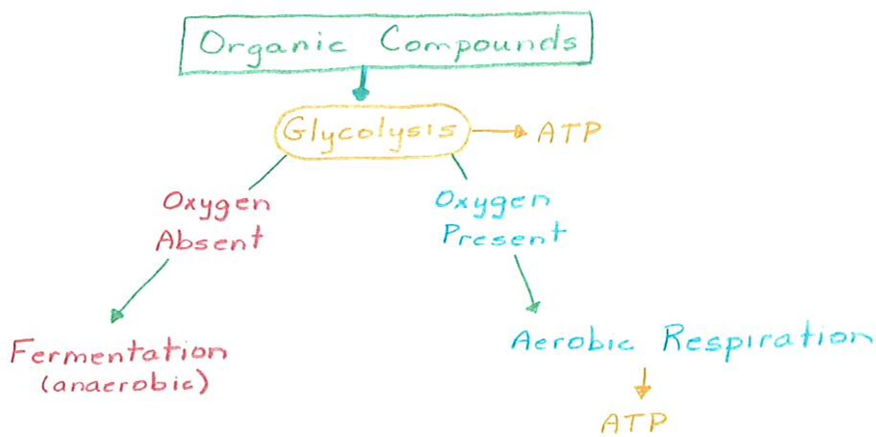
II CELLULAR RESPIRATION

- All cells break down complex organic compounds into simpler molecules.
- Cells use some of the energy that is released in this process to make ATP.

A. Glycolysis and Fermentation

1. Harvesting Chemical Energy

- Autotrophs, such as plants, use photosynthesis to convert light energy from the sun into chemical energy, which is stored in carbohydrates and other organic compounds.
- Both autotrophs and heterotrophs depend on these organic compounds for the energy to power cellular activities.
- By breaking down these compounds into simpler molecules, cells release energy.
- Some of the energy is used to make ATP from ADP and phosphate.
- The complex process in which cells make ATP by breaking down organic compounds is known as **cellular respiration**
- Cellular respiration begins with a biochemical pathway called **glycolysis**, which yields a relatively small amount of ATP.
- The other products of glycolysis can follow either of two main pathways, depending on whether there is oxygen in the cell.
- If oxygen is absent, the products of glycolysis may enter fermentation pathways that yield no additional ATP. Because they operate in the absence of oxygen, the fermentation pathways are said to be **anaerobic pathways**.
- If oxygen is present, the products of glycolysis enter the pathways of **aerobic respiration**. Aerobic respiration produces a much larger amount of ATP than does glycolysis alone
- Many of the reactions in cellular respiration are redox reactions



2. Glycolysis

- Glycolysis is a pathway in which one six-carbon molecule of glucose is oxidized to produce two three-carbon molecules of **pyruvic acid**
- Like other biochemical pathways, glycolysis consists of a series of chemical reactions catalyzed by specific enzymes.
- All the reaction of glycolysis take place in the cytosol of the cell
- These reactions can be condensed into four main steps.

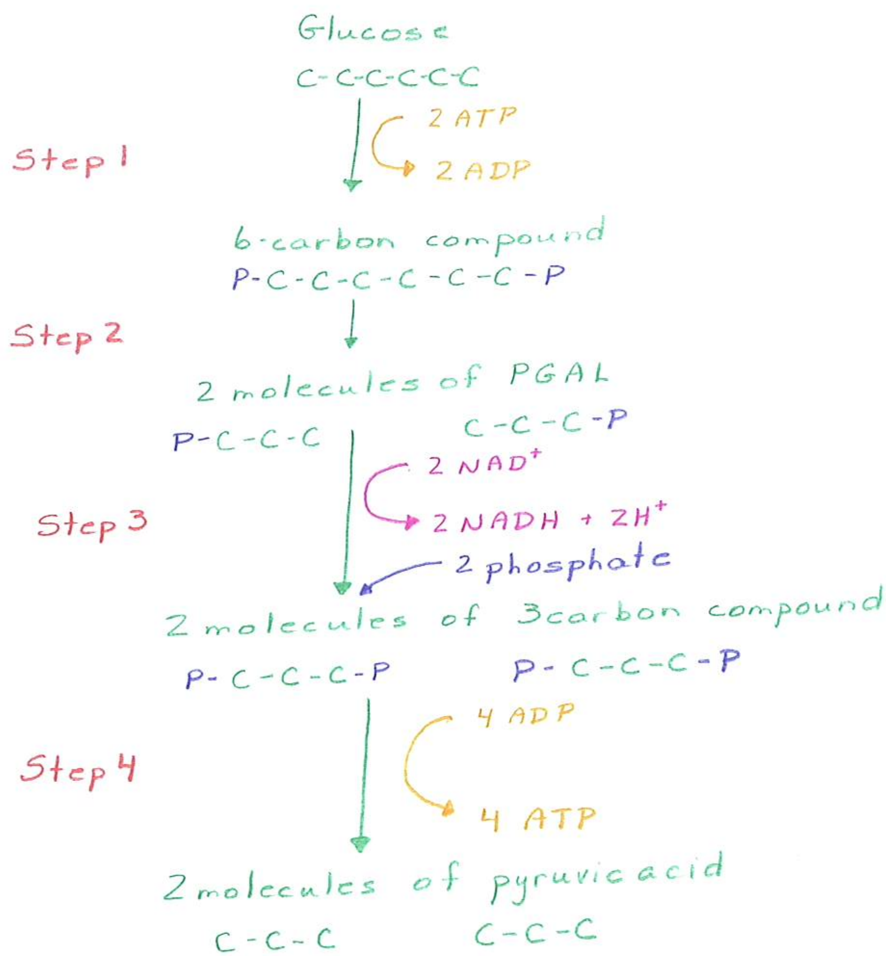
Step 1 – Two phosphate groups are attached to glucose, forming a new six-carbon compound. The phosphate groups are supplied by two molecules of ATP, which are converted into two molecules of ADP in the process.

