

CHAPTER 5
Cell Respiration and Metabolism

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Chapter 5 Outline

- ▶ Glycolysis and the Lactic Acid Pathway
- ▶ Aerobic Respiration
- ▶ Metabolism of Lipids and Proteins

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Metabolism

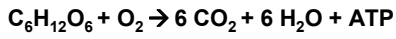
- ▶ Is all reactions in body that involve energy transformations
- ▶ **Divided into 2 categories:**
 - ▶ **Catabolism** breaks down molecules and releases energy
 - ▶ Is primary source of energy for making ATP
 - ▶ **Anabolism** makes larger molecules and requires energy
 - ▶ Source of body's large energy-storage compounds

Catabolism Drives Anabolism

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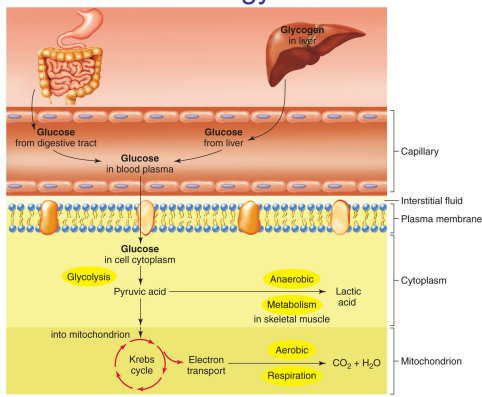
Complete Catabolism of Glucose

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



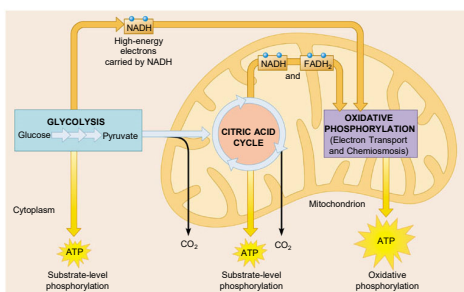
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Overview of Energy Metabolism



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► An overview of cellular respiration



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Glycolysis

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Glycolysis

- ▶ Is metabolic pathway by which **glucose** is converted into **2 pyruvic acid**
- ▶ **Does not require oxygen**
- ▶ Overall net equation is:
 - ▶ $\text{Glucose} + 2\text{NAD}^+ + 2\text{ADP} + 2\text{P}_i \rightarrow 2\text{Pyruvic acid} + 2\text{NADH} + 2\text{ATP}$

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▶ Glycolysis harvests chemical energy by oxidizing glucose to pyruvate

- ▶ In glycolysis, ATP is used to prime a glucose molecule
 - ▶ Which is split into two molecules of pyruvate

Figure 6.7A

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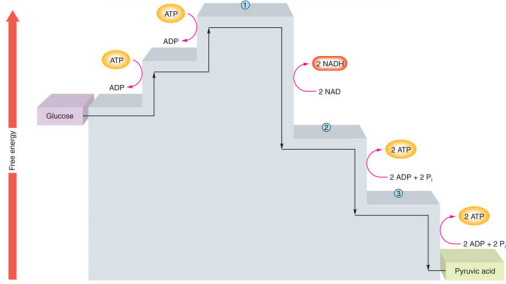
Glycolysis

- ▶ Glycolysis is exergonic - produces **net of 2ATPs** and **2NADHs**
- ▶ However, glucose must be activated with 2ATPs (**phosphorylation**) before energy can be obtained
 - ▶ Phosphorylation traps glucose inside cell

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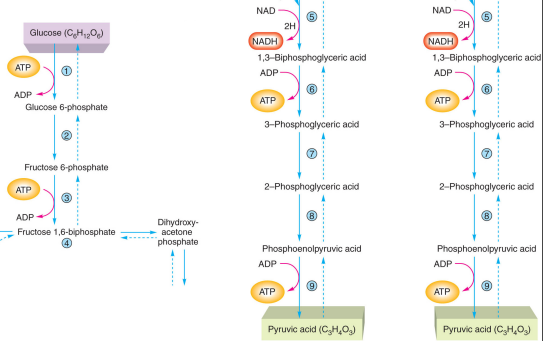
Glycolysis

