Summary of Metabolic Pathways (Ch 21, 23 and 25)

21.1 Energy and Life
- Energy can be converted from one form to another, but can’t be created or destroyed.
  - A consequence of this is that we need a constant supply of energy to power the external actions we take as well as the internal activities of our bodies.
- We can’t generate useful bodily energy by burning food:
  - Energy must be released gradually.
  - Energy must be stored until used.
  - The rate of energy release must be finely controlled.
  - We need just enough energy release to maintain a constant body temperature.
  - Energy must be available in forms other than heat.

21.2 Energy and Biochemical Reactions
- The free energy of a reaction describes the effect of a combination of changes in disorder as well as loss or gain of heat energy.
- Reactions in which the energy content of products is less than that of reactants (in which energy is produced) are said to have a negative value of free energy change and are called exergonic or exothermic. Exergonic reactions can occur spontaneously.
- Reactions in which the energy content of products is greater than that of reactants (in which energy is consumed) are said to have a positive value of free energy change and are called endergonic or endothermic. Endergonic reactions are thermodynamically unfavorable.

21.3 Cells and Their Structure
- Eukaryotic cells are larger and more complex than prokaryotic cells and contain internal components enclosed in organelles.
  - One of the most important types of organelles in prokaryotic cells is the mitochondrion, the so-called “power plant” of the cell.
- Mitochondria contain the enzymes of the electron transport chain, their own DNA, and enzymes that allow them to synthesize protein.
  - All our mitochondria come from our mothers. Does that seem fair?
- For simplicity, metabolic reactions can be classed in metabolic pathways.
  - Some pathways are linear, some are circular. Most are intertwined with other pathways.

Adapted From: Fundamentals of GOB, 5th ed. McMurry, Castellion, Ballantyne
• Breakdown of complex molecules to simpler molecules with release of energy is termed catabolism.
  - Breakdown of carbohydrates yields glucose and other sugars that can be oxidized to acetyl groups, which may be converted to carbon dioxide and water.
  - Breakdown of proteins yields amino acids, which may be further metabolized to simpler molecules.
  - Triglycerides (fats and oils) are broken down into long chain fatty acids. These may be broken down to acetyl groups and oxidized further to carbon dioxide and water.
  - Acetyl groups from carbohydrates and fatty acids are attached to coenzyme A for transport through metabolic pathways.
  - Energy produced in oxidative pathways is typically stored temporarily in molecules such as adenosine triphosphate (ATP).
• Synthesis of complex products from simple molecules uses energy and is called anabolism.

21.5 Strategies of Metabolism: ATP and Energy Transfer
• ATP is the most common molecular form of energy stored in cells.
  - The average person makes and uses his/her weight of ATP daily.
• ATP contains so-called high-energy bonds that yield energy upon hydrolysis to ADP and phosphoric acid.
  - Appropriate enzymes can reverse the hydrolysis of ATP to ADP and phosphoric acid; these reactions are endergonic.

Application—
Life without Sunlight
• While the sun is our major source of energy, life exists in some improbable locations.
  - Wherever it exists, life needs a source of energy in the form of some substance that the life form can metabolize.

21.6 Strategies of Metabolism: Metabolic Pathways and Coupled Reactions
• The free energy change of each step in a metabolic pathway can be measured.
  - Some steps in a metabolic pathway are endergonic and some are exergonic.
    - Endergonic reactions can be coupled to exergonic reactions (of higher negative free energy) so that a combination of the two will occur.
• The overall free energy change for a combination or series of reactions is the sum of the individual changes.

Adapted From: Fundamentals of GOB, 5th ed. McMurry, Castellion, Ballantyne
Application—
Basal Metabolism

- The basal metabolic rate is defined as the minimum amount of energy needed to stay alive.
- Basal metabolic rate is measured over a period of time in a person who is awake, lying down, comfortable, and has fasted for 12 hours.
- On average, the basal energy need per day is about 1 kcal/hr per kilogram of body weight for males and 0.95 kcal/hr per kilogram of body weight for females.
- The total number of kilocalories needed depends on physical condition and activities.
  A very active person may require twice as much energy per day as an inactive person.

