Chapter 12 Lecture

General, Organic, and Biological Chemistry: An Integrated Approach

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by Richard Triplett

Chapter 12

Food as Fuel—A Metabolic Overview

Chapter Outline

Introduction

- ***Metabolism*** refers to the chemical reactions occurring in the body during the break down or building up of molecules.
- A ***metabolic pathway*** is a series of steps in the chemical reactions in biological systems.
- In the body, the energy of chemical reactions is captured in the nucleotide, ATP, which is produced during the metabolism of glucose.

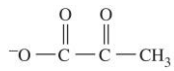
12.1 Overview of Metabolism

- Animals and humans get energy from the covalent bonds contained in carbohydrates, fats, and proteins.
- The first stage of metabolism involves the breakdown of large biomolecules into smaller units through hydrolysis reactions.
- Polysaccharides are hydrolyzed into monosaccharide units, triglycerides are hydrolyzed into glycerol and fatty acids, and proteins are hydrolyzed into amino acids.

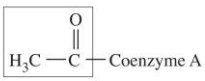
12.1 Overview of Metabolism, Continued

- Smaller molecules produced during metabolism are absorbed through the intestinal wall into the bloodstream and transported to different cells for use.
- Once in cells, further breakdown occurs into molecules containing two or three carbons.
- These smaller molecules are referred to as ***metabolites***, which are chemical intermediates formed by enzyme-catalyzed reactions.

12.1 Overview of Metabolism, Continued



a. *Pyruvate*



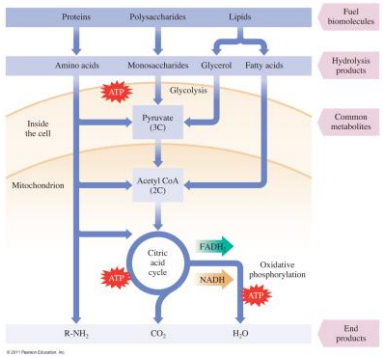
b. *Acetyl group*

If there is adequate oxygen in the cells and there is a need for energy, two-carbon metabolites, known as ***acetyl groups***, are broken down to carbon dioxide in the citric acid cycle.

12.1 Overview of Metabolism, Continued

- The citric acid cycle works in conjunction with electron transport and oxidative phosphorylation pathways to produce energy.
- Energy, in the form of ATP, nicotinamide adenine dinucleotide (NADH), and flavin adenine dinucleotide ($FADH_2$), is produced in these sequence of events.

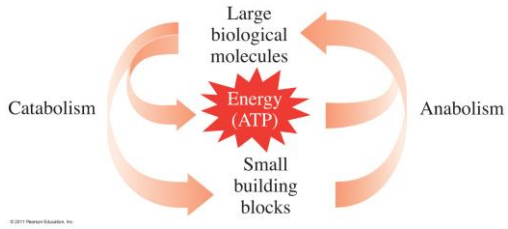
12.1 Overview of Metabolism, Continued



12.1 Overview of Metabolism, Continued

- Metabolism occurs in two parts: *catabolism* and *anabolism*.
- ***Catabolism*** refers to chemical reactions where large molecules are broken down into smaller molecules.
- ***Anabolism*** refers to chemical reactions where metabolites combine to form larger molecules.

12.1 Overview of Metabolism, Continued



The reactions of catabolism produce energy and are oxidative, while those of anabolism require energy and are reductive. Energy from catabolism is stored in ATP.

12.1 Overview of Metabolism, Continued

Metabolic Pathways in the Animal Cell

- Since metabolic pathways occur in cells, it is important to know major parts of an animal cell.
- The ***cell membrane*** separates the materials inside the cell from the exterior environment.
- The ***nucleus*** contains DNA that controls cell replication and protein synthesis.

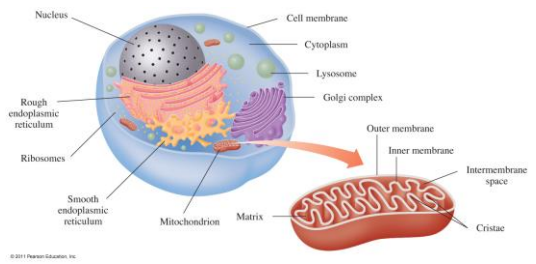
12.1 Overview of Metabolism, Continued

- The ***cytoplasm*** contains all the materials between the nucleus and cell membrane.
- The ***cytosol*** is the aqueous part of the cytoplasm that contains electrolytes and enzymes.
- Within the cytoplasm, there are specialized organelles that carry out specific cellular functions.

12.1 Overview of Metabolism, Continued

- ***Ribosomes*** are the sites of protein synthesis.
- Energy is produced in the ***mitochondria***. A mitochondrion is composed of an outer membrane and an inner membrane, with an intermembrane space between them.
- The fluid section encased by the inner membrane is referred to as the ***matrix***. Enzymes in the matrix and along the inner membrane catalyze the oxidation of carbohydrates, fats, and amino acids.

12.1 Overview of Metabolism, Continued



12.1 Overview of Metabolism, Continued

Oxidation pathways produce carbon dioxide, water, and energy.

