

Metabolism - Part 1

Glycolysis & Respiration



Cells harvest chemical energy from foodstuffs in a series of exergonic reactions. The harvested energy can then be used to power energy demanding processes including endergonic reactions.

1

Metabolism - the sum of all chemical processes carried out by living cells

Catabolism - the chemical reactions that break larger molecules into smaller molecules. It is usually an exergonic process.

Anabolism - the chemical reactions that form larger molecules from smaller molecules. It is usually an endergonic process.

Autotroph - an organism that obtains its energy from sunlight or inorganic chemicals. Plants, photosynthetic protists, and photosynthetic prokaryotes are autotrophs.

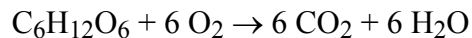
Heterotroph - an organism that obtains its energy by consuming and degrading organic molecules. Some eat other organisms, some parasitize, some degrade the remains of once-living organisms. Animals, Fungi, many protists and most prokaryotes are heterotrophs.

2

Glucose is the preferred energy source of all organisms and it is the principal product of photosynthesis.

Glucose breakdown can be aerobic (using oxygen) or anaerobic (without oxygen). Anaerobic metabolism of glucose is also known as **anaerobic glycolysis** or **fermentation**. Aerobic metabolism of glucose is known as **glycolysis and respiration**.

Complete aerobic metabolism of glucose produces water and carbon dioxide as products.



Energy is released in this process. The overall ΔG of glucose breakdown is -720 kcal/mole. Normally about 32% of the energy is released is captured through the formation of ATP the remainder is released as heat.

3

Aerobic breakdown of glucose consists of four stages

1. **Glycolysis** - a 10 step biochemical pathway where a glucose molecule (6 C) is split into 2 molecules of pyruvate (3 C). To begin the process 2 ATP must be invested. Energy released from the reactions is captured in the form of 4 molecules of ATP molecules and high energy electrons are trapped in the reduction of 2 molecules NAD to NADH.

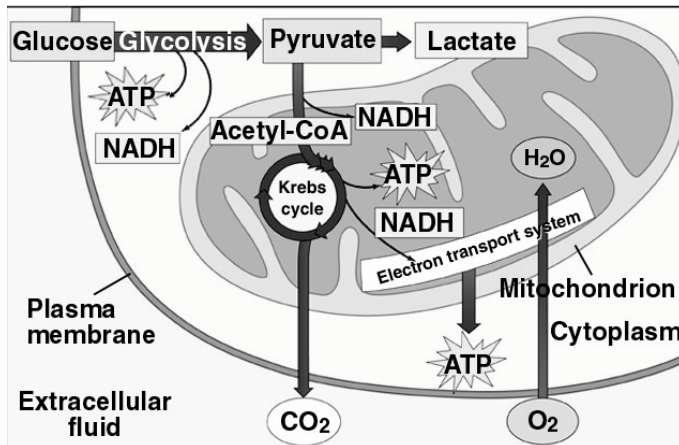
The remaining steps are collectively called **Respiration**.

2. **Pyruvate oxidation** - In a single step a carbon is removed from pyruvate (3C) as CO₂, leaving 2 of the original carbons attached to Coenzyme-A. The complex is called Acetyl Co-A. In this process one NADH molecule is produced.

3. **Krebs cycle** - A 9 step biochemical pathway that converts all of the carbon from the original glucose into CO₂, and yields 1 ATP, and traps high energy electrons in 3 NADH, and 1 FADH.

4

4. **Electron Transport Chain** - the high energy electrons trapped in NADH and FADH in the previous steps are used to produce ATP through chemiosmosis. O_2 is the final acceptor of high energy electrons.