Step 2 – The six-carbon compound formed in Step 1 is split into two three-carbon molecules of PGAL.

Step 3 – The two PGAL molecules are oxidized, and each receives a phosphate group. The product of this step is two molecules of a new three-carbon compound. The oxidation of PGAL is accompanied by the reduction of two molecules of NAD^+ to NADH. NAD^+ is very similar to $NADP^+$ in that it accepts hydrogen.

Step 4 – The phosphate groups added in Step 1 and Step 3 are removed from the three-carbon compounds formed in Step 3. This reaction produces two molecules of pyruvic acid. Each phosphate group is combined with a molecule of ADP to make a molecule of ATP. Because a total of four phosphate groups were added in Step 1 and Step 3, four molecules of ATP are produced.

GLYCOLYSIS – Production of PGAL

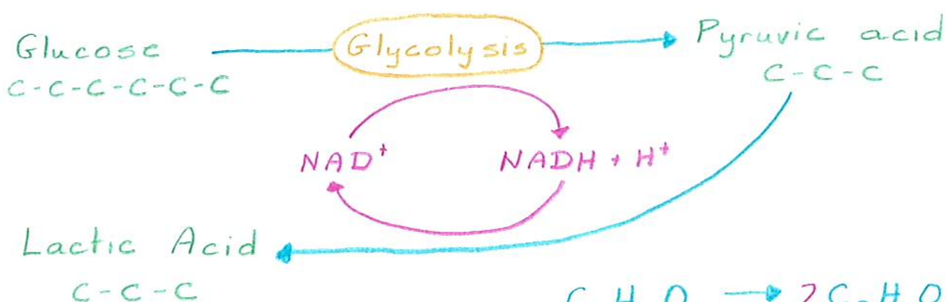


- Note that two ATP molecules were used in Step 1, but four were produced in Step 4. Therefore, glycolysis has a net yield of two ATP molecules for every molecule of glucose that is converted into pyruvic acid.
- What happens to the pyruvic acid depends on the type of cell and on whether oxygen is present

3. Fermentation
- In the absence of oxygen, some cells can convert pyruvic acid into other compounds through additional biochemical pathways that occur in the cytosol.
- The combination of glycolysis plus these additional pathways is known as **fermentation**
- The additional fermentation pathways do not produce ATP. However, they do regenerate NAD^+, which can be used to keep glycolysis going to make more ATP.
- There are many fermentation pathways, and they differ in terms of the enzymes that are used and the compounds that are made from pyruvic acid.
- Two common fermentation pathways result in the production of lactic acid and ethyl alcohol.

(a) Lactic Acid Fermentation

- In **lactic acid fermentation**, an enzyme converts pyruvic acid into another three-carbon compound, called lactic acid
- Lactic acid fermentation involves the transfer of two hydrogen atoms from NADH and H^+ to pyruvic acid.
- In the process, NADH is oxidized to form NAD^+.
- The resulting NAD^+ is used in glycolysis, where it is again reduced to NADH.
- Thus the regeneration of NAD^+ in lactic acid fermentation helps to keep glycolysis operating



