Cellular Respiration and Metabolism, Chapter 5
Outline of class notes
Objectives:
After studying this chapter you should be able to:
1. Define metabolism and explain the difference between catabolic and anabolic reactions.
2. Describe the two mechanisms involved in the breakdown of organic molecules.
3. Explain glycolysis.
4. Describe the process of aerobic respiration including details of glycolysis, Krebs cycle, and oxidative phosphorylation (electron transport chain and chemiosmotic theory).
5. Explain the difference between anaerobic and aerobic respiration and the effect of anaerobic respiration on skeletal muscles.
6. Explain the Cori Cycle
7. Describe the metabolism of lipids.
8. Explain the metabolism of amino acids.
9. Discuss the Clinical Applications from the study guide and be able to describe the disorders from the Applications to Health located at the end of this chapter.

Chapter Overview
• Metabolism
• Metabolic Pathway of Cellular Respiration
  – Glycolysis
  – Citric Acid Cycle
  – Electron Transport Chain
• Anaerobic vs. aerobic respiration
• Lipid and amino acid metabolism

Metabolism
• **Metabolism**: Total of all chemical reactions that occur in the body. Can be divided into two categories:
  – **Catabolic reactions**: Release energy by the breakdown of larger organic molecules into smaller molecules.
    • Breakdown of glucose, fatty acids, and amino acids serve as the primary sources of energy for the synthesis of ATP
    • ~40% of the energy released goes to the conversion of ADP to ATP and the rest escapes as heat.
  – **Anabolic reactions**:

Cellular Respiration
• **Cellular respiration**: Utilizes food energy to generate ATP and occurs by two mechanisms: Aerobic and Anaerobic respiration.
• **Anaerobic respiration**: Respiration pathway that does not use oxygen to generate ATP.
  – Occurs in the cell’s cytoplasm and generates ATP by glycolysis.
  – Process converts glucose to
• **Aerobic respiration**: Requires oxygen to generate ATP and occurs in three phases: glycolysis, the Krebs cycle, and oxidative phosphorylation.
  – Glycolysis takes place in the cells cytoplasm
  – Krebs cycle and the electron transport chain are
Equation for Aerobic Cellular Respiration

\[
\text{Glucose (C}_6\text{H}_{12}\text{O}_6) + 6 \text{O}_2 \rightarrow 6 \text{CO}_2 + 6 \text{H}_2\text{O} + \text{ATP}
\]

- Overall, aerobic cell respiration involves the transfer of electrons and hydrogen atoms from glucose to oxygen, forming H2O.
- **Main function is to generate ATP**
  - Aerobic respiration yields a great deal more ATP (38 ATP molecules/glucose) than

**Redox Reactions**

- **Cellular processes** that release energy from organic fuels is based on the transfer of high energy electrons.
  - Electron transfer releases energy which is ultimately used to make ATP.
- **Oxidation-reduction (Redox) reactions**: Chemical reactions that transfer electrons (e-) from one substance to another substance.
  - **Oxidation**: Loss of electrons from a substance
  - **Reduction**: Gains electron

**Redox Reactions and Cellular Respiration**

- In the process of **aerobic cellular respiration**:
  - **Glucose**
  - **Oxygen** is reduced, gaining electrons (and hydrogens) lost from glucose.
    - Oxygen’s gain of electrons + hydrogen atoms form water

**Cells use the energy released during the transfer of electrons (Redox reactions) to make ATP.**
- **Final step**: The high energy electrons are eventually transferred to

**NAD: Electron Carrier**

- **NAD+**: Nicotinamide Adenine Dinucleotide
  - **NAD+**: An electron carrier that binds to two electrons and one hydrogen atom (proton) as they are striped from food molecules. The other proton removed is released as a hydrogen ion (H+) into the surrounding solution.
    - **NAD is reduced to NADH when it binds to electrons**
    - The “H” represents the transfer of
Aerobic cellular respiration occurs in 3 stages
- Each stage takes place in a specific region of the cell
  1. **Glycolysis**: Glucose, a 6-carbon sugar, is split into two 3-carbon molecules of pyruvic acid
  - 2. **Krebs Cycle (Citric Acid Cycle)**: Completes the break down of glucose to CO2.
  - 3. **Oxidative Phosphorylation: Electron Transport Chain (ETC) and Chemiosmosis**: Electrons captured during glycolysis and Krebs cycle are used to generate ATP
    - Occurs in the inner membrane (cristae) of mitochondria