In eukaryotes, glycolysis occurs in the cytoplasm, pyruvate oxidation, the Krebs cycle and the Electron Transport System occur in the mitochondrion

5

Energy tally - starting with glucose and following all carbons

Glycolysis: Glucose \rightarrow 2 pyruvate + 2 ATP (net) + 2 NADH

Pyruvate oxidation: - 2 pyruvate \rightarrow 2 Acetyl Co-A + 2 NADH

Krebs Cycle:

2 Acetyl Co-A \rightarrow 4 CO_2 + 2 ATP + 6 NADH + 2 FADH

Electron transport system (ETS):

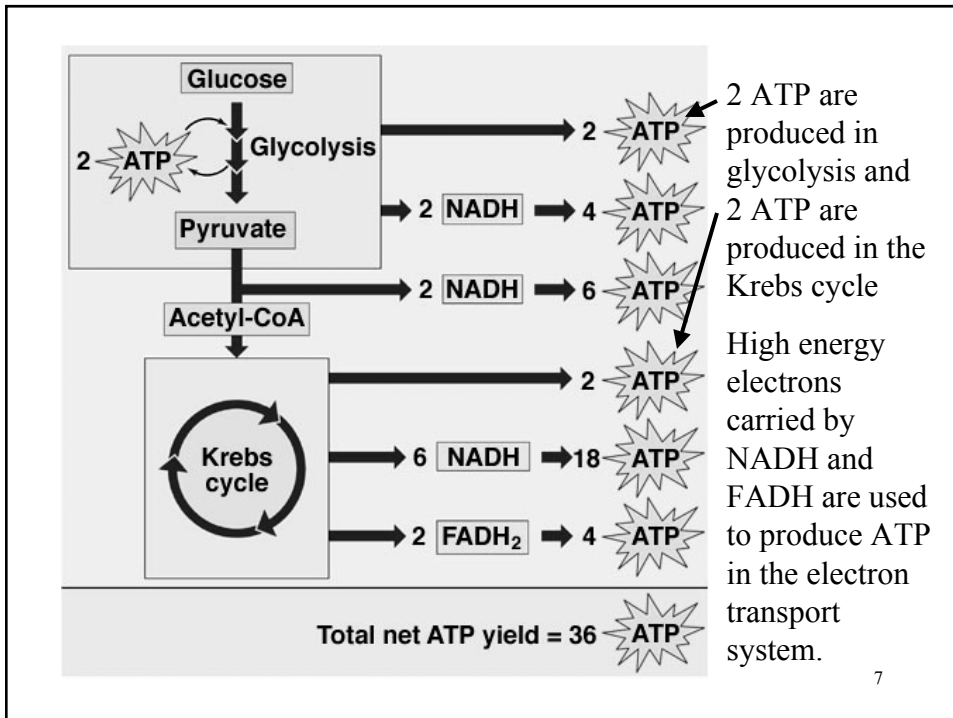
2 NADH from glycolysis allow production of 4 ATP

2 NADH from pyruvate oxidation allow production of 6 ATP

6 NADH from the Krebs cycle allow the production of 18 ATP

2 FADH from Krebs cycle allow the production of 4 ATP

6



Theoretical Energy Efficiency of Glycolysis and Respiration

Glucose contains 720 kcal/ mole

ATP contains 7.3 kcal/mole

36 ATP are harvested from each molecule of glucose:

2 from glycolysis

2 from Krebs cycle

32 from ETS

or 36 moles of ATP are harvested from 1 mole of glucose

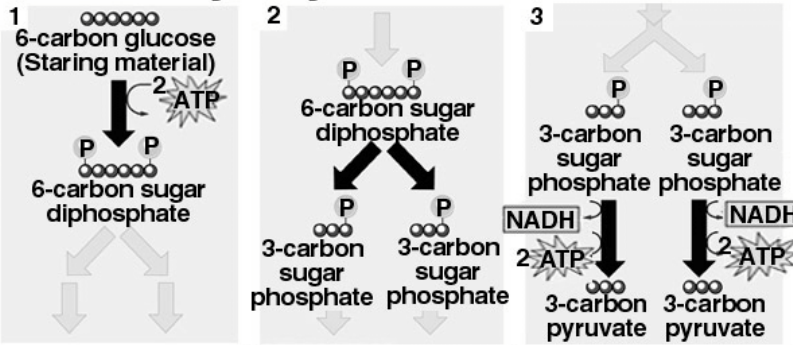
36 moles of ATP x 7.3 kcal/mole = 263 kcal trapped as ATP

efficiency:

$$263/720 \times 100 = 36\% \text{ efficiency}$$

Actual efficiency is slightly less (more on this later).