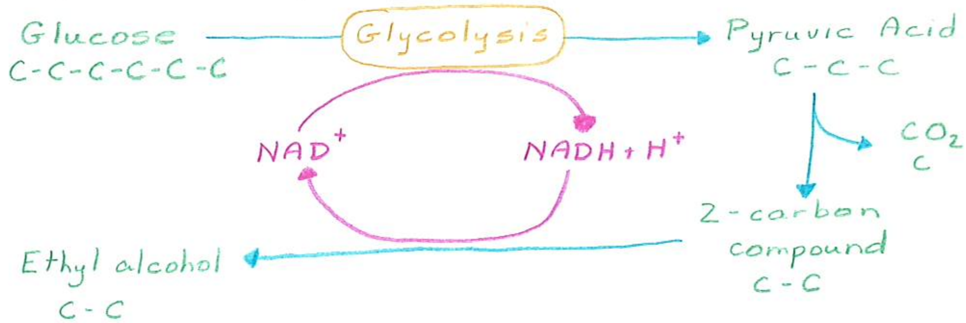
$C_6H_{12}O_6 \rightarrow 2C_3H_6O_3 + 2ATP$

- Lactic acid fermentation by microorganisms plays an essential role in the manufacture of food products such as yogurt and cheese
- Lactic acid also occurs in your muscle cells during very strenuous exercise, the muscle cells use up oxygen more rapidly than it can be delivered to them. As oxygen becomes depleted, the muscle cells begin to switch form aerobic respiration to lactic acid fermentation. Lactic acid accumulated in the muscle cells, making the cells' cytosol, more acidic. The increased acidity may reduce the capacity of the cells to contract, resulting in muscle fatigue,

pain, and even cramps. Eventually, the lactic acid diffuses into the blood and is transported to the liver, where it is converted back into pyruvic acid when oxygen becomes available.

(b) Alcoholic Fermentation

- Some plant cells and unicellular organisms, such as yeast, use a process called **alcoholic fermentation** to convert pyruvic acid into ethyl alcohol.
- This pathway requires two steps
- In the first step, a CO_2 molecules is removed from pyruvic acid, leaving a two-carbon compound.
- In the second step, two hydrogen atoms are added to the two-carbon compound to form ethyl alcohol.



$$C_6H_{12}O_6 \rightarrow 2C_2H_5OH + 2CO_2 + 2ATP$$

- As in lactic acid fermentation, these hydrogen atoms come from NADH and H^+, regenerating NAD^+ for use in glycolysis.
- Alcoholic fermentation is the basis of the wine and beer industries. Yeast cells added to the fermentation mixture to provide the enzymes needed for alcoholic fermentation
- As fermentation proceeds, ethyl alcohol accumulates in the mixture until it reaches a concentration that inhibits fermentation.
- Bread making also depends on alcoholic fermentation performed by yeast cells. In this case, the CO_2 that is produced by fermentation makes the bread rise by forming bubbles inside the dough, and the ethyl alcohol evaporates during baking.

4. Energy Yield
   - To determine the how efficient the anaerobic pathways are, the amount of energy available in glucose has to be compared with the amount of energy contained in the ATP that is produced by the anaerobic pathways.
   - In such comparisons, energy is often measured in units of **kilocalories** (kcal)
   - One kilocalorie equal 1,000 calories (cal).
   - Scientists have calculated that the complete oxidation of a standard amount of glucose releases 686 kcal.
   - Under the conditions that exist inside most cells, the production of a standard amount of ATP from ADP absorbs about 12 kcal.

- Recall that two ATP molecules are produced from every glucose molecules that is broken down by glycolysis

$$\text{Efficiency} = \frac{\text{Energy required to make ATP}}{\text{Energy released by oxidation of glucose}} \times 100\%$$

$$= \frac{2 \times 12}{686} \times 100\% = 3.5\%$$

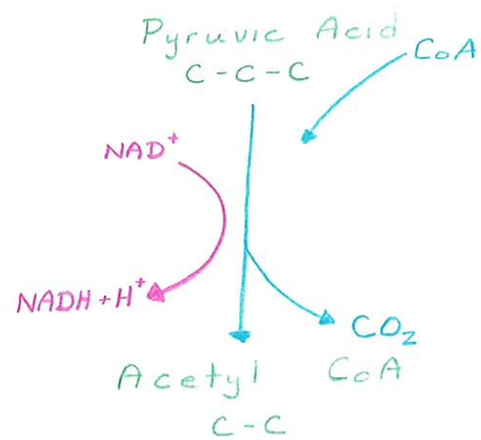
- So the two ATP molecules produced during glycolysis receive only a small percentage of the energy that could be released by the complete oxidation of each molecule of glucose.
- Much of the energy originally contained in the glucose is still held in pyruvic acid.
- Even if pyruvic acid is converted into lactic acid or ethyl alcohol, no additional ATP is synthesized.
- It's clear that the anaerobic pathways are not very efficient in transferring energy from glucose to ATP.
- The anaerobic pathways probably evolved very early in the history of life on Earth. The first organisms were bacteria, and they produced all of their ATP through glycolysis.
- It took more than a billion years for the first photosynthetic organisms to appear.
- The oxygen they released as a by-product of photosynthesis stimulated the evolution of organisms that make most of their ATP through aerobic respiration.
- By themselves, the anaerobic pathways provide enough energy for many present-day organisms.
- However, most of these organisms are unicellular, and those that are multicellular are very small. All of them have limited energy requirements.
- Larger organisms have much greater energy requirements that cannot be satisfied by the anaerobic pathways alone. These larger organisms meet their energy requirements with the more efficient pathways of aerobic respiration.

