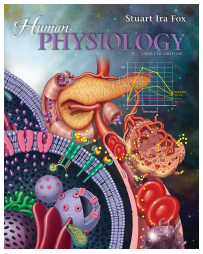


Chapter 5

Cell Respiration and Metabolism

Lecture PowerPoint

Metabolism

- All of the reactions in the body that require energy transfer. Can be divided into:
  - Anabolism: requires the input of energy to synthesize large molecules
  - Catabolism: releases energy by breaking down large molecules into small molecules

Catabolism Drives Anabolism

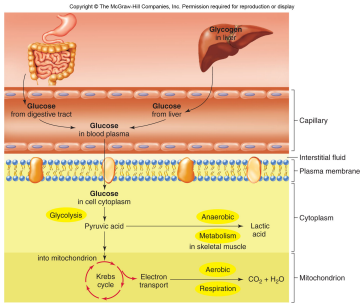
- The catabolic reactions that break down glucose, fatty acids, and amino acids serve as energy sources for the anabolism of ATP.
  - Involves many oxidation-reduction reactions.
  - Complete catabolism of glucose requires oxygen as the final electron acceptor.
  - This is therefore an aerobic reaction.
  - Called cellular respiration.
  - Breaking down glucose requires many steps, and the first ones are anaerobic.

Complete Catabolism of Glucose

- Often called cellular respiration (although the first part is anaerobic)

$$C_6H_{12}O_6 + O_2 \rightarrow 6\ CO_2 + 6\ H_2O + ATP$$

Overview of Energy Metabolism



Common Metabolic Processes

Table 5.1 | Common Terms for Some Metabolic Processes in the Body

Term	Process
Glycolysis	Conversion of glucose into two molecules of pyruvic acid
Glycogenesis	The production of glycogen, mostly in skeletal muscles and the liver
Glycogenolysis	Hydrolysis (breakdown) of glycogen; yields glucose 6-phosphate for glycolysis, or (in the liver only) free glucose that can be secreted into the blood
Gluconeogenesis	The production of glucose from noncarbohydrate molecules, including lactic acid and amino acids, primarily in the liver
Lipogenesis	The formation of triglycerides (fat), primarily in adipose tissue
Lipolysis	Hydrolysis (breakdown) of triglycerides, primarily in adipose tissue
Ketogenesis	The formation of ketone bodies, which are four-carbon-long organic acids, from fatty acids; occurs in the liver

I. Glycolysis and the Lactic Acid Pathway

Glycolysis

- First step in catabolism of glucose
- Occurs in the cytoplasm of the cell

6-carbon sugar → 2 molecules of 3-carbon pyruvate

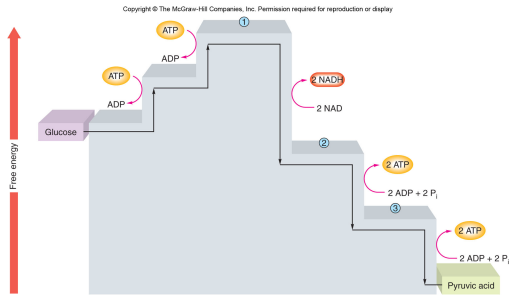
$C_6H_{12}O_6$ → 2 molecules $C_3H_4O_3$

- Note loss of 4 hydrogen ions. These were used to reduce 2 molecules of NAD.

Net Energy Gain in Glycolysis

- Glycolysis is exergonic, so some energy is produced and used to drive the reaction
  $ADP + P_i \rightarrow ATP$
- 4 ATP are generated.
- Glucose requires activation at the beginning provided by 2 P_i stripped from 2 ATP molecules.
- Net gain in glycolysis = 2 ATP

Use and Expenditure of Energy in Glycolysis

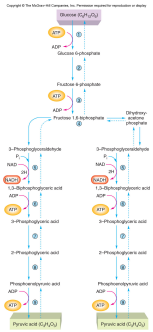


Reactants and Products of Glycolysis

Glucose + 2 NAD + 2 ADP + 2 P_i →

2 pyruvic acid + 2 NADH + 2 ATP

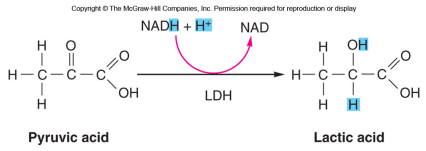
Glycolysis Pathway



Lactic Acid Pathway

- When there is no oxygen to complete the breakdown of glucose, NADH has to give its electrons to pyruvic acid. This results in the reformation of NAD and the conversion of pyruvate to lactic acid.