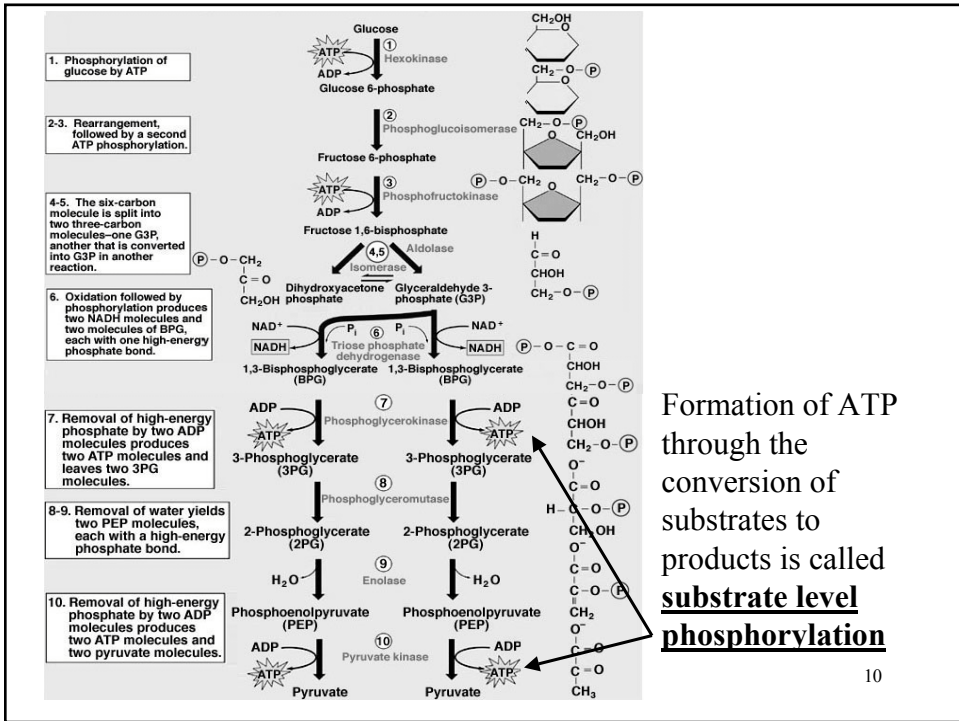
Glycolysis Overview



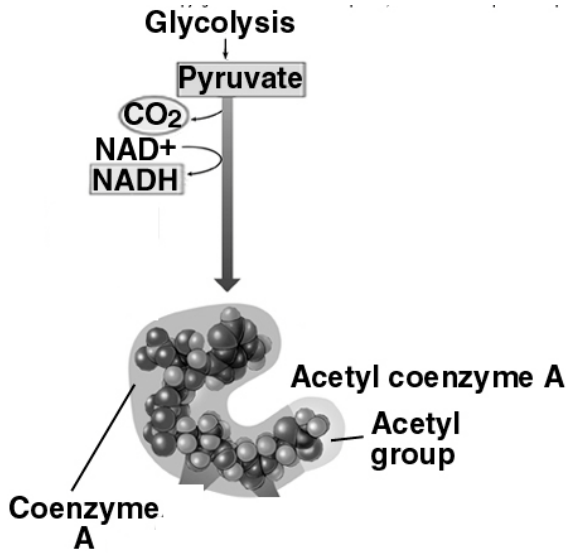
Priming reactions. Glycolysis begins with addition of energy. Two high-energy phosphates from two molecules of ATP are added to the six-carbon molecule glucose, producing a six-carbon molecule with two phosphates.

Cleavage reactions. Then, the six-carbon molecule with two phosphates is split in two, forming two three-carbon sugar phosphates.

Energy-harvesting reactions. Finally, in a series of reactions, each of the two three-carbon sugar phosphates is converted to pyruvate. In the process, an energy-rich hydrogen is harvested as NADH, and two ATP molecules are formed.



Respiration - pyruvate oxidation, the Krebs cycle, and the ETS

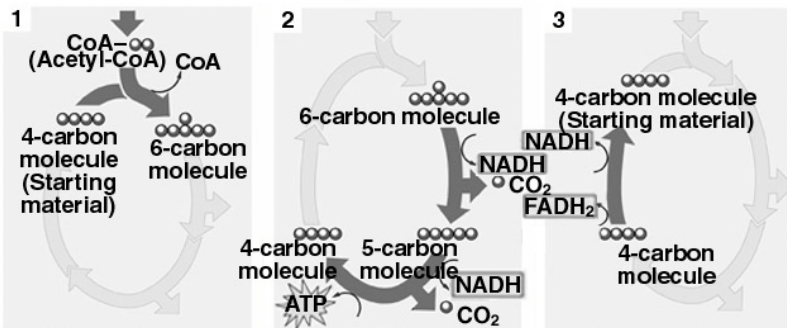


Pyruvate, a 3 carbon molecule is oxidized to acetate (producing CO₂ and NADH) and combined with Coenzyme-A to form Acetyl Co-A in preparation for sending the remaining carbons of acetate into the Krebs cycle.