B. Aerobic Respiration

- In most cells, the pyruvic acid that is produced in glycolysis does not undergo fermentation. Instead, if oxygen is available, pyruvic acid enters the pathways of **aerobic respiration**, or cellular respiration that requires oxygen.
- Aerobic respiration produces nearly 20 times as much ATP as is produced by glycolysis alone.

1. Overview of Aerobic Respiration
   - Aerobic respiration has two major states: the Krebs cycle and the electron transport chain.
   - In the Krebs cycle, the oxidation of glucose that began with glycolysis is completed. As glucose is oxidized, NAD^+ is reduced to NADH.
   - In the electron transport chain, NADH is used to make ATP.
   - Although the Krebs cycle also produces a small amount of ATP, the electron transport chain makes most of the ATP produced during aerobic respiration.

- The reactions of the Krebs cycle and the electron transport chain occur only if oxygen is present in the cell.
- In prokaryotes, the reactions of the Krebs cycle and the electron transport chain take place in the cytosol of the cell
- In eukaryotic cells these reactions take place inside mitochondria rather than in the cytosol.
- The pyruvic acid that is produced in glycolysis diffuses across the double membrane of the mitochondrion and enters the **mitochondrial matrix**. The mitochondrial matrix is the space inside the inner membrane of a mitochondrion.
- The mitochondrial matrix contains the enzymes needed to catalyze the reactions of the Krebs cycle.
- When pyruvic acid enters the mitochondrial matrix, it reacts with a molecule called coenzyme A to form **acetyl coenzyme A** abbreviated **acetyl CoA**
- The acetyl part of acetyl CoA contains two carbon atoms, but pyruvic acid is a three carbon compound. The carbon atom that is lost in the conversion of pyruvic acid to acetyl CoA is released in a molecule of CO_2.
- Also this reaction reduces a molecule of NAD^+ to NADH..



2. The Krebs Cycle
   - The **Krebs cycle** is a biochemical pathway that breaks down acetyl CoA, producing CO_2., hydrogen atoms, and ATP.
   - The reactions that make up the cycle were identified by Hans Krebs (1900-1981), a German-British biochemist.
   - The Krebs cycle has five main steps. In eukaryotic cells, all five steps occur in the mitochondrial matrix.

Step 1 – A two-carbon molecule of acetyl CoA combines with a four-carbon compound, **oxaloacetic acid**, to produce a six-carbon compound, **citric acid**. This reaction regenerates coenzyme A.