TABLE 12.1 LOCATIONS AND FUNCTIONS OF COMPONENTS IN ANIMAL CELLS

Component	Description and Function
Cell membrane	Separates the contents of a cell from the external environment and contains structures that communicate with other cells
Cytoplasm	Consists of all the cellular contents between the cell membrane and nucleus
Cytosol	Is the fluid part of the cytoplasm that contains enzymes for many of the cell's chemical reactions
Endoplasmic reticulum	Rough type processes proteins for secretion and synthesizes phospholipids; smooth type synthesizes fats and steroids
Golgi complex	Modifies and secretes proteins from the endoplasmic reticulum and synthesizes glycoproteins and cell membranes
Lysosomes	Contain hydrolytic enzymes that digest and recycle old cell structures
Mitochondria	Contain the structures for the synthesis of ATP from energy-producing reactions
Nucleus	Contains genetic information for the replication of DNA and the synthesis of protein
Ribosomes	Are the sites of protein synthesis using mRNA templates

12.2 Metabolically Relevant Nucleotides

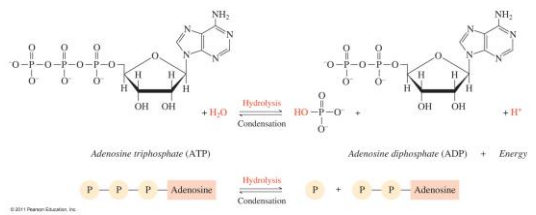
- Nucleotides have important cellular functions such as energy exchangers and coenzymes.
- Nucleotides have two forms:
  1. A high-energy form
  2. A low-energy form
- Recall that ***nucleotides*** consist of a nitrogenous base, a phosphate, and a five-carbon sugar. Many contain a vitamin within their structure.

12.2 Metabolically Relevant Nucleotides, Continued

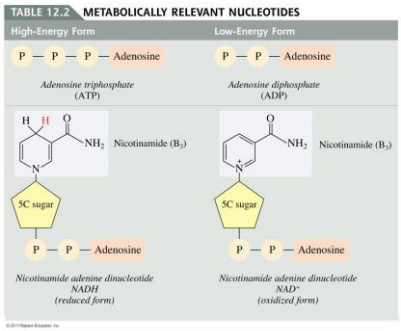
ATP/ADP

- ***ATP*** is referred to as the energy currency of the cell.
- ATP undergoes hydrolysis to ADP, during which energy is released.
- Released energy can be coupled to drive a chemical reaction that requires energy during anabolism.

12.2 Metabolically Relevant Nucleotides, Continued



12.2 Metabolically Relevant Nucleotides, Continued

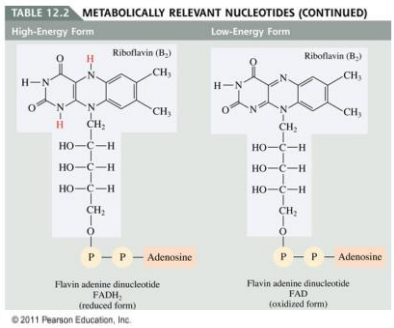


12.2 Metabolically Relevant Nucleotides, Continued

NADH/NAD^+ and $FADH_2$/FAD

- NAD^+ and FAD are energy transferring compounds whose high-energy form is reduced (hydrogen added) and whose low-energy form is oxidized (hydrogen removed).
- NADH is the reduced form of NAD^+, and $FADH_2$ is the reduced form of FAD. The active end of each molecule, the end being oxidized or reduced, contains a vitamin component.

12.2 Metabolically Relevant Nucleotides, Continued

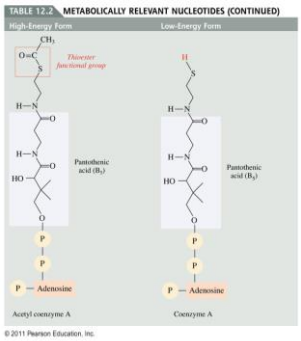


12.2 Metabolically Relevant Nucleotides, Continued

Acetyl Coenzyme A and Coenzyme A

- Acetyl coenzyme A is the high-energy form, and coenzyme A is the low-energy form, of this important energy exchanger.
- Energy is released from acetyl coenzyme A when the carbon–sulfur bond in the thioester functional group is hydrolyzed.
- CoA contains adenosine, three phosphates, and a vitamin-derived portion.

12.2 Metabolically Relevant Nucleotides, Continued



12.3 Digestion—From Fuel Molecules to Hydrolysis Products

- When we consume food, it is broken down in a process known as ***digestion***.
- In digestion, large biomolecules are broken down into smaller hydrolysis products.
- The hydrolyzed products are delivered to the cells for further catabolism.

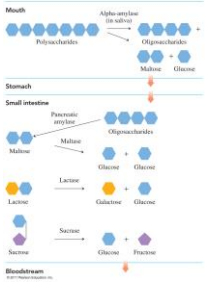
12.3 Digestion—From Fuel Molecules to Hydrolysis Products, Continued

Carbohydrates

- Starch (amylose and amylopectin) digestion begins in the mouth by the enzyme α-amylase secreted in saliva.
- Alpha-amylase hydrolyzes some of the α-glycosidic bonds in starch molecules, producing some glucose, the disaccharide maltose, and oligosaccharides.

12.3 Digestion—From Fuel Molecules to Hydrolysis Products, Continued

Complete digestion of starch molecules to monosaccharides takes place in the small intestine.



12.3 Digestion—From Fuel Molecules to Hydrolysis Products, Continued

- Other carbohydrates, like cellulose, cannot be digested because of the lack of the enzyme needed to hydrolyze the β-glycosidic bond.
- Indigestible fibers of cellulose are referred to as ***insoluble fiber*** and are important for a healthy digestive tract.
- Insoluble fiber stimulates the large intestine to excrete waste.

12.3 Digestion—From Fuel Molecules to Hydrolysis Products, Continued

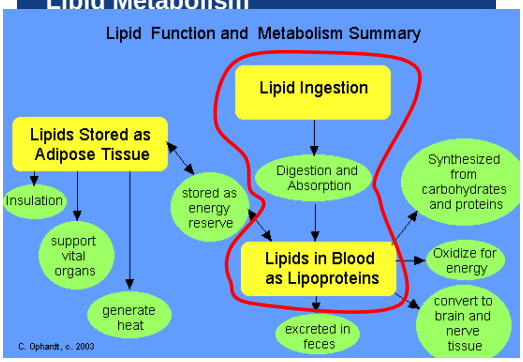
Fats

- Dietary fats are nonpolar and require bile, excreted from the gall bladder, to assist digestion.
- Bile contains soap-like molecules called ***bile salts***. They contain a polar and nonpolar part.
- Bile salts break up the larger nonpolar fat globules into smaller droplets called ***micelles***.