All steps of respiration occur in the mitochondrion.

11

Krebs Cycle Overview



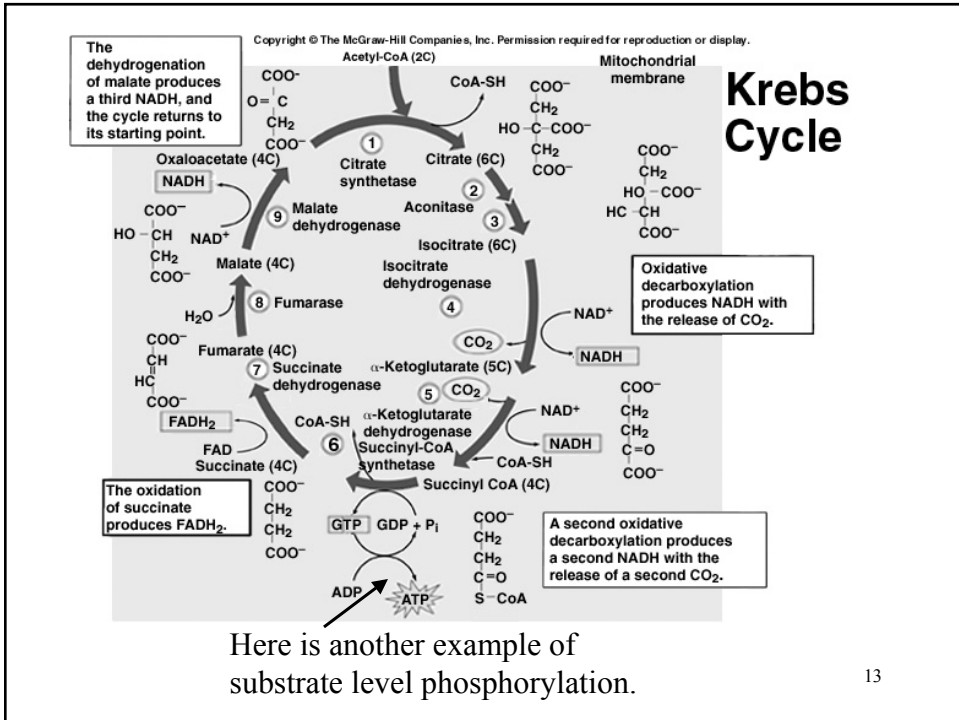
The Krebs cycle begins when a two-carbon fragment is transferred from acetyl-CoA to a four-carbon molecule (the starting material).

Then, the resulting six-carbon molecule is oxidized (a hydrogen removed to form NADH) and decarboxylated (a carbon removed to form CO₂). Next, the five-carbon molecule is oxidized and decarboxylated again, and a coupled reaction generates ATP.

Finally, the resulting four-carbon molecule is further oxidized (hydrogens removed to form FADH₂ and NADH). This regenerates the four-carbon starting material, completing the cycle.

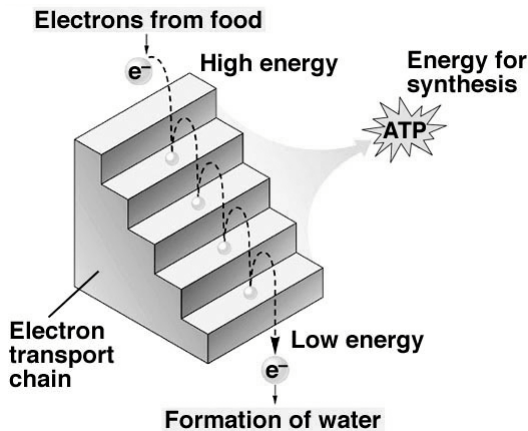
The Krebs cycle occurs in the mitochondrion.