**Stage 1: Glycolysis**
- **Glycolysis** ("sugar splitting")
  - Occurs in the
  - Two ATP are used to activate the glucose molecule, but in the end 4 ATP are produced yielding a net of 2 ATP.
  - **Net products**:
    - **2 pyruvic acid**
      - Breaks glucose \((\text{C}_6\text{H}_{12}\text{O}_6)\) in half forming 2 molecules of pyruvic acid \((\text{C}_3\text{H}_4\text{O}_3)\).
    - **2 NADH**
      - NADH is actually NADH + H carrying two extra electrons and two hydrogens, but is written as NADH (shorthand)
    - **2 ATP**
Link between Glycolysis and Citric Acid Cycle:

- To enter the **Citric Acid Cycle**, pyruvic acid is moved from the cytoplasm into the mitochondrion and converted to **Acetyl CoA**
- **Steps involved:**
  1. The carboxyl group of each pyruvic acid molecule is removed and given off as CO₂ which is carried by the blood to the lungs
  2. Oxidation of pyruvic acid generates **NADH** and a 2 carbon compound called **acetic acid**.
  3. **Acetic acid** is attached to a molecule called **coenzyme A (CoA)** to form **acetyl CoA**.
     - The CoA activates and escorts the acetic acid into the

Stage 2: The Citric Acid Cycle

- **The Citric Acid Cycle (Krebs Cycle or Tricarboxylic acid cyc)**
  - Takes place in the **matrix** of mitochondria.
    - Main Function:
      - **First step**, the **acetic acid subunit** (2 carbons long) of **acetyl CoA** combines with **oxaloacetic acid** (4 carbons long) to form a molecule of **citric acid** (6 carbons long).
      - Coenzyme A acts as a transporter of acetic acid then leaves to transport more.
      - **Citric acid** formation begins a cyclic metabolic pathway known as the citric acid cycle where **acetic acid** rides a "Ferris wheel" of chemical reactions that ultimately breaks the molecule apart.
      - **FAD**, flavin adenine dinucleotide, is an additional electron/proton carrier. **FADH₂ and NADH** shuttle protons and high energy electrons to the **electron transport chain**.
      - Each 2 carbon molecule of acetic acid releases:

What happens to the CO₂?

- CO₂ will diffuse out of the mitochondria, out of the cell, and into the blood stream which will take it to the lungs to be exhaled.

So far, what has happened to our glucose molecule?

- **Glycolysis:**

- **Pyruvic Acid conversion to Acetyl CoA**

- **Citric Acid Cycle:**

- **Next Step: Oxidative Phosphorylation by ETC and Chemiosmosis:**
  - NADH and FADH₂ will deliver their electrons and hydrogens to the electron transport chain.
Test Your Knowledge
1. Another name for a hydrogen ion (H+) is:
   a. Oxidation  b. Reduction  c. Hydrogenation
2. An atom or molecule gains an electron. This best describes:
   a. Oxidation  b. Reduction  c. Hydrogenation
3. When a molecule gains electrons, we say it becomes:
   a. Oxidized  b. Reduced
4. NADH is the_________ form of NAD+.
   a. Oxidized  b. Reduced

Mitochondrion Structure
- Site of aerobic cellular respiration: Cell’s Powerhouse
- Composed of two membranes:
  1. **Outer membrane**
  2. **Inner membrane**
     - Molecules that function in cellular respiration are built into the inner membrane (cristae)
     - **Matrix** is the thick fluid surrounded by the cristae and contains the enzymes for the **Citric Acid Cycle**
  3. **Intermembrane space** is the space between the outer and inner membrane.