21.7 Strategies of Metabolism: Oxidized and Reduced Coenzymes.

- Coenzymes accept electrons during redox reactions of metabolism.
  Among the most important redox coenzymes are NAD+, NADP+, FAD, and FMN, which act as electron carriers.
  In these coenzymes, electrons are carried along with or attached to hydrogen atoms.

21.8 The Citric Acid Cycle

- Catabolism of both carbohydrates and fatty acids yields acetyl groups, which are attached to coenzyme A (as acetyl coenzyme A) for further metabolism.
- Enzymes of the citric acid cycle are located inside mitochondria.
- At the beginning of the cycle, acetyl groups are added to oxaloacetate to form citric acid.
  - Citric acid is isomerized to form isocitric acid.
  - Isocitric acid is oxidized and decarboxylated to form α-ketoglutarate molecules.
  - NAD+ acts as a coenzyme, accepting the electrons removed from isocitric acid.
  - α-Ketoglutarate molecules lose carbon dioxide and are oxidized to form succinyl-SCoA.
    - Here, the coenzyme A acts as a carrier for the succinyl group.
    - Succinyl-SCoA is a relatively high-energy compound. Hydrolysis of succinyl coenzyme A to succinic acid and coenzyme A provides enough energy to synthesis ATP from ADP and phosphate.
    - Succinic acid is oxidized to fumaric acid.
    - FAD acts as an electron accepting coenzyme for the reaction.

Adapted From: Fundamentals of GOB, 5th ed. McMurry, Castellion, Ballantyne
- Fumaric acid is hydrated to form malic acid.
- Malic acid is oxidized to form oxaloacetic acid, which can react with acetyl coenzyme A again, forming citric acid and continuing the cycle.
- NAD+ acts as a coenzyme for this oxidoreductase reaction.

- The net result of the citric acid cycle is conversion of an acetyl group to two carbon dioxide molecules, four molecules of reduced coenzymes, and one ATP molecule.
- The reduced coenzyme molecules can pass electrons into the mitochondria, where they can result in generation of more ATP by oxidative phosphorylation.
- The citric acid cycle is controlled in part by the availability of reduced coenzymes and the body’s need for ATP.

23.1 Digestion of Carbohydrates
- In digestion, food is ground and mixed with lubricants and enzymes.
- Digestion begins in the mouth with the attack of α-amylase on starch.
- Large molecules are broken down to fatty acids, monosaccharides, glycerol, and amino acids prior to absorption from the intestine.

23.2 Glucose Metabolism: An Overview
- Glucose is a nearly universal fuel for cells (nearly the only fuel for red blood cells, nervous tissue, and anaerobic muscle), as well as the precursor for glycerol and for lactose.
- Upon entering a cell, glucose is phosphorylated to form glucose-6-phosphate.
- The glucose proceeds through glycolysis, forming acetyl coenzyme A, which feeds into the citric acid cycle.
- When extra glucose is available, it is converted to glycogen for storage or into fatty acids for formation of lipids.
- Some excess glucose may also enter the pentose phosphate pathway, supplying NADPH and pentoses needed for biosynthesis.

23.3 Glycolysis
- Glycolysis occurs in the cytoplasm of eukaryotic cells, converting glucose into pyruvic acid and yielding two moles of ATP per mole of glucose.
- Pyruvate can undergo further oxidation to acetyl coenzyme A.
- Formation of glucose-6-phosphate tags glucose for metabolism and locks it within the cell.
- Once attached to phosphate, carbons from glucose pass through a number of steps on the pathway to pyruvic acid.

Adapted From: Fundamentals of GOB, 5th ed. McMurry, Castellion, Ballantyne
-Two moles of reduced coenzyme NADH are formed per mole of glucose. Electrons from NADH can pass into the electron transport chain, yielding as much as three ATP per NADH.
-Two moles of ATP are formed directly from glycolytic oxidation of each glucose.