12



13

High energy electrons carried by NADH and FADH are used to produce ATP in the Electron Transport System.

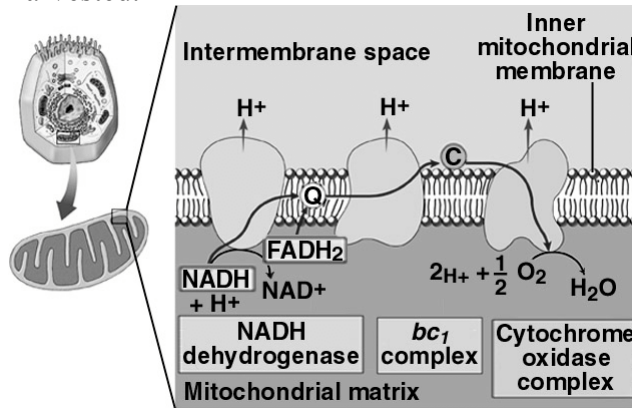


Electrons are passed through a series of oxidation-reduction reactions. The energy from those transfers is coupled to the production of ATP.

The electrons ultimately are passed to oxygen (protons follow) to produce water. Oxygen is a necessity for this process.

14

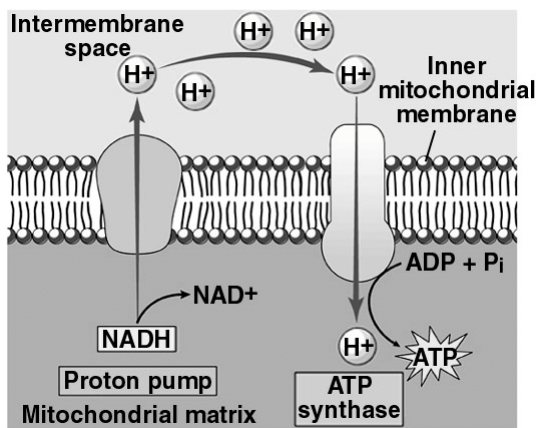
The Electron Transport System is located within the inner mitochondrial membrane. Electrons passed through the ETS release energy and are used to pump protons from the matrix into the intermembrane space. Oxygen is required as the final electron acceptor. Without oxygen, there is no place for NADH and FADH to donate their electrons and no energy can be harvested.



3 protons per NADH
2 protons per FADH

When the ETS is active, the intermembrane space has a lower pH than the matrix.¹⁵

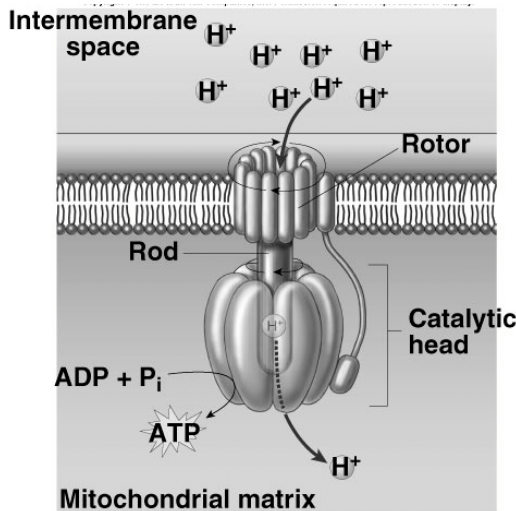
The protons pumped out of the matrix produce a proton gradient between the intermembrane space and the matrix. The proton gradient is used to produce ATP. This is the **Chemiosmotic Theory**.



ATP synthase couples ATP production to proton flow.

This production of ATP is called **oxidative phosphorylation** because it requires oxygen. It does not directly involve substrates.

