CELLULAR RESPIRATION

Cellular Respiration

One of my favorite television programs growing up was Mr. Wizard. Mr. Wizard, *aka* Don Herbert, would invite neighborhood kids over and have them perform science experiments, always having the kid explain what was going on, how it worked, and how it could be applied. Alas, Mr. Wizard went the way of all programs with declining ratings. Much to my surprise, some 20 years later, I returned from a day of teaching to find Mr. Wizard back at it. While channel surfing, I ran across the Nickelodeon network. Low and behold, there was Mr. Wizard with all new episodes.

The day I tuned in 20 years later, Mr. Wizard was in the process of burning a mole of glucose in a bomb calorimeter. For those of you who don't speak chemistry, a mole is 180 grams of glucose; not a very large amount. When he inserted the glucose in the bomb calorimeter and ignited it (remember, all materials will burn if you get them hot enough) the calorimeter shot a flame as high as the ceiling which burned very brightly for about 2 seconds. They don't call it a bomb calorimeter for nothing. That was a lot of energy released. Actually, a mole of glucose will release 686 kilocalories of energy.

As a human, you happen to have a lot more than a mole of glucose in your body. What would happen to you if you released all the energy of all the glucose in your body at the same time? I suspect you would auto-combust. Consequently, cells in your body do not release the energy locked in a glucose molecule all at once, but in stages. That process of burning glucose in the presence of oxygen in your cells is called "cellular respiration."

Many people mistakenly think respiration is breathing. That's not the case. Breathing is a physical act of inspiration (air intake) and expiration (air outflow). Respiration is a biochemical process that occurs at the cellular level.

The summary equation for cellular respiration is:

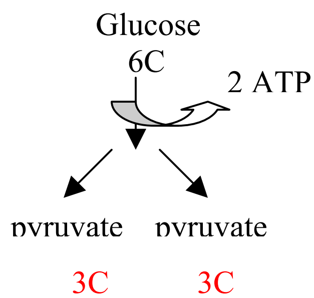
$$\underset{\text{oxygen}}{6O_2} + \underset{\text{glucose}}{C_6H_{12}O_6} \rightarrow \underset{\text{carbon dioxide}}{6CO_2} + \underset{\text{water}}{12H_2O}.$$

Remember, this is a "summary" equation and the process is actually a series of chemical reactions occurring in the cell.

Glucose is broken down in stages. The three major steps of glucose metabolism are (1) glycolysis (2) Kreb's cycle and (3) Electron Transport System. Remember, the whole purpose of cellular respiration is to release energy from glucose and produce ATP. That energy available to do work is called Gibb's Free Energy.

Glycolysis: An Overview

The word "lysis" means loosen or break apart. What we are doing is breaking apart glucose. We begin by taking glucose, a six carbon compound, and breaking it into two (3) carbon compounds, both of which are phosphoenol pyruvate (PEP).

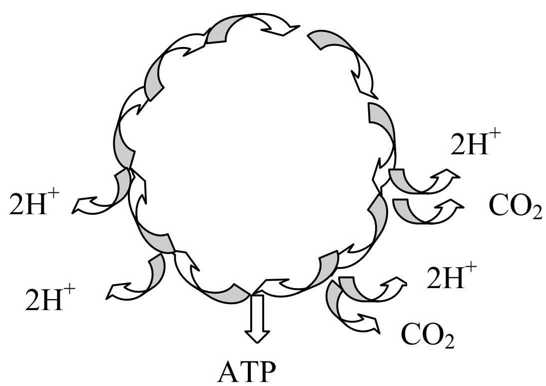


At the same time glucose is broken down into two pyruvates, a net of 2 ATP are produced.

Glycolysis occurs in the cytoplasm of eukaryotic cells and the protoplasm of prokaryotic cells. This is also an anaerobic process (occurs without the presence of oxygen).

Krebs' Cycle: An Overview

The pyruvate from glycolysis will be converted into an intermediate compound that feeds into the Krebs' cycle. As a cycle, you begin with a compound, change it, change it, change it, etc., and end with the same compound.