Lactic Acid Pathway



Lactic Acid Pathway

- Also called anaerobic metabolism or lactic acid fermentation
  - Similar to how yeasts ferment glucose into alcohol
- Still yields a net gain of 2 ATP
  - Muscle cells can survive for awhile without oxygen by using lactic acid fermentation.
  - RBCs can only use lactic acid fermentation because they lack mitochondria.

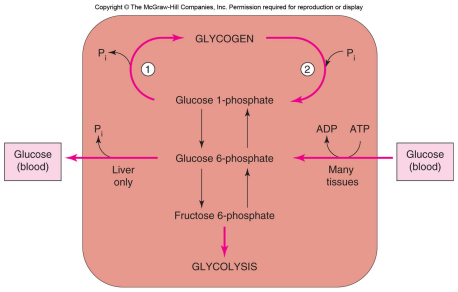
Glycogenesis

- Cells can't store much glucose because it will pull water into the cell via osmosis.
- Glucose is stored as a larger molecule called glycogen in the liver, skeletal muscles, and cardiac muscles.
- Glycogen is formed from glucose via glycogenesis.

Glycogenolysis

- When the cell needs glucose, it breaks glycogen down again.
  - Produces glucose 1-phosphate

Glycogenolysis



Glycogenolysis in the Liver

- Glucose from glycogen is in the form glucose 1-phosphate, so cannot leave muscle or heart cells.
- The liver has an enzyme called glucose 6-phosphatase that removes the phosphate so glucose can reenter the bloodstream.

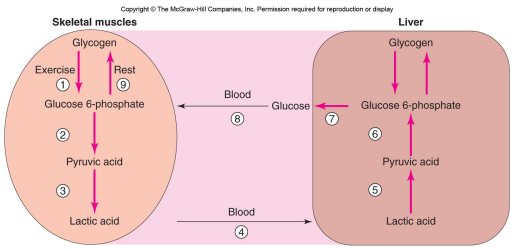
Lactic Acid

- Some lactic acid can be used in cellular respiration to produce carbon dioxide and water. Skeletal muscles make too much, so it is shipped to the liver.
- The liver has the enzyme lactic acid dehydrogenase, which converts lactic acid to pyruvic acid and NADH.

The Cori Cycle

- The liver can convert pyruvate to glucose 6-phosphate.
  - This can be used to make glycogen or glucose in a reverse of glycolysis.
  - Pyruvate → Glucose = gluconeogenesis
  - The glucose can return to the muscle cells, which completes the Cori Cycle.

The Cori Cycle



II. Aerobic Respiration

Cellular Respiration

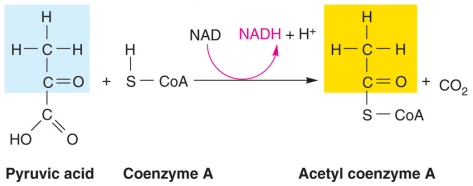
Equation: $C_6H_{12}O_6 + O_2 \rightarrow 6\ CO_2 + 6\ H_2O$

- Begins with glycolysis, which produces:
  - 2 molecules pyruvate, 2 NADH, and 2 ATP
  - The pyruvate will be used in a metabolic pathway called the Krebs cycle, and the NADH will be oxidized to make ATP.