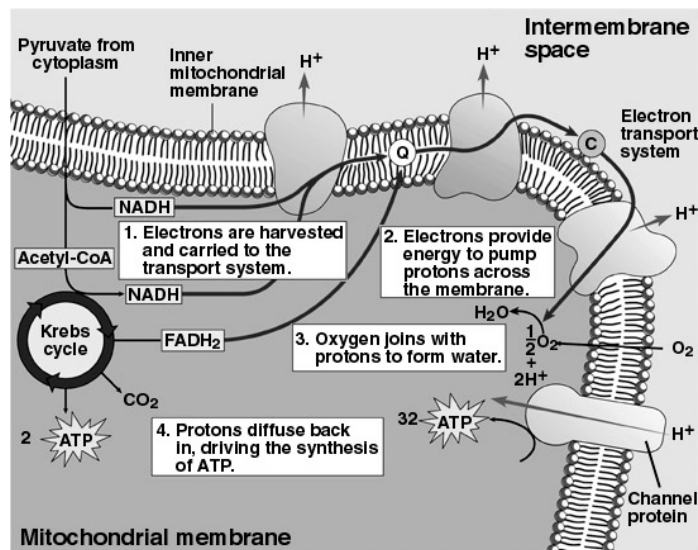
More detail on ATP synthase:

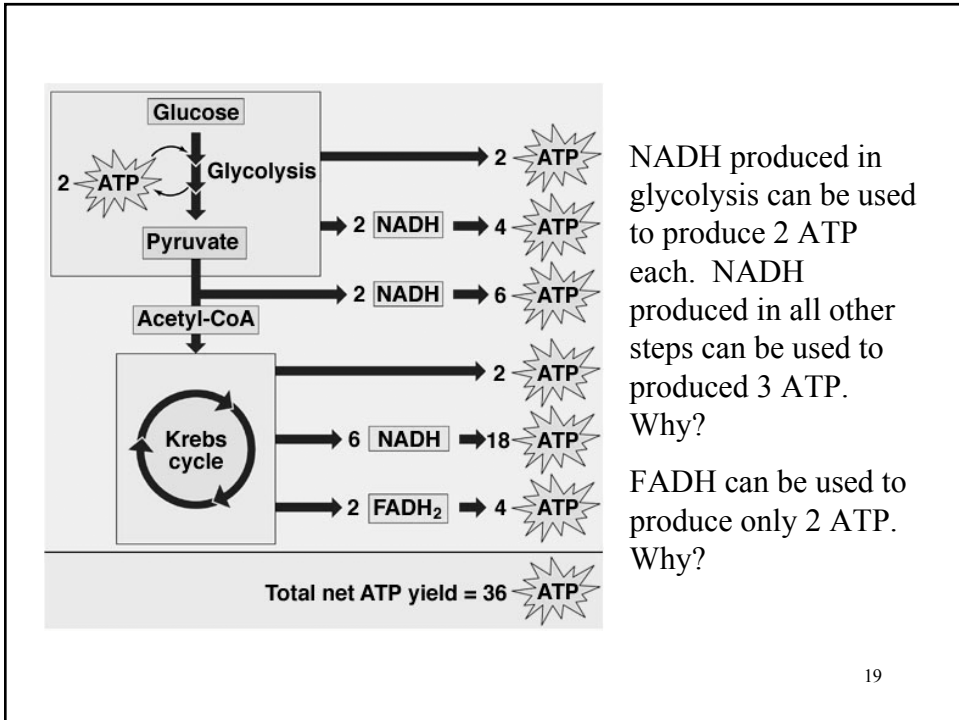


ATP synthase is a large enzyme that acts as a rotary motor.

The ETS creates a proton gradient. Proton flow causes the rotary motor to spin and the mechanical energy of the spinning motor is captured by combining ADP and P_i to form ATP.

ATP production in the mitochondrion (a summary of respiration):

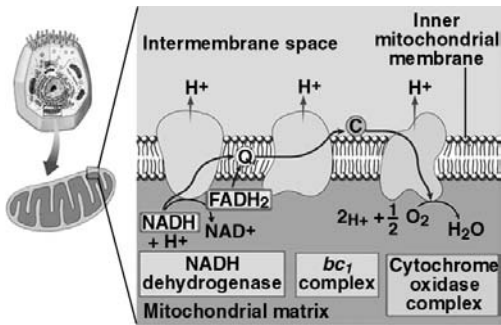




NADH produced in glycolysis can be used to produce 2 ATP each. NADH produced in all other steps can be used to produce 3 ATP. Why?

FADH can be used to produce only 2 ATP. Why?

The NADH produced in glycolysis are produced in the cytoplasm and they must be transported into the matrix of the mitochondrion before they can donate electrons to the ETS. It costs 1 ATP per NADH to transport NADH into the mitochondrial matrix. All other NADH are produced in the matrix.