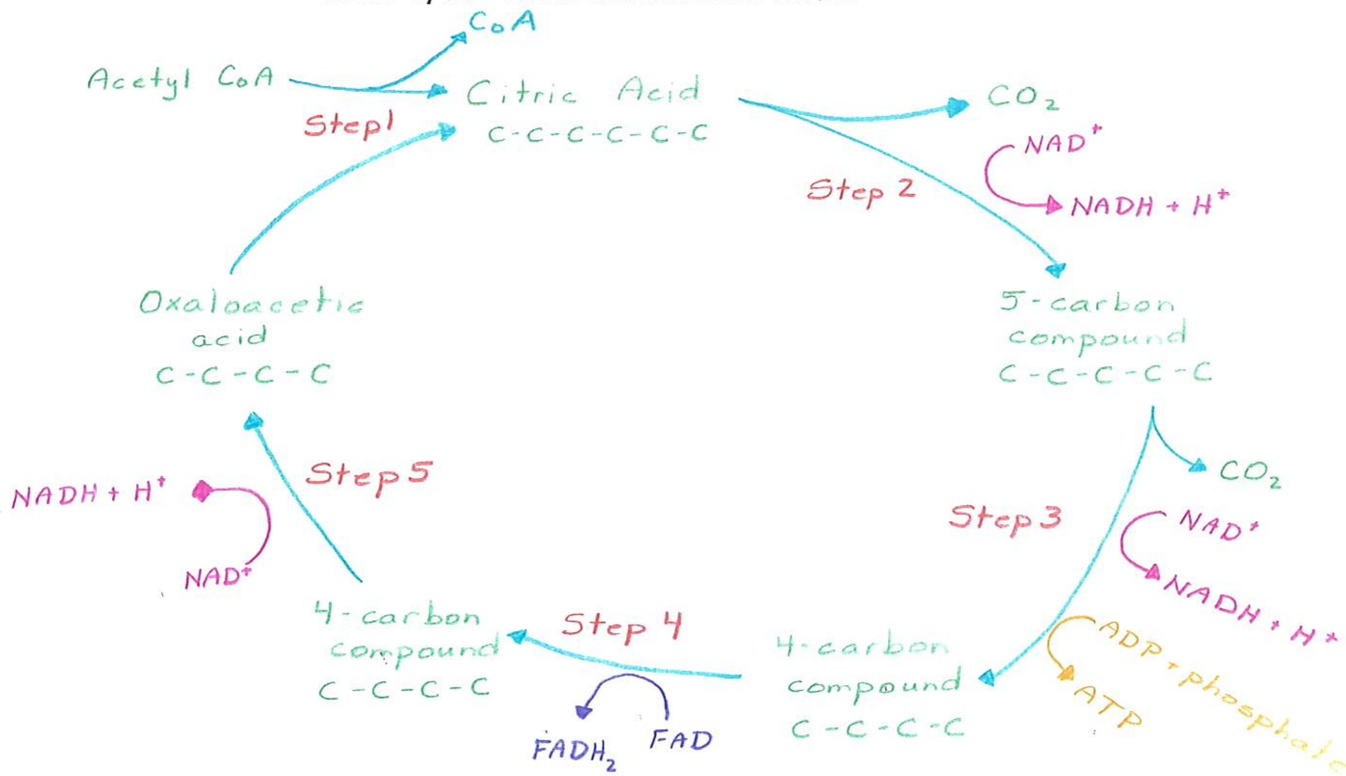
Step 2 – Citric acid releases a CO_2 molecule and a hydrogen atom to form a five-carbon compound. By losing a hydrogen atom with its electron, citric acid is oxidized. The hydrogen atom is transferred to NAD^+, reducing it to NADH.

Step 3 – The five-carbon compound formed in Step 2 also releases a CO_2 molecule and a hydrogen atom, forming a four-carbon compound. Again, NAD^+ is reduced to NADH. Notice that in this step a molecule of ATP is also synthesized from ADP.

Step 4 – The four-carbon compound formed in Step 3 releases a hydrogen atom to form another four-carbon compound. This time, the hydrogen atom is used to reduce FAD to $FADH_2$. **FAD**, or flavin adenine dinucleotide, is a molecule very similar to NAD^+, because FAD accepts electrons.

Step 5 – The four-carbon compound formed in Step 4 releases a hydrogen atom to regenerate oxaloacetic acid, which keeps the Krebs cycle operating. The hydrogen atom reduced NAD^+ to NADH.

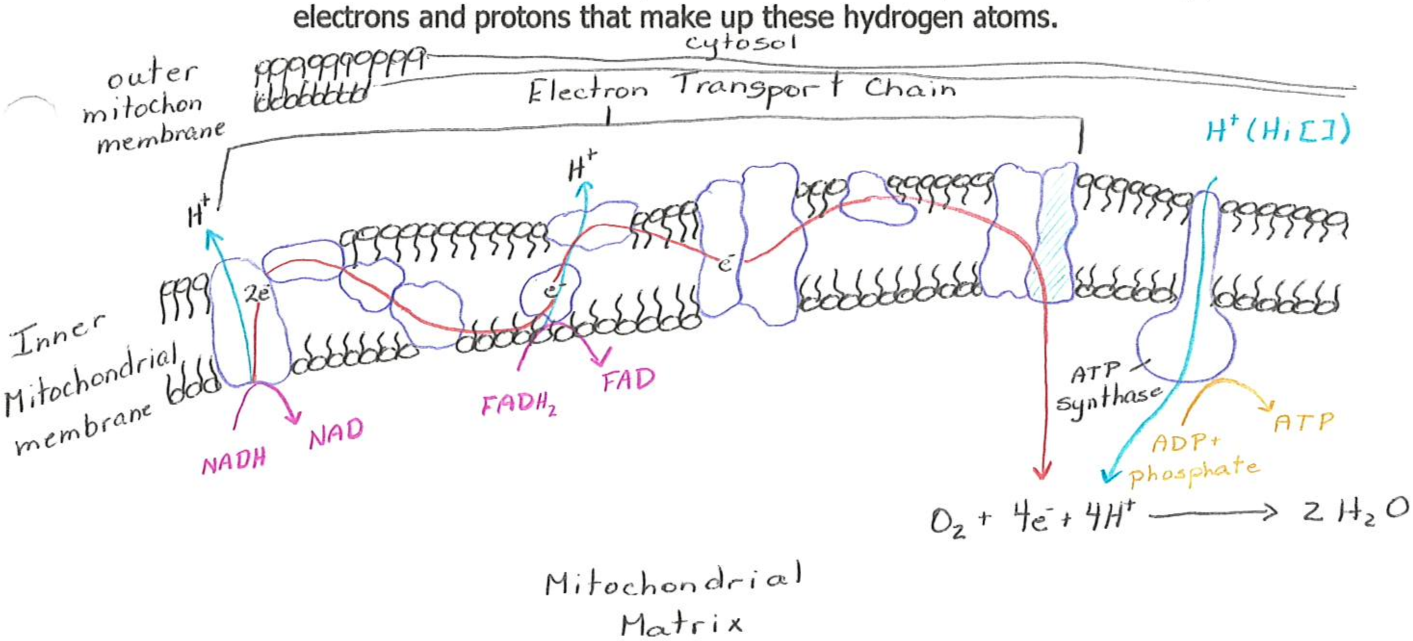
Krebs Cycle – in the mitochondrial matrix