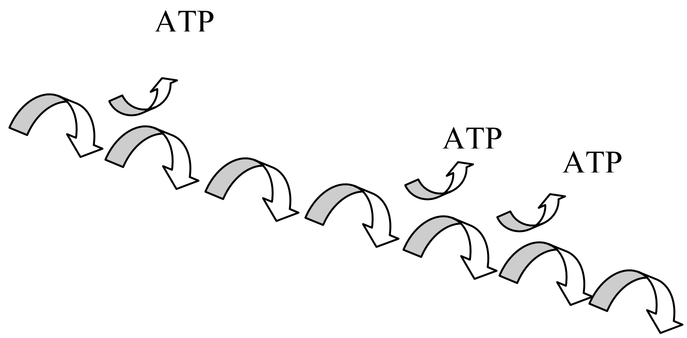


During this process of conversion from one compound to another, 2 carbon dioxides are released and the four pairs of hydrogen's are used to reduce compounds. One ATP is produced. This occurs for each pyruvate that feeds into the Kreb's cycle.

The Krebs' cycle occurs in the mitochondria of eukaryotic cells (and along membranes in prokaryotic cells) in the presence of oxygen (aerobic).

Electron Transport System: An Overview

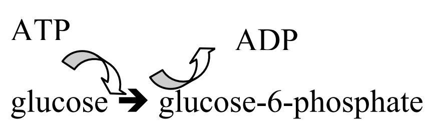
The hydrogen's from the Krebs' cycle were used to reduce two compounds. These two compounds will feed into the Electron Transport System and be passed from one molecule to another (along with electrons). As hydrogen and electrons are passed along, three ATP will be produced. The hydrogen are eventually passed to oxygen to form water.



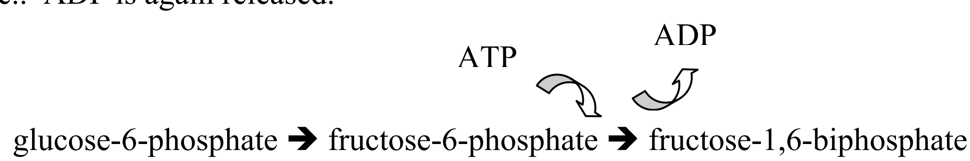
The Electron Transport System occurs in the mitochondria under aerobic conditions.

Glycolysis: A Detailed Look

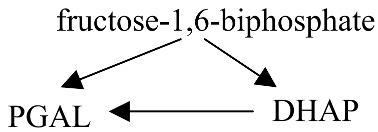
The first event of glycolysis is to *add* ATP. That seems strange until you consider the old adage "to make money, you have to have money to begin". To make ATP, we must first use some. We remove the phosphate group from ATP and add it to the number 6 carbon of glucose to form glucose-6-phosphate (G-6-P). ADP is left over from this reaction. All of these reactions of glycolysis which follow are catalyzed by enzymes.



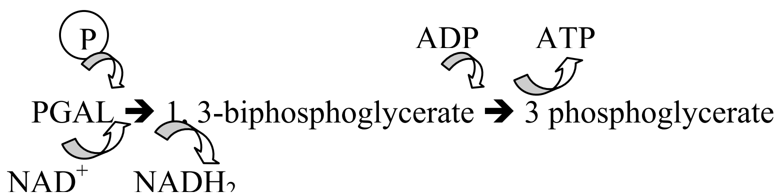
Glucose-6-phosphate (G-6-P) is converted to Fructose-6-phosphate (F-6-P), an isomer of G-6-P by an enzyme. F-6-P is converted to Fructose 1-6 biphosphate (or, as some chemists prefer, diphosphate) by the addition of another ATP to the number 1 carbon of glucose.. ADP is again released.



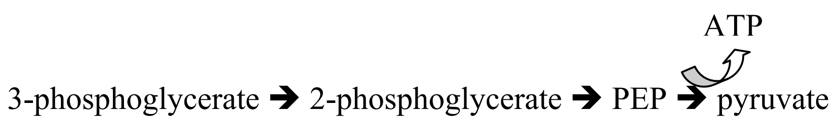
Fructose-1,6-biphosphate is broken down into two molecules: DHAP (dihydroxyacetone phosphate) and PGAL (phosphoglyceraldehyde). Both are three carbon compounds. Almost immediately, DHAP is converted into a second molecule of PGAL.