23.5 The Fate of Pyruvate
- Under aerobic conditions, pyruvic acid is oxidized to acetyl coenzyme A.
- Oxidation of pyruvate to acetyl coenzyme A yields energy in the form of NADH.
- Oxidation of pyruvate can only occur if the oxidized coenzyme (NAD+) is available.
- Under anaerobic conditions, the NADH which accumulates is not converted to NAD+. This prevents oxidation of pyruvate and stops the earlier step in glycolysis which requires NAD+.

- The net result of the citric acid cycle is conversion of an acetyl group to two carbon dioxide molecules, four molecules of reduced coenzymes, and one ATP molecule.
- The reduced coenzyme molecules can pass electrons into the mitochondria, where they can result in generation of more ATP by oxidative phosphorylation.
- The citric acid cycle is controlled in part by the availability of reduced coenzymes and the body’s need for ATP.
- ADP and NAD+ act as allosteric activators of the enzyme that oxidizes isocitric acid.
  - If insufficient NAD+ is available, it can be formed by reduction of pyruvate to lactate by passing electrons (attached to hydrogen) from NADH to pyruvate.

25.5 Oxidation of Fatty Acids
- After fatty acids cross the cell membrane into the cytosol of a cell, three actions are involved in fatty acid oxidation:
  - The fatty acid must be converted to fatty acyl-SCoA.
  - The fatty acyl-SCoA must be transported into the mitochondria.
  (The fatty acyl-SCoA is oxidized by enzymes in the matrix of the mitochondria, producing acetyl-SCoA and reduced coenzymes NADH and FADH2.)
  - ATP is needed for synthesis of acyl-SCoA, forming AMP and pyrophosphoric acid.
  The pyrophosphate is hydrolyzed rapidly; in effect, two ATP are used to form one acyl-SCoA.

Adapted From: Fundamentals of GOB, 5th ed. McMurry, Castellion, Ballantyne
-A carnitine shuttle carries acyl groups across the mitochondrial membrane.

**Process of Oxidation:**
- In the first step of oxidation, FAD removes two hydrogen atoms (and their electrons) from the second and third carbons of the acyl chain, forming a double bond. (This is referred to as β-oxidation.)
- In the second step, water is added across the double bond. The -OH group attaches to the β-carbon.
- A second β-oxidation occurs, removing two hydrogens (and their electrons) from the β-carbon. NAD+ is the electron-accepting coenzyme. A ketoacyl-SCoA molecule forms.
- In the next step, a coenzyme A molecule accepts the acyl group, forming a molecule of acetyl-SCoA and an acyl-SCoA molecule two carbons shorter than the original fatty acid.
- The new acyl-SCoA molecule may pass through the first four steps again, generating more FADH2 and NADH, along with another acetyl-SCoA molecule and another molecule of acyl-SCoA (again, two carbons shorter).

**25.6 Energy from Fatty Acid Oxidation**
- In effect, 2 ATP were used to form a fatty acyl-SCoA.
- In fatty acid oxidation, each acetyl-SCoA can pass carbons into the citric acid cycle, yielding 12 ATP.
- Each of the FADH2 molecules can be oxidized via the electron transport chain to form a maximum of 2 ATP, and each NADH can result in formation of 3 ATP.
- One mole of lauric acid weighs about the same as one mole of glucose.
- 12 carbons as lauric acid can form 6 acetyl-SCoA’s, each worth 12 ATP.
- 6 acetyl-SCoA yield 12 ATP/acetyl-SCoA 72 ATP
- β-oxidations occur, each yielding an FADH2 and a NADH.
- 5 FADH2 each yielding 2 ATP 10 ATP 5 NADH each yielding 3 ATP 15 ATP
- 2 ATP were used to start: ATP→ AMP + pyrophosphate –2 ATP
- Net energy production from 12 carbons as lauric acid: 95 ATP
- One mole of glucose (180 grams) yields 38 ATP. Obviously, a much higher energy yield is obtained by oxidation of fatty acids than glucose. Six carbons as glucose would yield 2 (38) ATP, or 76 ATP.
- In addition, glycogen is much more highly hydrated, so a typical person would need to weigh about 120 pounds more to carry his or her reserve energy supply as starch.

Adapted From: Fundamentals of GOB, 5th ed. McMurry, Castellion, Ballantyne