12.3 Digestion—From Fuel Molecules to Hydrolysis Products, Continued

- This process of is known as ***emulsification***.
- The smaller micelles move closer to the intestinal wall so cholesterol can be absorbed and triglycerides can be hydrolyzed by pancreatic lipase to free fatty acids and monoglycerides, which are then absorbed.
- Once across the intestinal wall, free fatty acids and monoglycerides are reassembled into triglycerides, and cholesterol forms a cholesterol ester with a free fatty acid.

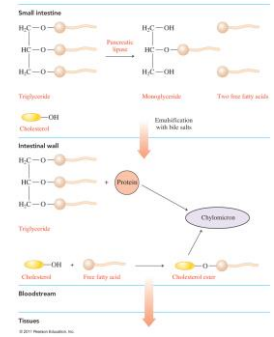
Lipid Metabolism

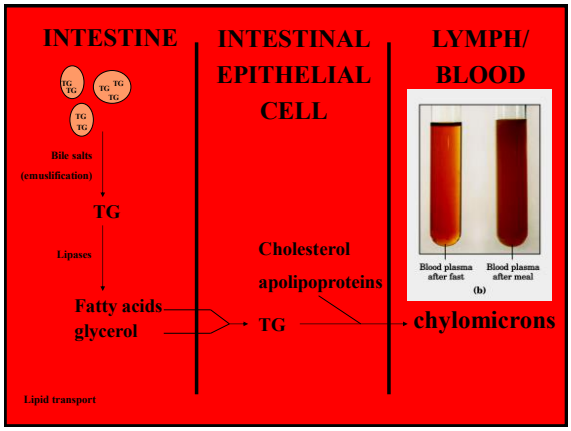


12.3 Digestion—From Fuel Molecules to Hydrolysis Products, Continued

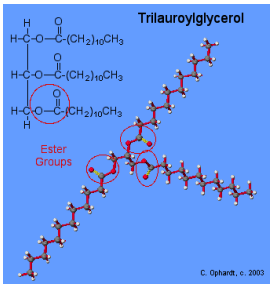
- Both are packaged with protein forming a lipoprotein called a ***chylomicron***.
- Chylomicrons transport triglycerides through the bloodstream to the tissues where they are used for energy production or stored in the cells.
- The process of fatty acid digestion is shown on the next slide.

12.3 Digestion—From Fuel Molecules to Hydrolysis Products, Continued





Lipid Metabolism



LIPID TRANSPORT

•Lipids are transported in the blood as lipoproteins

Lipids:

Cholesterol

Apolipoproteins +Cholesteryl esters → lipoproteins

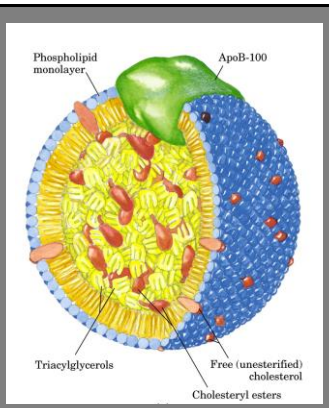
Triacylglycerols

Phospholids

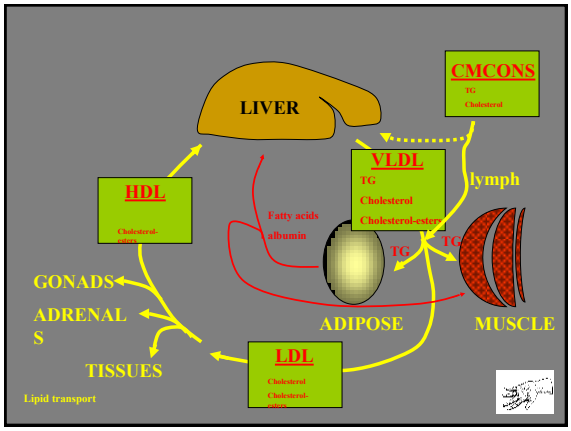
•There are 4 types of lipoprotein

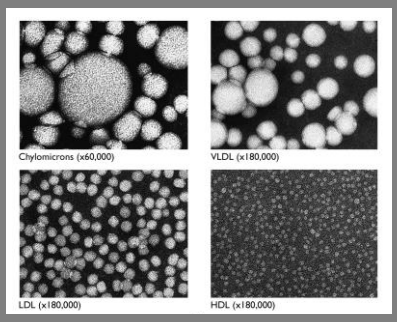
Lipid transport

LDL



Lipid transport





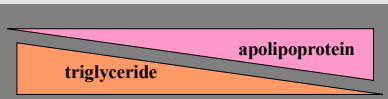
The lipoprotein formed depends on the constituent apoprotein and lipids

table 21–2

Major Classes of Human Plasma Lipoproteins: Some Properties

Lipoprotein	Density (g/mL)	Composition (wt %)				
		Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
Chylomicrons	<1.006	2	9	1	3	85
VLDL	0.95–1.006	10	18	7	12	50
LDL	1.006–1.063	23	20	8	37	10
HDL	1.063–1.210	55	24	2	15	4

Source: Modified from Kritchevsky, D. (1986) Atherosclerosis and nutrition. *Nutr. Int.* **2**, 290 – 297.



Chylo VLDL LDL HDL

Lipid transport

Atherosclerosis – fatty plaques in blood vessels

- High blood cholesterol – LDL receptor / hypercholesterolaemia

see Lehninger p811 for more info.

vessel occlusion – heart attack!