The Fate of Pyruvate

- Pyruvate leaves the cytoplasm and enters the interior matrix of the mitochondria.
  - Carbon dioxide is removed to form acetic acid.
  - Acetic acid is combined with coenzyme A to form acetyl CoA.
    - **1 glucose → 2 molecules acetyl CoA**

The Fate of Pyruvate



Krebs Cycle

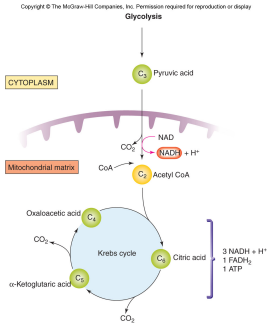
- Also called the citric acid cycle
- Acetyl CoA combines with oxaloacetic acid to form citric acid.
- Citric acid starts the Krebs cycle.
  - It is a cycle because citric acid moves through a series of reactions to produce oxaloacetic acid again.

Important Events in the Krebs Cycle

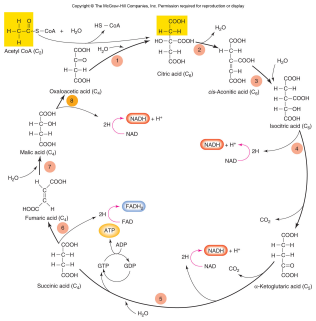
1. One guanosine triphosphate (GTP) is produced, which donates a phosphate group to ADP to form ATP.
2. Three molecules NAD are reduced to NADH.
3. One molecule FAD is reduced to $FADH_2$.

- These events occur for each acetic acid, so happen twice for each glucose molecule.

Abbreviated Diagram of the Krebs Cycle



The Complete Krebs Cycle



Products of Krebs Cycle

- For each glucose:
  - 6 NADH
  - 2 $FADH_2$
  - 2 ATP

(There were also 2 NADH and 2 ATP from glycolysis.)

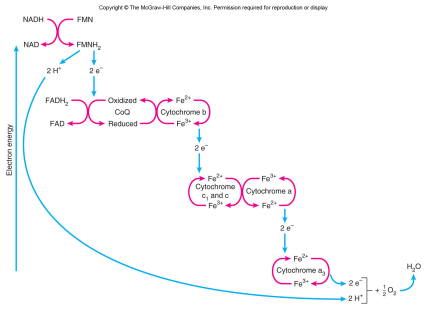
Electron Transport Chain

- In the folds or cristae of the mitochondria are molecules that serve as electron transporters.
  - Include FMN, coenzyme Q, and several cytochromes
  - These accept electrons from NADH and $FADH_2$. The hydrogens are not transported, however.
  - Oxidized FAD and NAD are reused.

Electron Transport Chain

- Electron transport molecules pass the electrons down a chain, with each being reduced and then oxidized.
- This is an exergonic reaction, and the energy produced is used to make ATP from ADP.
  - ADP is phosphorylated.
  - This process is called oxidative phosphorylation.

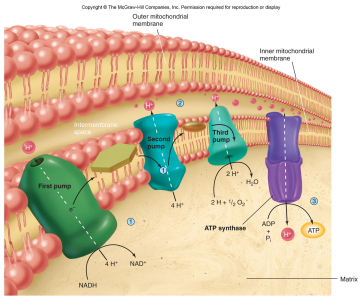
Electron Transport Chain



ATP Production

- Electron transport fuels proton pumps, which pump H^+ from the mitochondrial matrix to the space between the inner and outer membranes.
- This sets up a huge concentration gradient between the membranes. Movement of H^+ across the membrane provides energy to the enzyme ATP synthase, which converts ADP to ATP.

Oxidative Phosphorylation



The Role of Oxygen

- **Final electron acceptor**. Without a final acceptor, the whole process would come to a halt. The Krebs cycle and electron transport require oxygen to continue.
  - Water is formed in the following reaction:

$$O_2 + 4\ e^- + 4\ H^+ \rightarrow 2\ H_2O$$

ATP Balance Sheet

- Direct phosphorylation in glycolysis and the Krebs cycle yields 4 ATP.
  - These numbers are constant.
- Oxidative phosphorylation in electron transport yields varying amounts of ATP, depending on the cell and conditions.
  - Theoretically, each NADH yields 3 ATP and each $FADH_2$ yields 2 ATP.
  - Theoretical ATP yield is 36-38 per glucose.