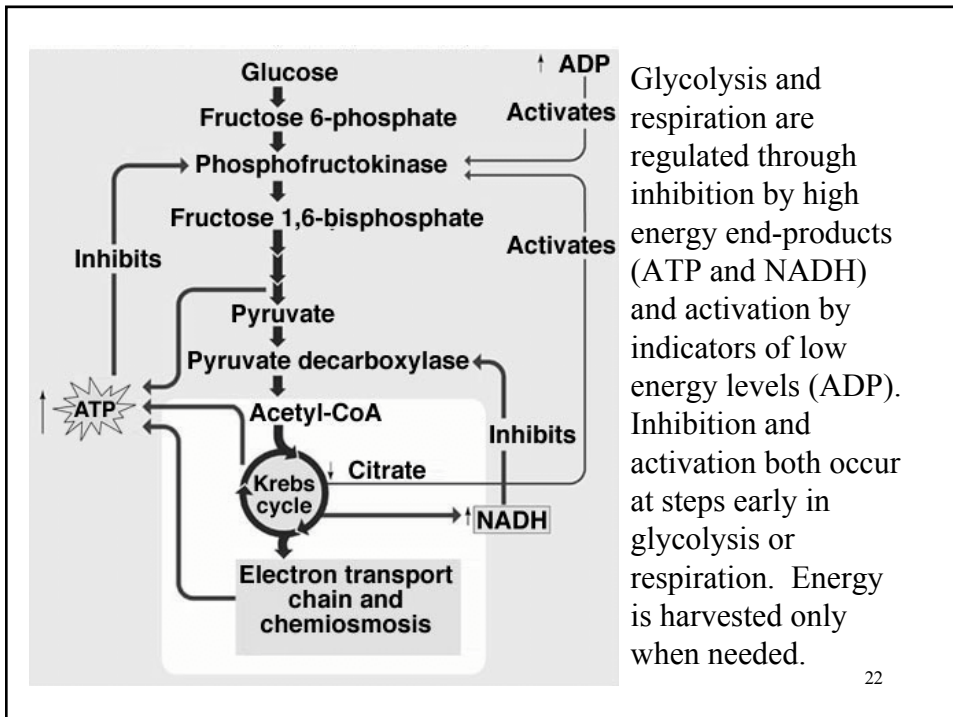
The electrons carried by FADH have less energy than the electrons carried by NADH. FADH electrons can be used to pump 2 protons. NADH electrons can be used to pump 3 protons. 1 ATP molecule can be produced per proton pumped.

The theoretical yield of ATP from glucose is 36 ATP per glucose. The actual number produced is closer to 30 because of several inefficiencies and complications:

1. The inner mitochondrial membrane is “leaky.” Some protons leak into the matrix without passing through ATP synthase.
2. The proton gradient is used for other things besides ATP synthesis. It is used to pump pyruvate from the cytoplasm into the mitochondrial matrix.

The actual yield of ATP is about 30 per glucose.

Actual efficiency: $(7.3 \times 30 / 720) \times 100 = 30\%$



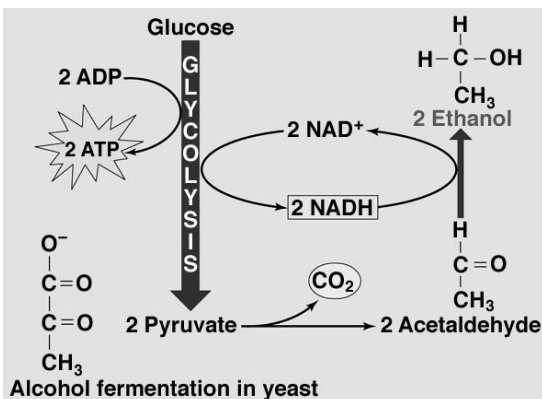
Metabolizing glucose without oxygen: **Anaerobic glycolysis** or **fermentation**

Many organisms live in environments completely devoid of oxygen and still metabolize glucose. Some organisms can switch between metabolizing glucose aerobically and anaerobically depending on oxygen availability. Our own muscles must metabolize glucose anaerobically when we work them vigorously because they deplete oxygen faster than the circulatory system can supply it.