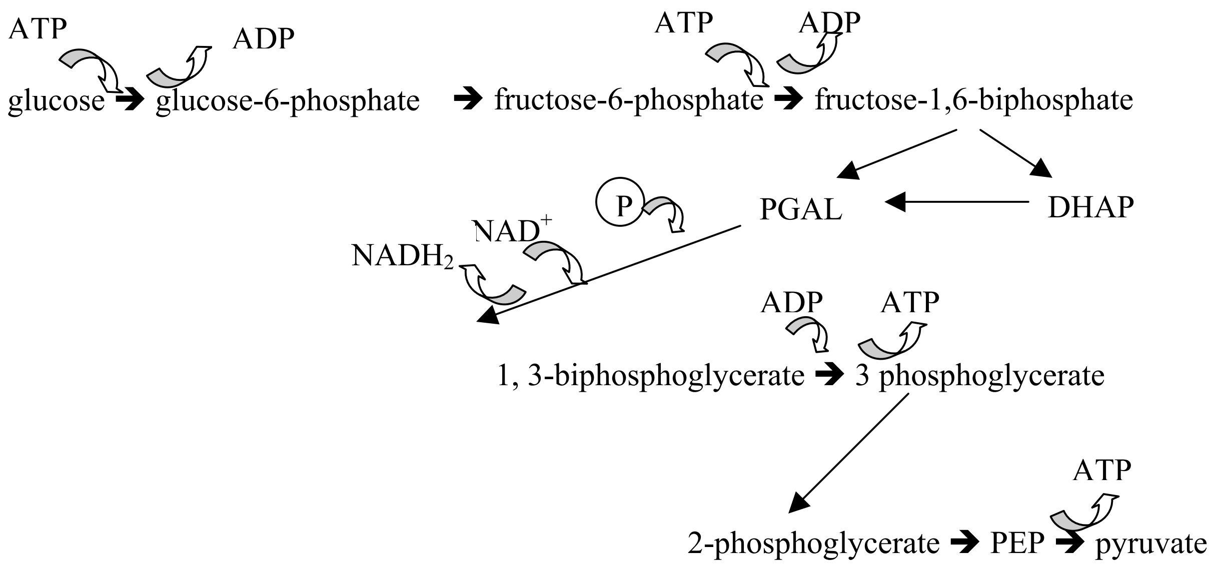
PGAL is converted into 1,3-biphosphoglycerate by the addition of a phosphate group (not from ATP this time) and by oxidized Nicotinamide Adenine Dinucleotide (NAD). NAD in the oxidized form now becomes reduced. 1,3-diphosphoglycerate is converted into 3-phosphoglycerate and we make our first ATP when we lose a phosphate group off the number 1 carbon of 1-3-diphosphoglycerate.



3-phosphoglycerate is converted into 2-phosphoglycerate. 2-phosphoglycerate is converted into phosphoenolpyruvate (PEP). PEP is converted into pyruvate with the formation of more ATP.



Anyone familiar with the business term net production immediately realizes there appears to be a problem. We, at first, appear to make two ATP and consume 2 ATP for a net production of zero. However, remember Fructose-1,6-biphosphate is converted into both DHAP and PGAL. DHAP is converted into a second molecule of PGAL and so everything after that step doubles. In reality, we have made 4 and used 2 ATP for a net production of 2.



Fates of Pyruvate

Pyruvate's fate may follow two courses: one aerobic, the other anaerobic. Under aerobic conditions, pyruvate is converted into acetyl Coenzyme A (acetyl CoA). That feeds into the Krebs' cycle. Under anaerobic conditions, pyruvate goes into the fermentation process.

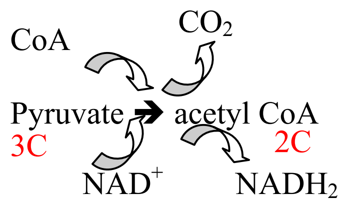
Pyruvate Under Anaerobic Conditions

Fermentation in eukaryotic cells and prokaryotic cells is different and it is even different within eukaryotic cells. Most plants, fungi, and some protistans produce ethyl alcohol and carbon dioxide as products of using pyruvate. One particular fungus, yeast, has been used for centuries to make bread (baker's yeast) and beer (brewer's yeast) both of which produce carbon dioxide and ethyl alcohol. Actually, you can make beer out of baker's yeast and bread out of brewer's yeast, it's just beer tastes better with brewer's yeast.