Detailed Accounting

Table 5.2 | ATP Yield per Glucose in Aerobic Respiration

Phases of Respiration	ATP Made Directly	Reduced Coenzymes	ATP Made by Oxidative Phosphorylation	
			Theoretical Yield	Actual Yield
Glucose to pyruvate (in cytoplasm)	2 ATP (net gain)	2 NADH, but usually goes into mitochondria as 2 $FADH_2$	If from $FADH_2$: 2 ATP (× 2) = 4 ATP or if stays NADH: 3 ATP (× 2) = 6 ATP	If from $FADH_2$: 1.5 ATP (× 2) = 3 ATP or if stays NADH: 2.5 ATP (× 2) = 5 ATP
Pyruvate to acetyl CoA (× 2)	None	1 NADH (× 2) = 2 NADH	3 ATP (× 2) = 6 ATP	2.5 ATP (× 2) = 5 ATP
Krebs cycle (× 2)	1 ATP (× 2) = 2 ATP	3 NADH (× 2) = 6 NADH 1 $FADH_2$ (× 2) = 2 $FADH_2$	3 ATP (× 6) = 18 ATP 2 ATP (× 2) = 4 ATP	2.5 ATP (× 6) = 15 ATP 1.5 ATP (× 2) = 3 ATP
Total ATP	**4 ATP**		**32 (or 34) ATP**	**26 (or 28) ATP**

III. Metabolism of Lipids and Proteins

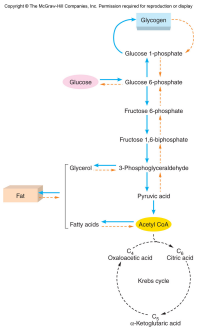
Energy from Other Molecules

- Lipids and proteins can also be used for energy via the same pathways used for the metabolism of pyruvate.

Too Much Energy?

- When more food energy is taken into the body than is needed to meet energy demands, we can't store ATP for later. Instead, glucose is converted into glycogen and fat.

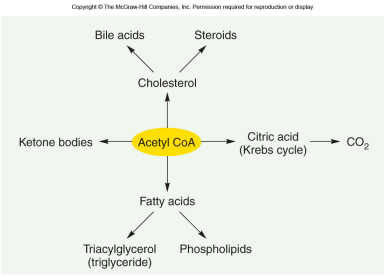
Too Much Energy?



Lipid Metabolism

- As ATP levels rise after an energy-rich meal, production of ATP is inhibited:
  - Glucose doesn't complete glycolysis to form pyruvate, and the acetyl CoA already formed is joined together to produce a variety of lipids, including cholesterol, ketone bodies, and fatty acids.
  - Fatty acids combine with glycerol to form triglycerides in the adipose tissue and liver = lipogenesis.

Acetyl CoA → Lipids



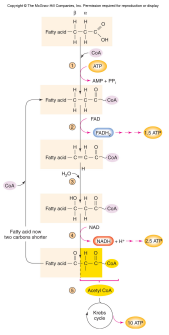
White Fat

- Fat stored in adipose tissue
- Great way to store energy: 1 gram fat = 9 kcal energy.
  - In a nonobese 155-pound man, 80-85% of his stored energy is in fat.
  - Lipolysis: breaking triglycerides down into fatty acids and glycerol using the enzyme lipase.
  - Fatty acids can then enter the blood and be used for energy elsewhere.

Fatty Acids as an Energy Source

- β-oxidation: Enzymes remove acetic acid molecules from the fatty acid to form acetyl CoA.
  - For every 2 carbons on the fatty acid chain, 1 acetyl CoA can be formed.
  - A 16-carbon fatty acid → 8 acetyl CoA
  - Each acetyl CoA → 10 ATP + 1 NADH + 1 $FADH_2$
  - A 16-carbon fatty acid → 80 ATP + 28 in electron transport = 108 ATP!!!

β-oxidation of Fat



Brown Fat

- Stored in different cells
- Involved in heat production, especially in newborns

Ketone Bodies

- When the rate of lipolysis exceeds the rate of fatty acid utilization (as in dieting, starvation, or diabetes), the concentration of fatty acids in the blood increases.
- Liver cells convert the fatty acids into acetyl CoA and then into ketone bodies.
- These are water-soluble molecules that circulate in the blood.