- High levels of LDL – probably bad
- High levels of HDL – probably good

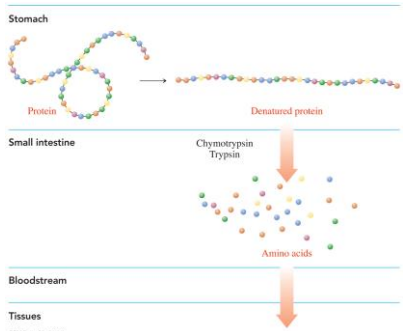
Lipid transport

12.3 Digestion—From Fuel Molecules to Hydrolysis Products, Continued

Proteins

- Protein digestion begins in the stomach. Proteins are denatured by the acidic digestive juices and are partially digested by pepsin.
- Complete digestion of proteins occurs in the small intestine by the enzymes trypsin and chymotrypsin. Free amino acids are absorbed into the bloodstream for delivery to the tissues.

12.3 Digestion—From Fuel Molecules to Hydrolysis Products, Continued



12.4 Glycolysis—From Hydrolysis Products to Common Metabolites

- ***Glycolysis*** is the chemical pathway for the catabolism of glucose, the main source of fuel for the body.
- When there is insufficient glucose entering the body, glucose is made in the body from noncarbohydrate molecules through a process called ***gluconeogenesis***.
- Glucose enters the cell with the aid of a transporter protein.

12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

- Glycolysis occurs in the cytosol where glucose is broken down into two three-carbon molecules of pyruvate.
- Molecules like fructose, amino acids, and free fatty acids can be used as fuel by the cells.
- These molecules enter glycolysis later in the pathway or by chemical conversion to one of the common metabolites.

12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

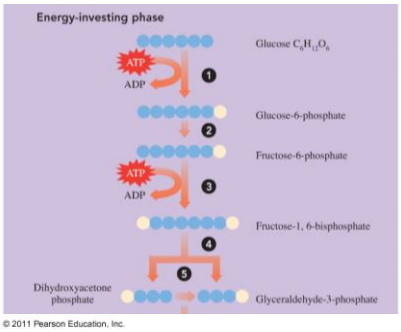
The Chemical Reactions in Glycolysis

- Energy must be transferred in small amounts to minimize the heat released during the process of glycolysis. Reactions that produce energy are coupled with reactions that require energy.
- In glycolysis, energy is transferred through phosphate groups undergoing condensation and hydrolysis reactions.

12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

- There are 10 chemical reactions in glycolysis to produce two molecules of pyruvate.
- The first five reactions require the investment of energy from two molecules of ATP, which are used to add a phosphate group to glucose and to fructose-6-phosphate.
- Two sugar phosphate molecules are formed in reaction 5.

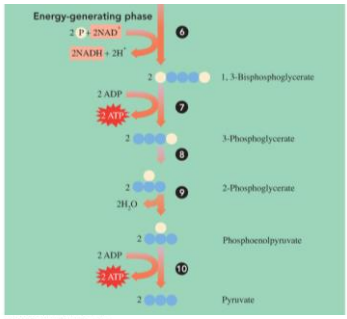
12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued



12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

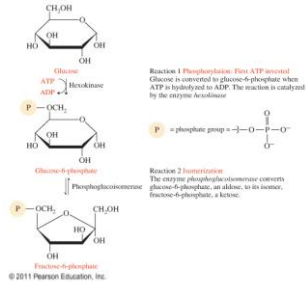
- Reactions 6–10 generate two high-energy NADH molecules and four ATP molecules.
- Two molecules of pyruvate are formed in reaction 10.

12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

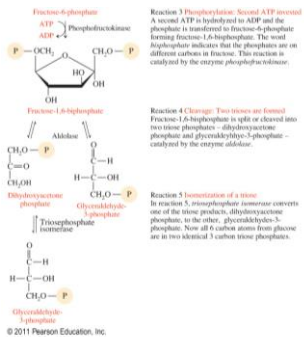


12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

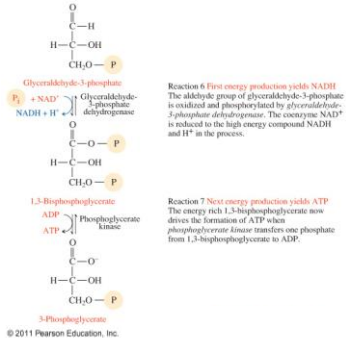
The complete sequence of events of glycolysis is shown in the next series of slides.



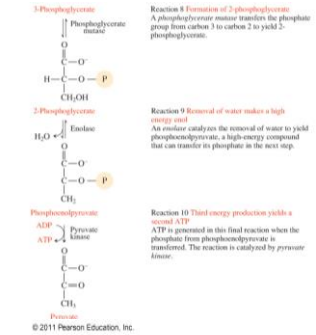
12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued



12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

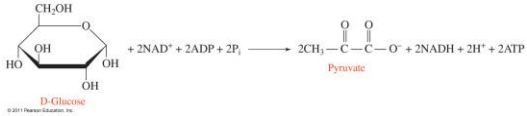


12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued



12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

- The net result of 10 reactions in glycolysis is that one molecule of glucose is converted to two molecules of pyruvate.
- The net energy output is two NADH and two ATP (4 ATP produced in reactions 6 through 10 minus 2 ATP used in reactions 1 through 5).



12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

Regulation of Glycolysis

- Metabolic pathways have one or more steps that regulate the flow of reactants to final product.
- Glycolysis is regulated at reaction 3 of the pathway.
- Phosphofructokinase, the enzyme formed in reaction 3, is regulated by ATP. ATP acts as an inhibitor to this enzyme. If the cells have enough ATP, glycolysis slows down.

12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

The Fates of Pyruvate

- Pyruvate can be broken down further to produce more energy. The availability of oxygen determines how this breakdown will occur.
- In ***aerobic conditions*** (ample oxygen), pyruvate is oxidized further to acetyl coenzyme A.
- In ***anaerobic conditions*** (lacking oxygen), pyruvate is reduced to lactate.