- ▶ In glycolysis 2ATPs are added and 4 are produced for a **net gain of 2 ATP**



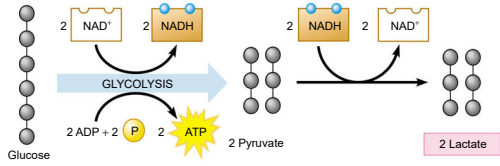
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Glycolysis



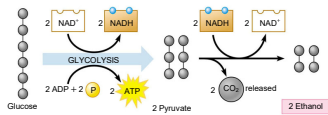
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- ▶ In lactic acid fermentation
 - ▶ NADH is oxidized to NAD⁺ as pyruvate is reduced to lactate



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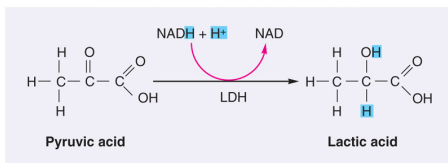
- ▶ In alcohol fermentation
 - ▶ NADH is oxidized to NAD⁺ while converting pyruvate to CO₂ and ethanol



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Lactic Acid Pathway

- ▶ To avoid end-product inhibition NADHs produced in glycolysis need to give Hs away
- ▶ In absence of O₂ NADH gives its Hs to pyruvic acid creating lactic acid (anaerobic metabolism or lactic acid fermentation)



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Lactic Acid Pathway

- ▶ Only yields a **net gain of 2 ATPs per glucose**
- ▶ RBCs don't have mitochondria; use only lactic acid pathway
- ▶ Occurs in skeletal and heart muscle when oxygen supply falls below critical level
 - ▶ During heavy exercise or vascular blockage

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Glycogenesis and Glycogenolysis

- ▶ For osmotic reasons cells can't store many free glucoses
 - ▶ Instead store glucose as glycogen (**glycogenesis**)
 - ▶ Skeletal muscle and liver store lots of glycogen
 - ▶ **Glycogenolysis** clips glucose out of glycogen as glucose 6-phosphate
 - ▶ Phosphate groups trap molecules in cells

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Glycogenesis and Glycogenolysis

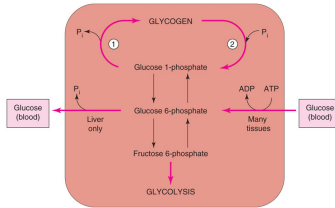
Table 5.1 | Common Terms for Some Metabolic Processes in the Body

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

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Glycogenesis and Glycogenolysis

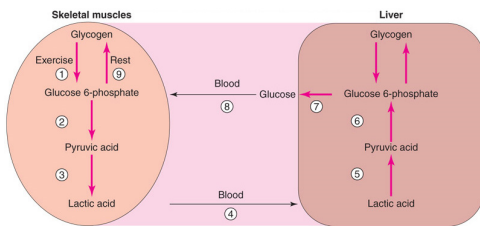
- ▶ Skeletal muscles use trapped glucose-6-phosphate for own energy needs
- ▶ Only liver has glucose-6-phosphatase that removes phosphate groups
 - ▶ So it can secrete free glucose into blood



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Cori Cycle

- ▶ Some skeletal muscle lactic acid goes to liver
 - ▶ Where it is converted back through pyruvic acid to glucose and glycogen
 - ▶ Called **gluconeogenesis**
 - ▶ Also can happen with amino acids and glycerol