– Recall that in glycolysis one glucose molecule produces two pyruvic acid molecules, which can then form two molecules of acetyl CoA.
– Thus, one glucose molecule causes two turns of the Krebs cycle.
– These two turns produce six NADH, tow $FADH_2$, two ATP, and four CO_2 molecules.
– The CO_2 is a waste product that diffuses out of the cells and is given off by the organism.
– The ATP can be used for energy. But note that each glucose molecule yields only two molecules of ATP through the Krebs cycle – the same number as in glycolysis.
– The bulk of the energy released by the oxidation of glucose still has not been transferred to ATP.

- That transfer requires the NADH and $FADH_2$ made in the pathways you have learned about so far.
- Recall that glycolysis produces two NADH molecules and that the conversion of pyruvic acid to acetyl CoA produces two more.
- Adding the six NADH molecules form the Krebs cycle gives a total of 10 NADH molecules for every glucose molecule that is oxidized.
- These 10 NADH molecules and the two $FADH_2$ molecules from the Krebs cycle drive the next stage of aerobic respiration. That is where most of the energy transfer from glucose to ATP actually occurs.

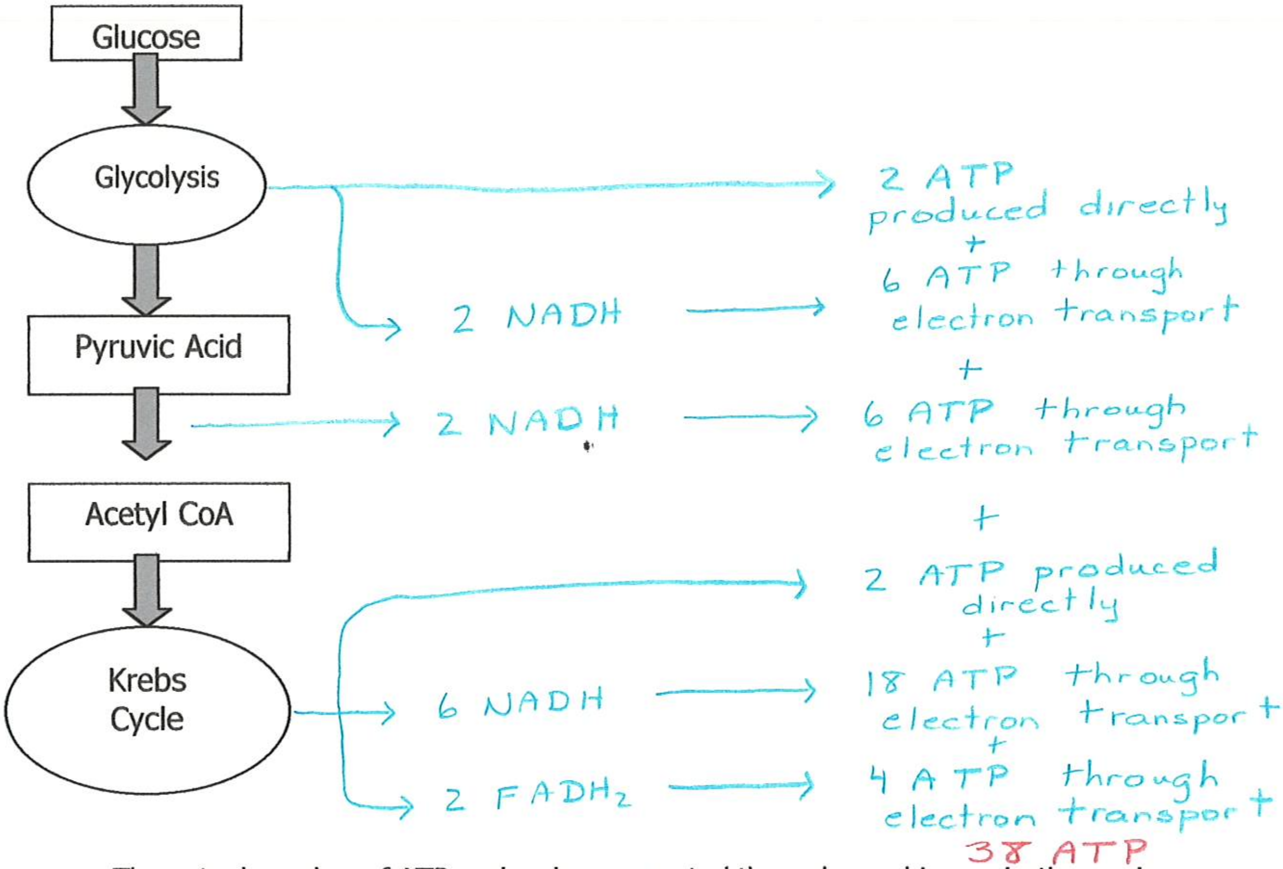
3. Electron Transport Chain
   - The **electron transport chain** constitutes the second stage of aerobic respiration.
   - In eukaryotic cells, the electron transport chain lines the inner membrane of the mitochondrion.
   - In prokaryotes, the electron transport chain lines the cell membrane.
   - The electron transport chain produces ATP when NADH and $FADH_2$ release hydrogen atoms, regenerating NAD^+ and FAD.
   - To understand how ATP is produced it is necessary to follow what happens to the electrons and protons that make up these hydrogen atoms.



- The electrons in the hydrogen atoms from NADH and $FADH_2$ are at a high energy level. In the electron transport chin, these high-energy electrons are passed along a series of molecules.
- As they move from molecule to molecule, the electrons lose some of their energy.
- The energy they lose is used to pump the protons of the hydrogen atoms form the mitochondrial matrix to the other side of the inner mitochondrial membrane. This pumping builds up a high concentration of protons in the space between the inner and outer mitochondrial membranes.