12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

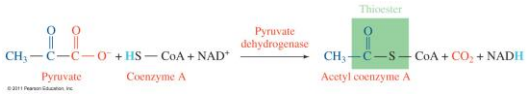
Aerobic Conditions

- The carboxylate functional group of pyruvate is liberated as CO_2, producing a two-carbon acetyl group and NADH.
- The acetyl group reacts with coenzyme A to produce acetyl coenzyme A.
- A high-energy thioester functional group is formed when acetyl coenzyme A is formed.

12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

Aerobic Conditions, Continued

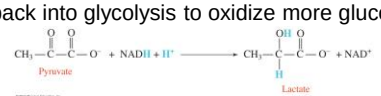
This reaction occurs in the mitochondria.



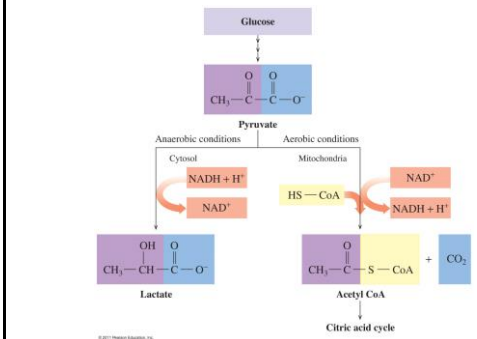
12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

Anaerobic Conditions

- During strenuous exercise, oxygen is in short supply.
- The middle carbonyl in pyruvate is reduced to an alcohol group, and lactate is formed.
- NADH supplies the hydrogen needed in the reaction. NAD^+ is produced.
- No energy is produced, so NAD^+ is funneled back into glycolysis to oxidize more glucose.

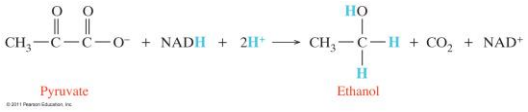


12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued



12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

- Yeast converts pyruvate to ethanol under anaerobic conditions. This process is known as ***fermentation***.
- Yeast is used in the preparation of alcoholic beverages.



12.4 Glycolysis—From Hydrolysis Products to Common Metabolites, Continued

Fructose and Glycolysis

- Fructose is converted to fructose-6-phosphate in the muscles and enters glycolysis at reaction 3.
- In the liver, it is converted to dihydroxyacetone phosphate and glyceraldehyde-3-phosphate, used in reaction 5. These two products provide an excess of reactants for glycolysis, creating excess pyruvate and acetyl CoA that is not needed and is ultimately converted to fat.

12.5 The Citric Acid Cycle—Central Processing

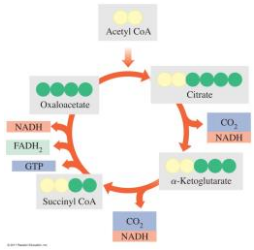
- When there is sufficient oxygen, glucose, fats, and amino acids enter the citric acid cycle.
- The ***citric acid cycle*** is a series of reactions that degrade the two-carbon acetyl groups from acetyl CoA into carbon dioxide while generating the high-energy molecules NADH and $FADH_2$.
- The citric acid cycle is also known as the ***Krebs cycle*** or the ***tricarboxylic acid cycle***.

12.5 The Citric Acid Cycle—Central Processing, Continued

- The first reaction in the cycle involves the condensation between acetyl CoA and a four-carbon molecule, oxaloacetate, which produces a six-carbon molecule, citrate. Hence, the name citric acid cycle.
- Citrate loses two carbons as CO_2 to form succinyl CoA.
- The breaking of the carbon–carbon bonds transfers energy to produce NADH from NAD^+.

12.5 The Citric Acid Cycle—Central Processing, Continued

Succinyl CoA, in a series of reactions, regenerates oxaloacetate, which starts the cycle again. NADH, $FADH_2$, and GTP are produced in these series of reactions.

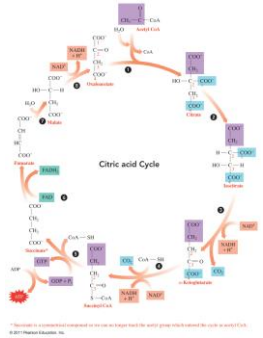


12.5 The Citric Acid Cycle—Central Processing, Continued

Reactions of the Citric Acid Cycle

- There are eight enzyme-catalyzed reactions in the citric acid cycle.
- The citric acid cycle occurs in the mitochondrial matrix.

12.5 The Citric Acid Cycle—Central Processing, Continued



12.5 The Citric Acid Cycle—Central Processing, Continued

Eight Reactions Shown in Figure 12.11

Reaction 1. *Formation of Citrate.* The acetyl group from acetyl CoA combines with oxaloacetate to form citrate.

Reaction 2. *Isomerization to Isocitrate.* Citrate contains a tertiary alcohol, which cannot be oxidized, so citrate isomerizes to isocitrate, which contains a secondary alcohol that can be oxidized to a carbonyl group. This step is necessary for the citric acid cycle to continue.

12.5 The Citric Acid Cycle—Central Processing, Continued

Eight Reactions Shown in Figure 12.11, Continued

Reaction 3. *First Oxidative Decarboxylation (Release of CO_2)*. Isocitrate is being oxidized to a ketone called α-ketoglutarate. The coenzyme NAD^+ is reduced to NADH. Decarboxylation of isocitrate occurs when a carboxylate (COO^-) is removed as CO_2.

Reaction 4. Second Oxidative Decarboxylation. A second redox reaction takes place. CO_2 is released, NAD^+ is reduced to NADH, and succinyl CoA is formed.

12.5 The Citric Acid Cycle—Central Processing, Continued

Eight Reactions Shown in Figure 12.11, Continued

- **Reaction 5. *Hydrolysis of Succinyl CoA.*** Succinyl CoA undergoes hydrolysis to succinate and coenzyme A. The energy that is released during this hydrolysis produces the high-energy nucleotide GTP, which is readily converted to ATP.
- **Reaction 6. *Dehydrogenation of Succinate.*** One hydrogen from each of the central carbon's of succinate loses a hydrogen (oxidation) to form fumarate. In the process, FAD is reduced to $FADH_2$.