Fortunately, you, as an animal, do not make ethyl alcohol and carbon dioxide. If you did, as you exercise, you'd get drunk. Instead, fermentation in animals results in the production of lactic acid. Some authorities attribute the accumulation of lactic acid in muscles as a cause of muscle fatigue.

Pyruvate Under Aerobic Conditions

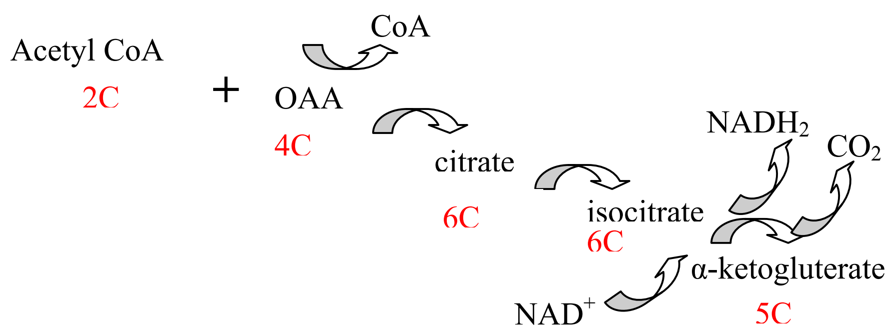
Pyruvate, a three carbon compound, under aerobic conditions is converted into acetyl Coenzyme A (Acetyl CoA), a two carbon compound. During this conversion, carbon dioxide is released. In order to form acetyl CoA, Coenzyme A must be added and at the same time, NAD is reduced to NADH + H^+.



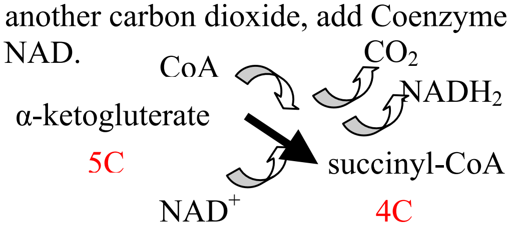
Acetyl Coenzyme A then feeds into the Krebs' cycle.

Kreb's Cycle

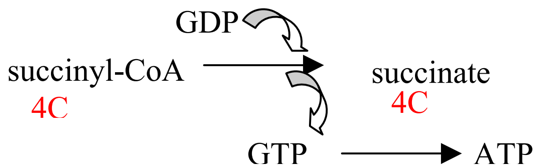
Acetyl CoA combines with oxaloacetate (OAA) in the Krebs' cycle under aerobic conditions, in the mitochondrion. OAA is a four carbon compound. This combination results in a six carbon compound called citrate. CoA is removed during this process. Citrate is converted into isocitrate, also a six carbon compound. Isocitrate is converted into alpha-ketogluterate, a five carbon compound. While this occurs, carbon dioxide is lost and NAD is reduced.



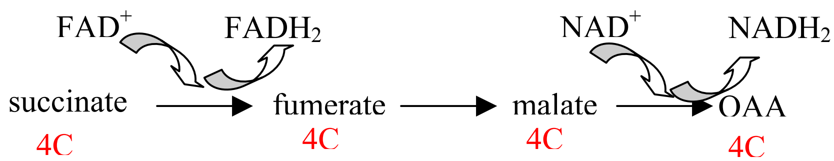
Alpha-ketogluterate is converted in succinyl-CoA, a four carbon compound. This means we lose another carbon dioxide, add Coenzyme A back to the compound, and also reduce another NAD.



Succinyl CoA is converted into succinate (a four carbon compound). Guanosine diphosphate is, at the same time, converted into Guanosine Triphosphate (GTP) and CoA is lost again. GTP is immediately converted into one ATP.