- The concentration gradient of protons drives the synthesis of ATP by chemiosmosis, the same process that generates ATP in photosynthesis. ATP synthase molecules are located in the inner mitochondrial membrane, so ATP is created from ADP as protons move down their concentration gradient into the mitochondrial matrix.
- ATP can be synthesized by chemiosmosis only if electrons continue to move form molecule to molecule in the electron transport chain.
- The last molecule in the electron transport chin cannot keep all the electrons it accepts. If it did, the electron transport chain would come to a halt. This is where oxygen comes into play in aerobic respiration.
- The oxygen serves as the final acceptor of electrons.
- By accepting electrons form the last molecule in the electron transport chain, oxygen allows additional electrons to pass along the chain.
- As a result, ATP can continue to be synthesized by chemiosmosis.
- Oxygen also accepts the protons that were once part of the hydrogen atoms supplied by NADH and $FADH_2$
- By combining with both electrons and protons, oxygen forms water

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

4. Energy Yield
   - Many ATP molecules are made in aerobic respiration
   - Glycolysis and the Krebs cycle each produce two ATP molecules for every glucose molecules that is oxidized.
   - Each NADH molecule that supplies the electrons transport chain can generate three ATP molecules.
   - Each $FADH_2$ molecule can generate two ATP molecules.
   - Thus, 10 NADH and two $FADH_2$ molecules made through aerobic respiration can produce up to 34 ATP molecules by the electron transport chain.
   - Adding the four ATP molecules form glycolysis and the Krebs cycle give a maximum yield of 38 ATP molecules per molecule of glucose



- The actual number of ATP molecules generated through aerobic respiration varies from cell to cell
- In most eukaryotic cells, the NADH that is made in the cytosol during glycolysis cannot diffuse through the inner membrane of the mitochondrion. Instead, it must be actively transported into the mitochondrial matrix. The active transport of NADH consumes ATP.
- As a result, most eukaryotic cells produce only about 36 ATP molecules per glucose molecule.
- So the efficiency of aerobic respiration is

$$\text{Efficiency} = \frac{38 \times 12 \text{ kcal}}{686 \text{ kcal}} \times 100\%$$

$$= 66\%$$

- This means that aerobic respiration is nearly 20 times more efficient than glycolysis alone.