12.5 The Citric Acid Cycle—Central Processing, Continued

Eight Reactions Shown in Figure 12.11, Continued

- **Reaction 7. *Hydration of Fumarate.*** Water adds to the double bond of fumarate to form malate.
- **Reaction 8. *Dehydrogenation Forms Oxaloacetate.*** The secondary alcohol of malate is oxidized to the ketone, oxaloacetate. NAD^+ is reduced to NADH.

12.5 The Citric Acid Cycle—Central Processing, Continued

Citric Acid Cycle Summary

- One turn of the citric acid cycle produces three NADH, one $FADH_2$, one GTP (forms ATP), two CO_2, and one CoA.
- The reactants in the cycle are regenerated, so the net reaction is:

$$\text{Acetyl CoA} + 3\,NAD^+ + FAD + GDP + P_i + 2\,H_2O \longrightarrow 2\,CO_2 + 3\,NADH + 2\,H^+ + FADH_2 + CoA + GTP$$

12.6 Electron Transport and Oxidative Phosphorylation

- A single molecule of glucose entering glycolysis and the citric acid cycle will produce two ATPs during glycolysis and two ATPs in the cycle.
- So, where is all the energy produced? It is produced in the mitochondria by a process called *oxidative phosphorylation*.
- The high-energy forms of the nucleotides NADH and $FADH_2$ are produced in glycolysis and the citric acid cycle.

12.6 Electron Transport and Oxidative Phosphorylation, Continued

- Electrons and hydrogens are transferred from the high-energy forms of the nucleotides through the inner mitochondrial membrane and combine with oxygen to produce water.
- Energy from this process drives the reaction ADP + P_i to form ATP. This process of producing ATP from reduced nucleotides is called ***oxidative phosphorylation***.

12.6 Electron Transport and Oxidative Phosphorylation, Continued

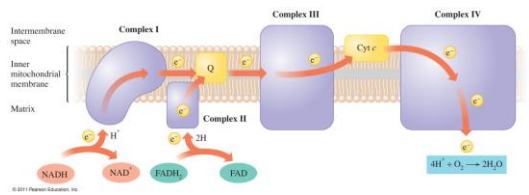
Electron Transport

- Mitochondria are the ATP factories of the cell.
- Reduced nucleotides are produced in the mitochondria, and their energy upon oxidation is used to produce ATP.
- The citric acid cycle occurs in the mitochondrial matrix, and the reduced nucleotides begin their journey through the inner membrane here.

12.6 Electron Transport and Oxidative Phosphorylation, Continued

- Complexes I and IV, a set of enzyme complexes, are located in the inner membrane of mitochondria.
- Electron carriers located in these complexes carry the electrons and protons of NADH and $FADH_2$ through the inner mitochondrial membrane.
- Electron carriers, coenzyme Q and cytochrome *c*, are not membrane-bound, so they serve to shuttle electrons between complexes.

12.6 Electron Transport and Oxidative Phosphorylation, Continued



12.6 Electron Transport and Oxidative Phosphorylation, Continued

- ***Complex I NADH Dehydrogenase***
  - NADH enters here. Two electrons and two protons are transferred to coenzyme Q. NAD^+ is regenerated and returns to the citric acid cycle.

$$NADH + H^+ + Q \rightarrow NAD^+ + QH_2$$

- ***Complex II Succinate Dehydrogenase***
  - $FADH_2$ enters at this complex. Two electrons and two protons from $FADH_2$ are also transferred to a coenzyme Q to form QH_2.

$$FADH_2 + Q \rightarrow FAD + QH_2$$

12.6 Electron Transport and Oxidative Phosphorylation, Continued

- ***Complex III Coenzyme Q—Cytochrome c Reductase***
  - QH_2 molecules are reoxidized to Q. Electrons are transferred to cytochrome *c*, which moves the electrons from complex III to complex IV.
- ***Complex IV Cytochrome c Oxidase***
  - Electrons are transferred from cytochrome *c* to combine with hydrogen ions and oxygen to form water. This is the final stop for electrons.

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

12.6 Electron Transport and Oxidative Phosphorylation, Continued

Oxidative Phosphorylation

- Energy is produced as a result of electron transport generating a proton (H^+) difference, or ***gradient***, on either side of the inner membrane. This is known as the ***chemiosmotic model***.
- Complexes I, III, and IV span the inner membrane and pump protons from the matrix into the intermembrane space as electrons are shuttled through the complexes.

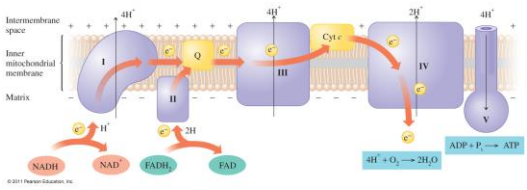
12.6 Electron Transport and Oxidative Phosphorylation, Continued

- An electrical charge difference, as well as a difference in concentration of protons on either side of the membrane, results in an ***electrochemical gradient***.
- The proton gradient provides the energy necessary for ATP synthesis.
- Protons move back to the matrix by passing through a protein complex called complex V, or ATP synthase.

12.6 Electron Transport and Oxidative Phosphorylation, Continued

The movement of protons from an area of high concentration of protons to an area of fewer protons releases energy that drives ATP synthase.

$$ADP + P_i + \text{energy} \rightarrow ATP$$



12.6 Electron Transport and Oxidative Phosphorylation, Continued

Thermogenesis—Uncoupling ATP Synthase

- ***Thermogenesis*** is the generation of body heat. It occurs when the proton pump is disrupted and ATP is not produced.
- Some animals adapted to cold climates produce small organic molecules called ***uncouplers***, which uncouple electron transport and oxidative phosphorylation, thereby assisting in regulating their body temperatures.