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How Glycolysis Works

6-carbon glucose

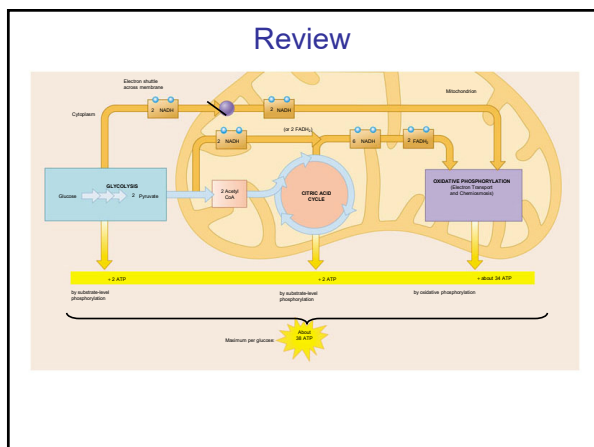
Cells derive energy from the oxidation of nutrients such as glucose. The oxidation of glucose to pyruvate occurs through a series of steps called glycolysis.

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Aerobic Respiration

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Aerobic Respiration

- Begins when pyruvic acid formed by glycolysis enters mitochondria
- CO₂ is clipped off pyruvic acid forming acetyl CoA (coenzyme A is a carrier for acetic acid)
- CO₂ goes to lungs
- Energy in acetyl CoA is extracted during aerobic respiration in mitochondria

$$\begin{array}{c}
 \text{H} \\
 | \\
 \text{H}-\text{C}-\text{H} \\
 | \\
 \text{C}=\text{O} \\
 | \\
 \text{HO}-\text{C} \\
 || \\
 \text{O}
 \end{array}
 + \text{S}-\text{CoA}
 \xrightarrow{\text{NAD} \rightarrow \text{NADH} + \text{H}^+}
 \begin{array}{c}
 \text{H} \\
 | \\
 \text{H}-\text{C}-\text{H} \\
 | \\
 \text{C}=\text{O} \\
 | \\
 \text{S}-\text{CoA}
 \end{array}
 + \text{CO}_2$$

Pyruvic acid Coenzyme A Acetyl coenzyme A

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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.

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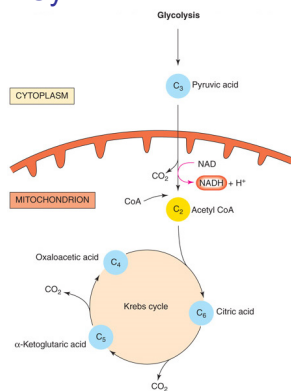
Important Events in the Krebs Cycle

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 FADH₂.
- ▶ These events occur for each acetic acid, so happen twice for each glucose molecule.

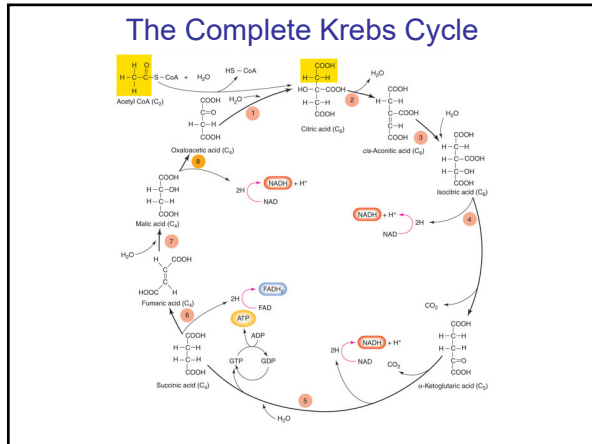
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Krebs Cycle

- ▶ Begins with acetyl CoA combining with **oxaloacetic acid** to form **citric acid**
- ▶ In a series of reactions citric acid converted back to oxaloacetic acid to complete the pathway



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Products of Krebs Cycle

- ▶ For each glucose:
 - ▶ 6 NADH
 - ▶ 2 FADH_2
 - ▶ 2 ATP
 - ▶ 4 CO_2

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

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How the Krebs Cycle Works

Cell cytoplasm

Mitochondrion

Play Pause Audio Text

During glycolysis, glucose is broken down to pyruvate.