Stage 3: Oxidative Phosphorylation: Electron Transport Chain (ETC) and Chemiosmosis:
- **Oxidative phosphorylation** is the process in which ATP is formed as a result of the transfer of electrons from NADH or FADH₂ to O₂ by a series of electron carriers found in the mitochondrial inner membrane. It consists of the **electron transport chain** and **chemiosmosis**
- **The Electron Transport Chain (ETC):**
  - The ETC is a series of molecules **embedded in the inner membrane** of the mitochondria specialized in the transport of electrons and pumping of protons
  - Consists mostly of **protein complexes** (numbered I - IV), coenzyme Q, and cytochromes.
- Electrons, obtained from NADH and FADH2, move ("cascade") down the ETC giving up a small amount of energy with each transfer.
- That energy or "downhill" fall of the electrons is used to **pump H⁺ into the intermembrane space**, forming a huge H⁺ gradient and a transmembrane electrical potential referred to as a **proton-motive force**.
- **H⁺ (proton) gradient** is then used by **ATP synthase** (an enzyme) to make ATP as H⁺ flow back across the innermembrane due to the **proton-motive force**!
  - This process of ATP production using a proton gradient is known as **chemiosmosis or the chemiosmotic theory**
  - ATP production powered by redox reactions of the ETC is called **oxidative phosphorylation**.
- **Oxygen** is the final (terminal) electron acceptor, combining with electrons and H⁺ ions to produce water
  - **This is the reason we need to breathe oxygen!**

Poisons and the Electron Transport Chain
- The action of some of the deadliest poisons is to disrupt the electron transport chain resulting in a decrease in ATP production.
  - **Cyanide** kills by blocking the transfer of
    - Causes the back up of electrons, no proton (H⁺) gradient to be produced resulting in a drastic decrease in ATP production – cell/organism dies

Test Your Knowledge!
- Where do the electrons and hydrogen atoms come from that feed that electron transport chain?

Test Your Knowledge
- At the end of the electron transport chain, what type of atom is the final electron acceptor?
  - What molecule is formed when this atom accepts the electrons/hydrogen atoms?

Test Your Knowledge
- What is the potential energy source that drives ATP production by ATP synthase?
  - Concentration Gradient of
  - Of the three main stages of cellular respiration (glycolysis, citric acid cycle, ETC), which one:
    - uses oxygen directly?
    - occurs in the cytosol?
    - Occurs only in the mitochondrial matrix?
Adding up the ATP from Cellular Respiration
- From a molecule of glucose you get **36 to 38 ATP** molecules from the following stages:
  - Glycolysis =
  - Citric Acid Cycle =
  - Electron Transport Chain =
- High energy electrons delivered by NADH and FADH2 are used to pump protons across the inner membrane and establish the **proton-motive force**
  - Each NADH that transfers a pair of electrons to the ETC can generate
  - Each FADH2 that transfers a pair of electrons to the ETC can generate
  - Since FADH2 drops off its electrons further down the ETC (at protein complex II) it is responsible for transport of only enough H+ to make 2 ATPs.

**Why Uncertainty of 36 to 38 ATP/Glucose?**
- The uncertainty results from which shuttle is used to transport electrons from the NADH made in the cytosol to the mitochondrial matrix.
  - The NADH molecules made during glycolysis cannot directly enter the mitochondria; instead a mechanism exists to “shuttle” these electrons into the mitochondrial matrix.
  - Depending on which shuttle is used, the electrons are passed either to FAD or to NAD+, and either two or three ATP can be produced, respectively.
The Versatility of Cellular Respiration
- The process of cellular respiration utilizes a variety of food molecules for energy.
- Utilizes:
  - 
  - 
  - 
- The macromolecules are broken down to their individual monomers and used in this process to make ATP.