12.6 Electron Transport and Oxidative Phosphorylation, Continued

- These animals have high amounts of ***brown fat***, so called because this fat contains high concentrations of mitochondria.
- Iron ions contained in the cytochrome molecules in the mitochondria are responsible for the color of brown fat.
- Babies have higher concentrations of brown fat than adults because they do not have much stored fat.

12.7 ATP Production

How Many ATPs Are Synthesized for Each Reduced Nucleotide Entering Electron Transport?

- NADH and $FADH_2$ enter the electron transport chain at different complexes, so the amount of energy produced for each is different.
- Ten H^+ are pumped for each NADH, and six H^+ are pumped for each $FADH_2$.

12.7 ATP Production, Continued

- Four H^+ are required for each ATP synthesized.
- The number of ATPs/NADH is 10/4 = 2.5.
- The number of ATPs/ $FADH_2$ is 6/4 = 1.5.

Nucleotide Input	Protons (H^+) Pumped	ATP Output
NADH	10	2.5
$FADH_2$	6	1.5

12.7 ATP Production, Continued

Counting ATP from One Glucose

How much ATP is generated from one molecule of glucose during oxidative catabolism?

- Glycolysis
  - One molecule of glucose produces two molecules of pyruvate, two molecules of ATP, and two molecules of NADH.
  - The direct shuttling of two NADH into the matrix results in the production of five ATPs.

12.7 ATP Production, Continued

Counting ATP from One Glucose, Continued

- Oxidation of pyruvate
  - The two pyruvate molecules are oxidized to produce two acetyl CoA, two CO_2, and two NADH.
  - The two NADH account for five ATPs.
- Citric acid cycle
  - Each acetyl CoA produced enters the citric acid cycle.
  - A total of six NADH, two $FADH_2$, and two ATPs are produced.
  - Note the accompanying art at the top of the next slide.

12.7 ATP Production, Continued

Counting ATP from One Glucose, Continued

6 NADH	$\longrightarrow$ 15 ATP
2 $FADH_2$	$\longrightarrow$ 3 ATP
Directly in pathway	$\longrightarrow$ 2 ATP
Total ATP for two acetyl CoAs: 20 ATP	

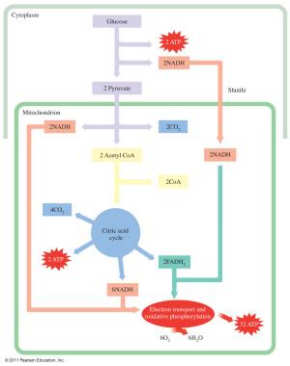
Total ATP from glucose oxidation: By summing the ATPs produced from glycolysis, pyruvate oxidation, and the citric acid cycle, a net number of ATPs/glucose can be estimated.

12.7 ATP Production, Continued

TABLE 12.3 ATP PRODUCED BY THE COMPLETE OXIDATION OF GLUCOSE

Pathway	Reduced Nucleotides Produced	ATP Yield
Glycolysis	$2NADH_{cytosol} \longrightarrow 2NADH_{matrix}$	5 ATP
(Produced directly in pathway)		2 ATP
2 Pyruvate $\longrightarrow$ 2 Acetyl CoA	2NADH	5 ATP
Citric acid cycle Two turns of the cycle accommodates 2 acetyl CoA	6 NADH 2$FADH_2$	15 ATP 3 ATP
(Produced as GTP in pathway)		2 ATP
	TOTAL ATP	32 ATP

12.7 ATP Production, Continued



12.8 Other Fuel Choices

- Glucose is our primary source of fuel. It is stored as glycogen in the liver and muscles.
- ***Glycogenolysis*** (hydrolysis of glycogen) produces glucose quickly when glucose concentrations are low.
- Once glycogen stores are depleted, glucose is synthesized from noncarbohydrate sources through ***gluconeogenesis***.

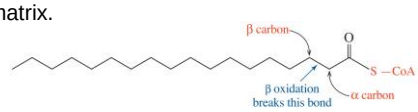
12.8 Other Fuel Choices, Continued

Energy from Fatty Acids

- When glucose and glycogen are not available, fatty acids can be oxidized to acetyl CoA through a process known as ***beta oxidation***.
- In beta oxidation, carbons are removed two at a time from an activated fatty acid.
- An activated fatty acid consists of a fatty acid bonded to a CoA, called a ***fatty acyl CoA***.

12.8 Other Fuel Choices, Continued

- Removal of two carbons during oxidation produces an acetyl CoA and a fatty acyl CoA shortened by two carbons.
- The cycle is repeated until the original fatty acid is completely degraded to acetyl CoA units.
- Beta oxidation occurs in the mitochondrial matrix.



Fatty acyl CoA containing 18 carbons

12.8 Other Fuel Choices, Continued

The Beta Oxidation Cycle

- **Reaction 1. *Oxidation (Dehydrogenation).*** One hydrogen from each of the α and β carbons is removed and a double bond is formed. $FADH_2$ is produced.
- **Reaction 2. *Hydration*.** Water is added across the double bond between the α and β carbons.
- **Reaction 3. *Oxidation (Dehydrogenation).*** The alcohol formed is oxidized to a ketone. NADH is produced.

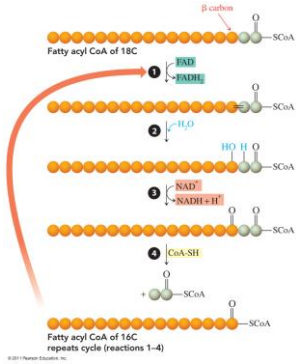
12.8 Other Fuel Choices, Continued

The Beta Oxidation Cycle, Continued

- **Reaction 4. *Removal of Acetyl CoA.*** The bond between the alpha and beta carbon is broken. A second CoA is added forming a fatty acyl CoA shortened by two carbons. The cycle continues.
- The net for one cycle of beta oxidation is:

$$\text{Fatty acyl CoA}_{n \text{ carbons}} + NAD^+ + FAD + H_2O + CoA \longrightarrow \text{Fatty acyl CoA}_{n-2 \text{ carbons}} + \text{Acetyl CoA} + NADH + H^+ + FADH_2$$

12.8 Other Fuel Choices, Continued



12.8 Other Fuel Choices, Continued

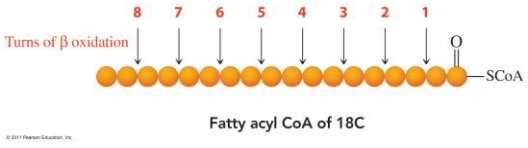
Cycle Repeats and ATP Production

- Consider the saturated 18-carbon fatty acid, stearic acid.
- Two carbons will produce an acetyl CoA, so nine acetyl CoA are produced from stearic acid.
- This will take eight turns of the beta oxidation cycle since the last turn produces two acetyl CoA.