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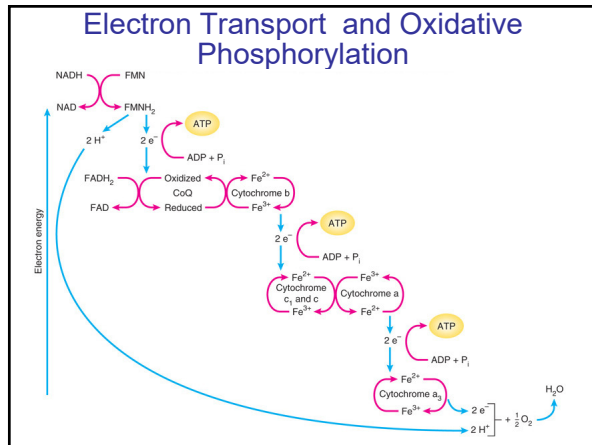
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Electron Transport and Oxidative Phosphorylation

- ▶ The electron transport chain is a linked series of proteins on the cristae of mitochondria
 - ▶ Proteins are FMN, coenzyme Q, and cytochromes
- ▶ NADH and FADH₂ from Krebs carry electrons to ETC
 - ▶ Which are then shuttled in sequence through ETC
 - ▶ NAD and FAD are regenerated to shuttle more electrons from Krebs Cycle to ETC

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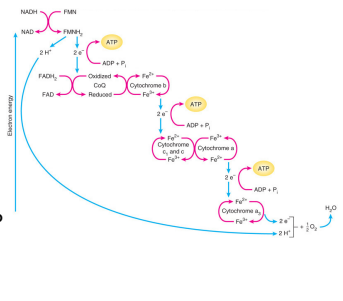
Electron Transport and Oxidative Phosphorylation



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Electron Transport and Oxidative Phosphorylation

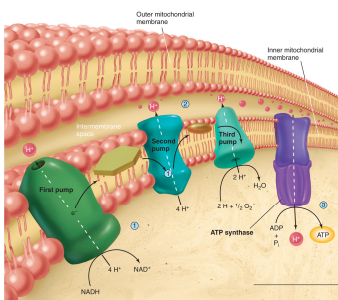
- ▶ As each protein in ETC accepts electrons it is reduced
 - ▶ When it gives electrons to next protein it is oxidized
- ▶ This process is exergonic
 - ▶ Energy is used to phosphorylate ADP to make ATP
 - ▶ Called oxidative phosphorylation



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Chemiosmotic Theory

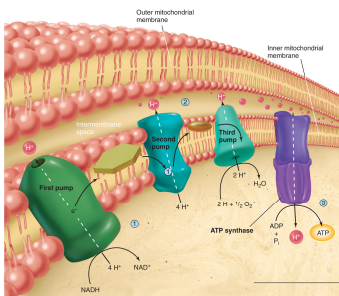
- ▶ Energy gathered by ETC is used to pump H⁺s into mitochondrial outer chamber
- ▶ Creating high H⁺ concentration there
- ▶ As H⁺s diffuse down concentration and charge gradient thru **ATP synthase**, and back into inner chamber, their energy drives ATP synthesis (**Chemiosmotic theory**)



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Function of Oxygen

- ▶ Electrons added to beginning of ETC are passed along until reach end
- ▶ Have to be given away or would stop ETC
- ▶ O₂ accepts these electrons and combines with 4H⁺s
- ▶ $O_2 + 4 e^- + 4 H^+ \rightarrow 2 H_2O$



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ATP Formation

- ▶ ATP can be made 2 ways:
 - ▶ **Direct (substrate-level) phosphorylation**
 - ▶ Where ATP is generated when bonds break
 - ▶ Both ATPs in glycolysis made this way
 - ▶ 2 ATPs/glucose in Kreb's made this way
 - ▶ **Oxidative phosphorylation** in Kreb's
 - ▶ Where ATP generated by ETC
 - ▶ 30-32 ATPs made this way