Amino Acid Metabolism

- Amino acids from dietary proteins are needed to replace proteins in the body.
- If more amino acids are consumed than are needed, the excess amino acids can be used for energy or converted into carbohydrates or fat.

Essential Amino Acids

- Our bodies can make 12 of the 20 amino acids from other molecules. Eight of them (9 in children) must come from the diet and are called essential amino acids.

Essential Amino Acids

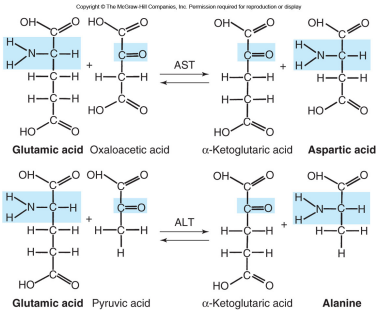
Table 5.3 | The Essential and Nonessential Amino Acids

Essential Amino Acids	Nonessential Amino Acids
Lysine	Aspartic acid
Tryptophan	Glutamic acid
Phenylalanine	Proline
Threonine	Glycine
Valine	Serine
Methionine	Alanine
Leucine	Cysteine
Isoleucine	Arginine
Histidine (in children)	Asparagine
	Glutamine
	Tyrosine

Transamination

- Pyruvate and several Krebs cycle intermediates (called keto acids) can be converted to amino acids by adding an amine group (NH_2).
  - Usually obtained from other amino acids
  - Called transamination
  - Requires vitamin B_6 as a coenzyme

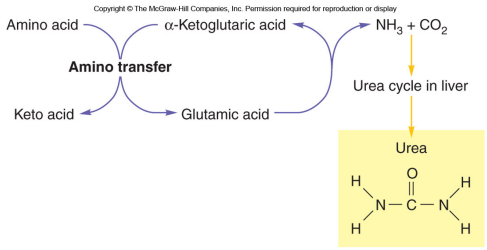
Transamination



Oxidative Deamination

- If there are more amino acids than needed, the amine group can be stripped and excreted as urea in the urine.

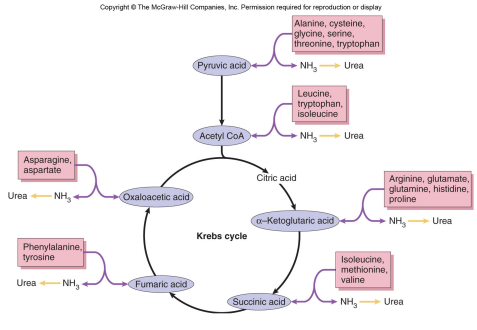
Oxidative Deamination



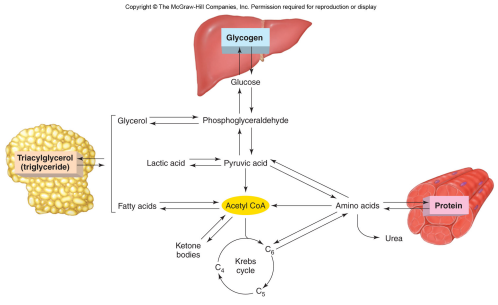
Amino Acids as Energy

- Oxidative deamination sometimes leaves pyruvate or another Krebs cycle intermediate.
  - These can be used to make energy or converted to glucose or fat.
  - The formation of glucose from amino acids is called gluconeogenesis and occurs in the Cori cycle.

Amino Acids as Energy



Different Energy Sources



Uses of Different Energy Sources

- Relative importance of different energy sources to different organs

Table 5.4 | Relative Importance of Different Molecules in the Blood with Respect to the Energy Requirements of Different Organs

Organ	Glucose	Fatty Acids	Ketone Bodies	Lactic Acid
Brain	+ + +	–	+	–
Skeletal muscles (resting)	+	+ + +	+	–
Liver	+	+ + +	+ +	+
Heart	+	+ +	+	+