12.8 Other Fuel Choices, Continued

Cycle Repeats and ATP Production, Continued

Turns of beta oxidation for the 18-carbon fatty acyl CoA is shown as:



12.8 Other Fuel Choices, Continued

The Beta Oxidation Cycle

ATP production from beta oxidation for a stearic acid molecule is:

ATP PRODUCTION FROM β OXIDATION FOR A STEARIC ACID (18C) MOLECULE	
9 Acetyl CoA 9 Acetyl CoA × 10 ATP/acetyl CoA	90 ATP
8 turns of β oxidation 8 NADH × 2.5 ATP/NADH	20 ATP
8 $FADH_2$ × 1.5 ATP/$FADH_2$	12 ATP
Total	122 ATP

12.8 Other Fuel Choices, Continued

Too Much Acetyl CoA—Ketosis

- In the absence of glucose, the body breaks down its body fat to continue ATP production.
- Oxidation of fatty acids cause large amounts of acetyl CoA to accumulate in the liver.
- When this occurs, two acetyl units condense, forming the four-carbon ketone molecules β-hydroxybutyrate and acetoacetate. Acetone is also produced.

12.8 Other Fuel Choices, Continued

- These three ketones are referred to as ***ketone bodies***.
- Their formation is termed ***ketogenesis***.
- ***Ketosis*** occurs when an excessive amount of ketone bodies are present in the body.
- Ketosis is often seen in individuals with diabetes.

12.8 Other Fuel Choices, Continued

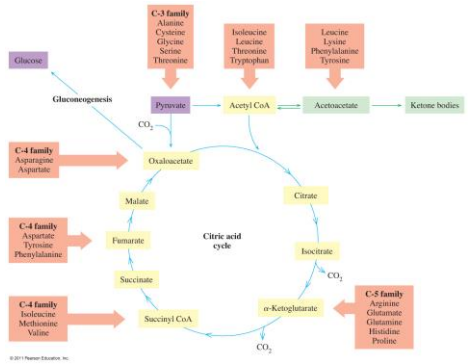
Energy from Amino Acids

- Nitrogen is produced when amino acids from proteins are metabolized.
- The α-amino group is removed yielding an α-keto acid through a process called ***transamination***.
- The α-keto acid can be converted into intermediates for other metabolic pathways.

12.8 Other Fuel Choices, Continued

- Ammonium ions produced during transamination are toxic to the body and are removed as urea through a series of reactions called the ***urea cycle***.
- Amino acids can replenish the intermediates in the citric acid cycle and therefore, have the ability to produce ATP.
- The number of carbons in the amino acid determines which intermediates are replenished.

12.8 Other Fuel Choices, Continued



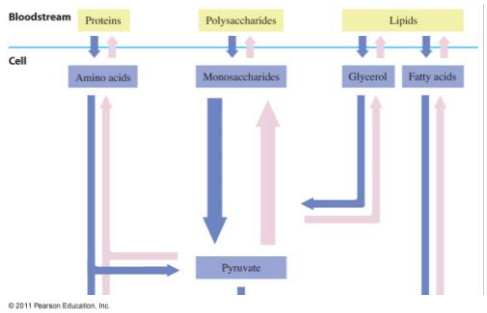
12.8 Other Fuel Choices, Continued

- We get about 10% of our energy from amino acids.
- More energy is extracted from amino acids during periods of fasting or starvation.
- When amino acids are our only source of energy, proteins in body tissues are degraded.

12.8 Other Fuel Choices, Continued

- Catabolic pathways produce high-energy molecules.
- Anabolic pathways synthesize larger molecules from smaller metabolites when necessary.
- Degradation of food biomolecules begins with digestion, where larger molecules are metabolized into smaller metabolites so they can enter the cell, where they eventually produce pyruvate or enter into the mitochondria to produce acetyl CoA.

12.8 Other Fuel Choices, Continued

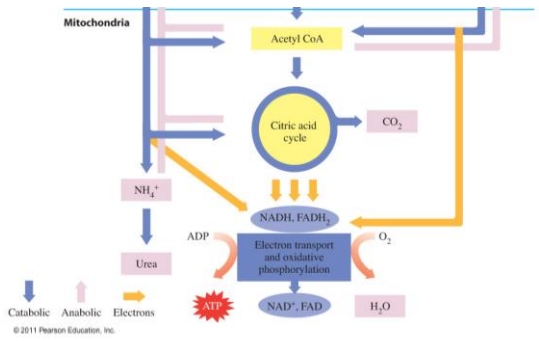


12.8 Other Fuel Choices, Continued

Putting It Together: Linking the Pathways

- Glucose is the body's main source of energy. It is degraded to acetyl CoA, then enters the citric acid cycle to produce energy. Glucose can be converted to glycogen for storage.
- Large biomolecules are metabolized into smaller metabolites, which eventually produce acetyl CoA that enters the citric acid cycle, followed by electron transport and oxidative phosphorylation.

12.8 Other Fuel Choices, Continued



12.8 Other Fuel Choices, Continued

- Amino acids provide nitrogen for anabolism of nitrogen compounds.
- Their carbons can enter the citric acid cycle as α-keto acids if necessary.