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ATP Formation

- ▶ 3H⁺s pass thru ATP synthase to generate 1 ATP
- ▶ This yields 36-38 ATPs/glucose
 - ▶ However some of these are used to pump ATPs out of mitochondria
 - ▶ So net yield is 30-32 ATPs/glucose
 - ▶ Really takes 4H⁺s to generate 1 exported ATP

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Production of ATP by ETC

- ▶ 2.5 ATP produced for each pair of electrons NADH donates
- ▶ 1.5 ATP produced for each pair of electrons FADH₂ donates
- ▶ Net of 26 ATP produced in ETC

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Net Production of ATP

- ▶ 34 ATP produced in ETC
- ▶ 2 from glycolysis
- ▶ 2 from direct phosphorylation in Krebs
- ▶ For total of 38 ATPs for each glucose

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Detailed Accounting

Table 5.2 | ATP Yield per Glucose in Aerobic Respiration

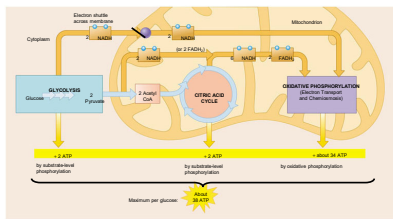
Phases of Respiration	ATP Made Directly	Reduced Coenzymes	ATP Made by Oxidative Phosphorylation	
			Theoretical Yield	Actual Yield
Glucose to pyruvate (in cytoplasm)	2 ATP (net gain)	2 NADH, but usually goes into mitochondria as 2 FADH ₂	If from FADH ₂ : 2 ATP (× 2) = 4 ATP or if stays NADH: 3 ATP (× 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

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Review

Each molecule of glucose yields many molecules of ATP
Oxidative phosphorylation, using electron transport and chemiosmosis

Produces up to 38 ATP molecules for each glucose molecule that enters cellular respiration



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Metabolism of Lipids and Proteins

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Energy from Other Molecules

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

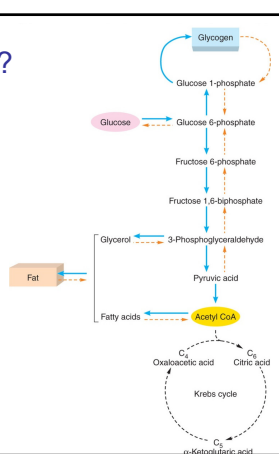
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Too Much Energy?

- ▶ 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.

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Too Much Energy?



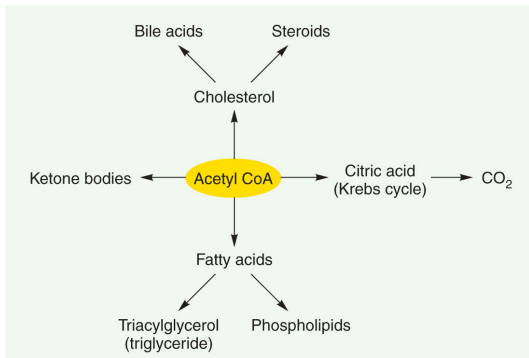
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Lipid Metabolism

- ▶ 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.

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Acetyl CoA → Lipids



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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.

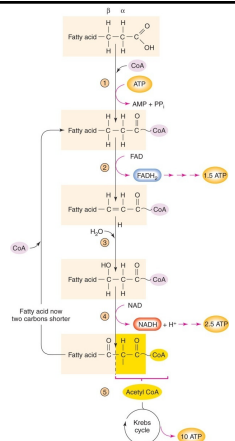
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Fatty Acids as an Energy Source

- ▶ 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 \rightarrow 8 acetyl CoA
 - ▶ Each acetyl CoA \rightarrow 10 ATP + 1 NADH + 1 FADH_2
 - ▶ A 16-carbon fatty acid \rightarrow 80 ATP + 28 in electron transport = **108 ATP!!!**

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β -oxidation of Fat



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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.