Relatively little ATP can be obtained from fermentation of a single molecule of glucose, but the process is very quick so many glucose molecules can be broken down to provide a large amount of ATP very quickly. If there is no oxygen available, fermentation is the only option for cells to harvest energy.

23

Yeast (a fungus), and some prokaryotes, metabolize glucose, harvesting 2 ATP. Since the ETS can't be used without oxygen the NADH can't be used to generate more ATP. Without oxygen the pyruvate can't be metabolized either because its metabolism depends on NADH being oxidized in the ETS.

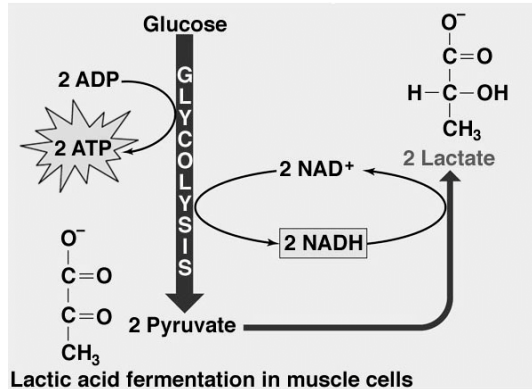


Without a mechanism to recycle NADH back to NAD, glycolysis would stop. NADH is recycled to NAD through the production of ethanol from pyruvate.

Ethanol and CO₂ are metabolic by-products of the anaerobic metabolism of glucose.

24

Our muscle cells and some microorganisms can metabolize glucose anaerobically. To recycle the NADH they produce lactic acid. The regenerated NAD can be used to keep glycolysis and ATP production going even when oxygen is absent.



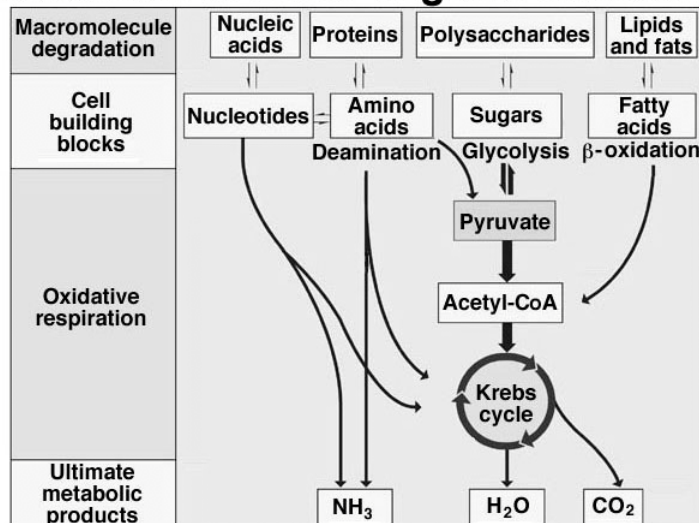
Lactic acid produced during activity must be reconverted into pyruvate by reducing NAD to NADH when oxygen is available to remove it. The NADH ultimately donates electrons to O_2 in the ETS.

Accumulated lactic acid is called **oxygen debt** because oxygen must be used to metabolize it after exercise has stopped. 25

All organic molecules metabolized as a source of energy are converted to one of the intermediates of glycolysis or respiration.

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

Catabolism of Other Organic Molecules



Metabolism of fatty acids yields more trapped ATP than metabolism of carbohydrates on a per carbon basis.

The preliminary steps are called β -oxidation

For a 6 carbon fatty acid, 1 ATP must be invested for every 2 carbons to prime the process.

From every 2 carbons of the 6 carbon fatty acid, the yield is 1 FADH and 1 NADH and 1 acetyl Co-A.

The acetyl Co-A can be metabolized in the Krebs cycle and generates 3 NADH, 1 FADH, and 1 ATP, as seen previously.

27

2 carbons thus generates a total of 2 FADH, 4 NADH, and 1 ATP with a cost of 1 ATP.

6 carbons generates 6 FADH, 12 NADH and 3 ATP with a cost of 3 ATP. The total yield:

6 FADH * 2 ATP/FADH \rightarrow 12 ATP
 12 NADH * 3 ATP/NADH \rightarrow 36 ATP

Total yield for 6 carbons from fat = 48 ATP
 Total yield for 6 carbons from sugar = 36 ATP.

Fats cannot be metabolized anaerobically - fat metabolism requires oxygen.

28