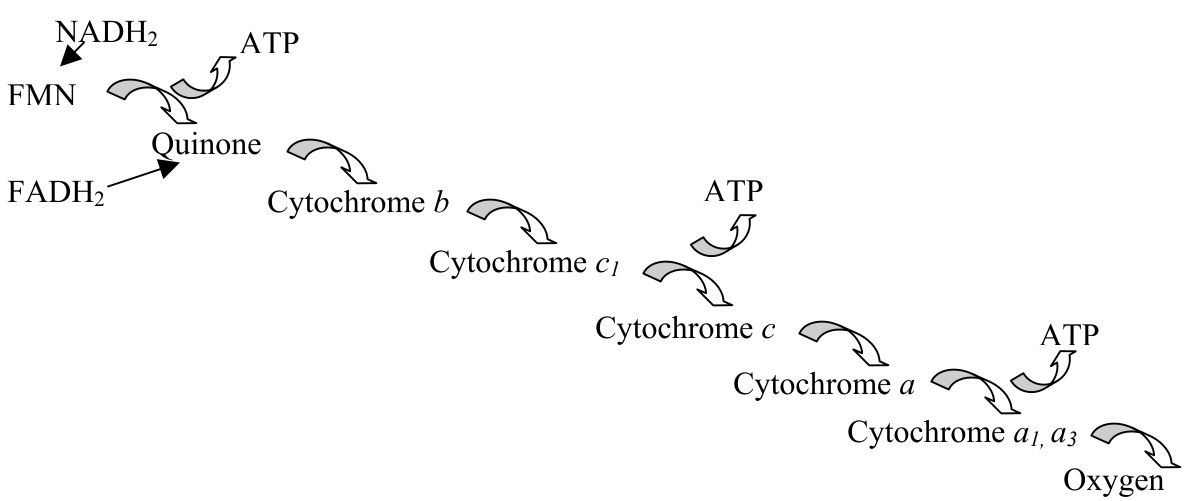
Succinate is converted into fumerate with the reduction of FAD. Fumerate is converted into malate. Malate is converted into OAA with the reduction of another NAD, and the cycle begins again.



Electron Transport System (ETS)

The reduced forms of NAD and FAD feed into the electron transport system under aerobic conditions (also in the mitochondria).

NAD reduced feeds into Flavin Mononucleotide (FMN). As it does, it passes two hydrogen atoms and two electrons to FMN and FMN becomes reduced. This process produces one ATP. FMN passes the hydrogen's and electrons to Quinone. Quinone becomes reduced (and FMN is oxidized). Quinone passes hydrogen's and electrons to cytochrome *b*. Cytochrome *b* passes them to cytochrome c_1, which passes them to cytochrome *c*. Another ATP is produced. Cytochrome *c* passes them to cytochrome *a* which in turn passes them to cyctochrome a_3. Another ATP is produced as a_3 passes them to oxygen to form water.



When NAD feeds through the electron transport system, 3 ATP are produced. However, FAD produced in the Krebs' cycle cannot enter the electron transport system at FMN. Instead, its entry is Quinone. As a consequence, only 2 ATP are produced for every molecule of FAD entering the ETS.

How Much ATP Is Produced from One Molecule of Glucose?

The answer is based on how many ATP are produced directly through glycolysis and Krebs' cycle plus the number of NAD reduced and FAD reduced that feed into the electron transport system.

Direct Production of ATP ATP

- Glycolysis ………………………………………………….2
- Krebs' cycle – one ATP per pyruvate
  - 2 pyruvate's from glycolysis…………………………..2

Indirect Production of ATP

- Glycolysis
  - 2 NAD reduced x 3 ATP per NAD in ETS……………6
- Pyruvate to Acetyl CoA
  - 1 NAD reduced per pyruvate x 2 pyruvate's……………6
- Krebs' cycle
  - 3 NAD reduced per pyruvate x 2 pyruvate's…………..18
- Krebs' cycle
  - 1 FAD reduced per pyruvate x 2 pyruvate's…………….4

Total 38 ATP

Actually, prokaryotic cells produced 38 ATP per glucose molecule, eukaryotic cells are a little less efficient at 36ATP.

The real question now becomes is this all the energy there is in a glucose molecule? Is there potential for more ATP in a molecule of glucose. The answer is yes, there is. Actually, mother nature is only about 36% efficient in ATP production from glucose. Approximately 64% of the energy of a glucose molecule is lost, usually in the form of heat or light. That doesn't sound too impressive.

What about our most prized possession, the automobile. Out of a gallon of gasoline, how much energy goes to turn the wheels? Our most efficient is around 25%. 75% of the energy in a gallon of gasoline is wasted. This is lost in the form of heat. That's why automobiles must have radiators – to prevent the engine block from melting down.