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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.

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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**.

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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

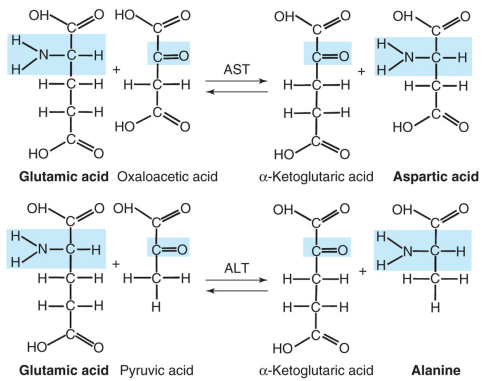
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Transamination

- ▶ Pyruvate and several Krebs cycle intermediates (called **keto acids**) can be converted to amino acids by adding an amine group (NH₂).
- ▶ Usually obtained from other amino acids
- ▶ Called **transamination**
- ▶ Requires vitamin B₆ as a coenzyme

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Transamination

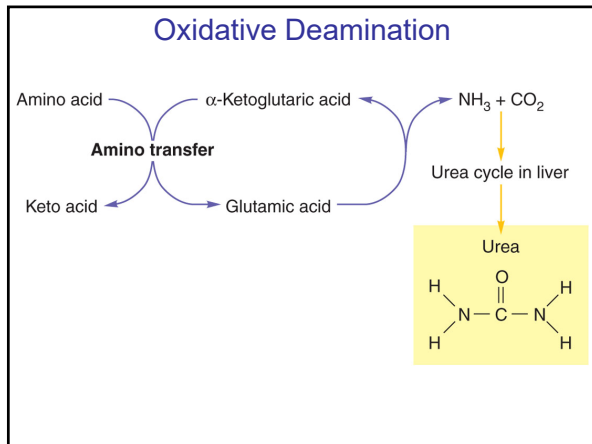


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Oxidative Deamination

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

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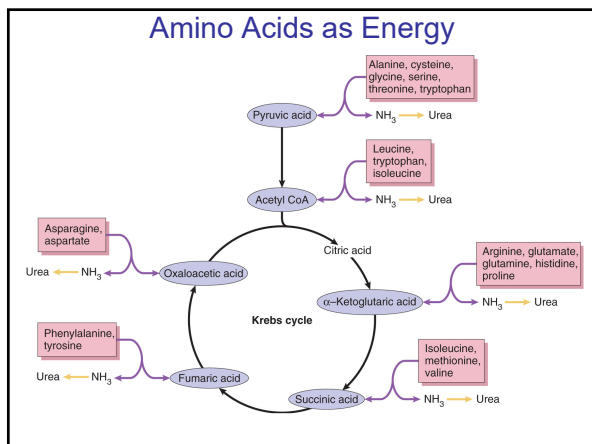


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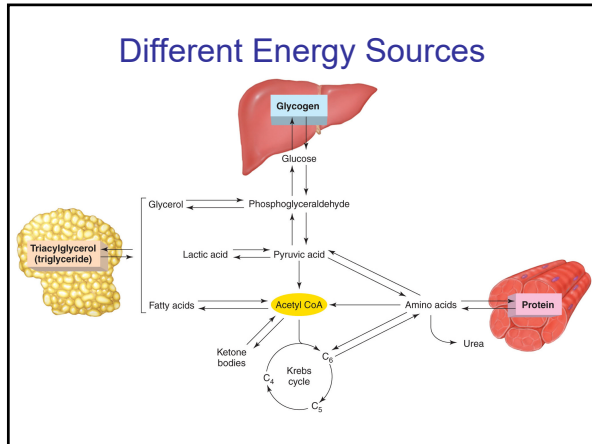
Amino Acids as Energy

- ▶ 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.

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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	+	++	+	+

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