5. Summarizing Cellular Respiration
   - The complete oxidation of glucose in aerobic respiration is summarized by the following equation:

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + 36\ ATP$$

   - Notice that the equation above is the opposite of the overall equation for photosynthesis, if glucose is considered to be a product of photosynthesis.
   - That is, the products of photosynthesis are reactants in aerobic respiration, and the products of aerobic respiration are reactants in photosynthesis.
   - However, it is important to remember that aerobic respiration is not the reverse of photosynthesis. As you have seen, these two processes involve different biochemical pathways and occur at different sites inside the cells
   - Cellular respiration provides the ATP that all cells need to support the activities of life. But providing cells with ATP is not the only important function of cellular respiration.
   - Cells also need specific organic compound from which to build the macromolecules that compose their own structure.
   - Some of these specific compounds may not be contained in the food a heterotroph consumes. However, the molecules formed at different steps in glycolysis and the Krebs cycle are often used by cells to make the compounds that are missing in food.
   - Thus another important function of cellular respiration is to provide carbon skeletons that can be built up into larger molecules needed by cells.

CELLULAR RESPIRATION REVIEW

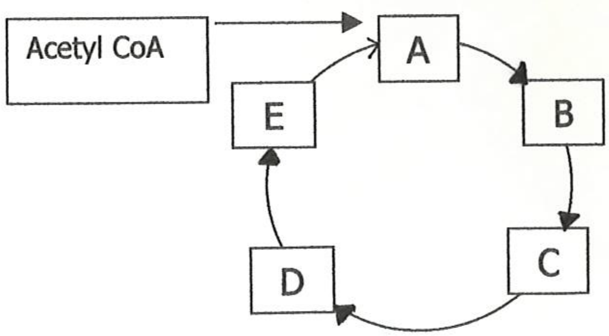
TERMS TO KNOW

Acetyl coenzyme A
Aerobic respiration
Alcoholic fermentation
Anaerobic pathway
Cellular respiration
Citric acid
Electron transport chain
FAD
Fermentation
Glycolysis
Kilocalorie
Krebs cycle
Lactic acid fermentation
Mitochondrial matrix
NAD^+
Oxaloacetic acid
Oxidation
Pyruvic acid

QUESTIONS FOR REVIEW

1. Define cellular respiration.
2. What six-carbon molecule begins glycolysis, and what three-carbon molecules are produced at the end of glycolysis?
3. For each six-carbon molecule that begins glycolysis, how many ATP molecules are used and how many ATP molecules are produced?

4. What condition must exist in a cell for the cell to engage in fermentation?
5. How efficient is glycolysis?
6. A large amount of ATP in a cell inhibits the enzymes that catalyze the first few steps of glycolysis. How will this inhibition eventually affect the amount of ATP in the cell? Explain your answer.
7. What four-carbon compound is regenerated at the end of the Krebs cycle? With what two-carbon compound does it combine at the start of the Krebs cycle?
8. How is the synthesis of ATP in the electron transport chain of mitochondria similar to the synthesis of ATP in chloroplasts?
9. What role does oxygen play in aerobic respiration? What molecule does oxygen become a part of as a result of aerobic respiration?
10. In what part of the mitochondrion does the Krebs cycle occur? In what part of a mitochondrion is the electron transport chain located?
11. Calculate the efficiency of aerobic respiration if a cell generates 32 ATP molecules per molecule of glucose.
12. What molecule made during glycolysis is used in the later steps in fermentation?
13. Summarize the events that occur from the end of glycolysis through the first reaction of the Krebs cycle.
14. Why do most eukaryotic cells produce fewer than 38 ATP molecules for every glucose molecule that is oxidized by aerobic respiration?
15. How do the anaerobic pathways differ from the pathways of aerobic respiration, at the sites they occur in eukaryotic cells?
16. How does aerobic respiration ultimately depend on photosynthesis?
17. What role does oxygen play in aerobic respiration?
18. Refer to the diagram of the Krebs cycle shown below. How many carbon atoms are in each of the compounds represented by the letters A – E?



19. The enzyme that converts pyruvic acid into acetyl CoA requires vitamin B_1, also called thiamine. Like many other vitamins, thiamine cannot be made in the human body. What can you infer about the nutritional requirements of humans?
20. Yeast can produce ATP through either fermentation or aerobic respiration, depending on whether oxygen is present. If oxygen is present, yeast cells consume glucose much more slowly than if oxygen is absent. How can you explain this observation?