Aerobic vs. Anaerobic Respiration
- Basic definitions:
  - **Aerobic respiration**: respiration pathway that requires oxygen.
    - Includes
  - **Anaerobic respiration (Fermentation)**: respiration pathway that does not require oxygen.
    - Includes

Anaerobic Conditions and Working Muscle
- Unfortunately, without O2, we cannot generate large amounts of ATP by the electron transport chain.
- Anaerobic respiration
- **Glycolysis** does not need oxygen to produce ATP, but it does need NAD+ to remove electrons from glucose.
  - To regenerate the NAD+, the NADH transfers its electrons to pyruvic acid making it lactic acid.
    - The regenerated NAD⁺ can then be reused for glycolysis.

Feel the Burn
- **Anaerobic metabolism** is inefficient.
  - Net
    - Compare this to the 36 ATP from aerobic respiration
  - The temporary accumulation of lactic acid in muscle cells contributes to the burning feeling during exercise.
  - **Lactic acid** is then transported to the liver where it is converted back to glucose as part of the Cori Cycle.
    - **Oxygen Debt**: Continue to breath heavy after activity – provide
Cori Cycle
- The Cori cycle (also known as the Lactic acid cycle), refers to the metabolic pathway in which lactate produced by glycolysis during anaerobic respiration in the muscles moves to the liver and is converted to glucose by gluconeogenesis, which then returns to the muscles and can be metabolized back to lactate.
- If intense muscle activity has stopped, the glucose is used to replenish the

Metabolism of Lipids and Proteins
- Triglycerides can be hydrolyzed into glycerol and fatty acids
  - Fatty acids can be converted to acetyl CoA that can enter the Krebs cycle and generate a large amount of ATP
- Amino acids can be used for energy
  - Requires removal of the

Lipid Metabolism
- Lipogenesis (fat formation) can occur due to excess glucose
  - Glucose is converted to pyruvic acid and then to acetyl CoA
  - Acetic acid subunits of Acetyl CoA can be used to produce a variety of lipids including cholesterol, ketone bodies, and fatty acids
    - Acetyl CoA is considered
- Fat is the major form of energy storage in the body
  - One gram of fat contains
  - One gram of protein contains
  - One gram of carbohydrates contains

Food Calories
- A calorie is a unit of measurement for energy.
  - One mole of glucose burned in air, will release **686 kcal** (2,870 kJ) of heat.
  - One mole of glucose is equal to 180 grams and has \( 6.02 \times 10^{23} \) molecules of glucose.
The name calorie can be used in two ways:
- The small calorie or gram calorie (symbol: cal) is the approximate amount of energy needed to raise the temperature of one gram of water by one degree Celsius.
- The large calorie, kilogram calorie, food calorie (Symbol: capital C) is used to describe the amount of energy in food
  - Food calories: 1 Calorie = 1 kilocalorie
  - One Calorie is approximately the amount of energy needed to raise the temperature of one kilogram of water by one degree Celsius. The large calorie is thus equal to 1000 small calories or one kilocalorie (symbol: kcal).

Lipid Metabolism (cont)
- **Lypolysis**: Process of breaking down
  - Glycerol can be converted to phosphoglyceraldehyde and enter glycolysis as an intermediate
  - Fatty acids, by process of β-oxidation, are broken into numerous 2 carbon acetic acid molecules and from acetyl CoA, which can enter the Krebs cycle.

- **Triglycerides** in adipose tissue are continuously being broken down (glycerol and fatty acids) and resynthesized.
  - Ensures adequate blood levels of fatty acids for aerobic respiration by skeletal muscle and other organs.
  - When rate of lypolysis exceeds rate of fatty acid utilization – as in starvation, dieting, and diabetes mellitus – the blood concentrations of fatty acids increases.
  - The liver takes the excess acetyl CoA made from

- **Ketone Bodies**: Include the 4 carbon acetoacetic acid and β-hydroxybutyric acid, and the 3 carbon acetone.
  - Used for energy by many organs and normally found in blood in relatively low concentrations
  - Elevated levels can produce ketosis or ketoacidosis which
  - Person may have a sweet-smelling breath due to the presence of acetone, which is volatile and leaves the blood in the exhaled air

Amino Acid Metabolism
- When excess amino acids are ingested, the amine group can be removed and carbon skeletons are used for energy or converted to carbohydrate (glucose) or fat.