 3 ATP
        - Each FADH₂ → 2 ATP (enters chain at lower energy than NADH)
  - **Net ATP yield from Glucose catabolism = 36 ATP**

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<td>Phosphocreatine</td>
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<tr>
<td>Adenylate Kinase</td>
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<td>Glycolysis</td>
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Citric Acid Cycle produces ~ 34 ATP via Oxidative Phosphorylation
**Lipid (Fat) Metabolism**

- Occurs only under Aerobic conditions and in mitochondria
- Lipids stored as Triacylglycerol within muscle fibers

<table>
<thead>
<tr>
<th>Hydrolysis of Triacylglycerol</th>
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<tr>
<td>Triacylglycerol + 3H₂O → Glycerol + 3 Fatty Acids</td>
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<tr>
<td>(enzyme is Lipase)</td>
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- Fatty Acids (FFAs)
  - Transferred in blood by Abumin across muscle plasma membrane
  - Bind to intramuscular proteins once in cytosol to enter mitochondria
  - In mitochondria
    - FFA (through Beta Ox.) → Acetyl CoA = NADH + FADH₂ → ETC = ATP
    - Each Triacylglycerol consisting of 3 Fatty Acids (18 carbons each) = 441 ATP from Beta Ox and Citric Acid Cycle/ETC
- Glycerol
  - Glycerol → Pyruvate which forms ATP via oxidative phosphorylation = 19 ATP
- Each Triacylglycerol molecule = 460 ATP
- Increased epinephrine, norepinephrine, glucagon, growth hormone = increased lipase activation

**Protein Metabolism**

- NOT a preferred source of energy
- Can be used to resynthesize ATP under aerobic conditions
- Occurs in mitochondria
- 1) Deamination of amino acids
  - Takes place in liver and skeletal muscles
- 2) Deaminated products → pyruvate or Acetyl CoA (depending on amino acid)
- Glucogenic: amino acid → pyruvate → AcetylCoA → citric acid cycle
  - Threonine, Serine, Cysteine, Glycine
  - Contribute to Gluconeogenesis (glucose synthesis) during prolonged exercise
- Ketogenic: amino acid → AcetylCoA → citric acid cycle
  - Isoleucine, Leucine, Lysine, Tyrosine, Phenylalanine, Tryptophan
  - Synthesize Triacylglycerol
- Some amino acids enter Citric acid cycle directly
  - Arginine, Glutamine, Tyrosine
Summary

- Fats and Glycogen = major sources for ATP resynthesis
- Carbs are ONLY macronutrient capable of generating ATP anaerobically
- Glycogen supplies energy for ATP synthesis during maximal exercise
- Carb → energy is faster than fatty acid → energy
- Carbs most useful for immediate energy release
- Fat provides energy for high-intensity, long duration exercise
- Carbohydrate metabolism is needed for fat oxidation
  - Oxaloacetate is regenerated from pyruvate (a product of glycolysis) and is required for entry of fatty acids into citric acid cycle
  - Fat oxidation is slower than glucose/glycogen catabolism

Simplified Glycolysis diagram. Molecule names contain extra capitals to illustrate components. 21/02/2010 followchemistry.wordpress.com
Exercise + Physiology

Fuel

[Diagram of the Krebs cycle and electron transport chain]

[a] Complex I receives 2 electrons from NADH and passes them to CoQ via FMN and an Fe-S protein. During this process, 4 H⁺ are pumped out of the matrix by complex I.

[b] Complex III passes electrons from CoQH₂ to cytochrome c via cytochromes b and c, and an Fe-S protein. CoQH₂ carries 2 H⁺ across the inner membrane and 2 more H⁺ are pumped out of the matrix.

[c] Complex IV receives electrons from cytochrome c and, via cytochrome a and a₅, passes them to molecular oxygen, which is reduced to water as 2 more H⁺ are pumped from the matrix by complex IV.

[d] ATP synthase uses the energy from the proton gradient generated during electron transport to synthesize ATP from ADP and Pᵢ.