CHEM121

Unit 2: Carbohydrate Metabolism

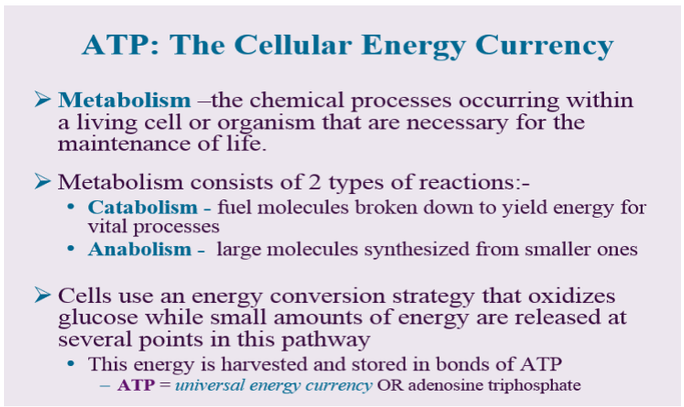
Lecture 3

At the end of the lecture, students should be able to:

- Define metabolism
- Discuss the structure and function of ATP in metabolism
- Discuss glycolysis in terms of its three major stages:
  - Activation
  - Cleavage
  - Harvest
- Write an equation for the overall reaction of aerobic glycolysis
- Discuss the practical and metabolic role of anaerobic glycolysis
- Give the main products of anaerobic glycolysis

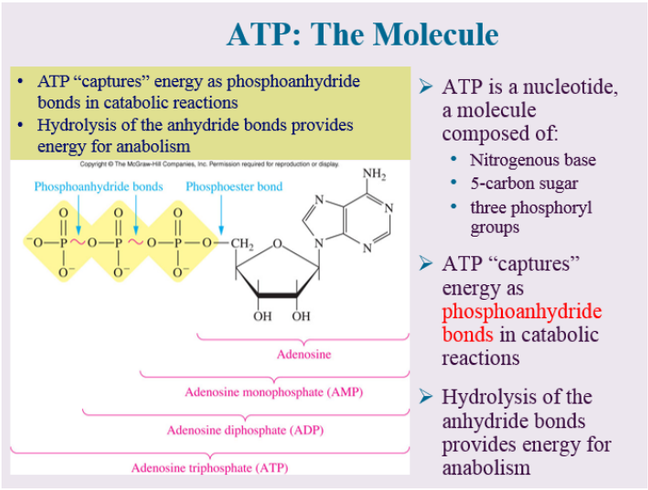
Lecture will be done through: a) Lecturer and students follow with the use of notes
b) Open discussion
c) Formative assessment through oral questioning

1. Define metabolism



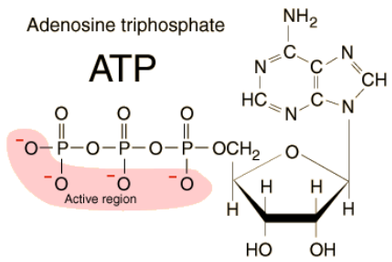
- Metabolism - The chemical processes by which cells produce the substances and energy needed to sustain life. Many metabolic processes are brought about by the action of enzymes
- As part of metabolism, organic compounds are **broken down** to provide heat and energy in the process called **catabolism** (BREAKDOWN)
- Catabolic reactions often involve oxidation or hydrolysis
- An example of an enzyme involved in catabolism is AMYLASE
- Starch and Water will get broken down to Maltose in the presence of amylase
- Simpler molecules are also used to **build more** complex compounds like proteins for growth and repair of tissues as part of **anabolism** (SYNTHESIS)
- The overall speed at which an organism carries out its metabolic processes is termed its metabolic rate (or, when the organism is at rest, its basal metabolic rate). Birds, for example, have a high metabolic rate, since they are warm-blooded, and their usual method of locomotion, flight, requires large amounts of energy. Accordingly, birds usually need large amounts of high-quality, energy-rich foods such as seeds or meat, which they must eat frequently.

2. (a) Discuss the function of ATP in metabolism



- Adenosine triphosphate (ATP) is considered by biologists to be the energy currency of life.
- It is the high-energy molecule that stores the energy we need to do just about everything we do.
- It is present in the cytoplasm and nucleoplasm of every cell, and essentially all the physiological mechanisms that require energy for operation obtain it directly from the stored ATP.
- As food in the cells is gradually oxidized, the released energy is used to re-form the ATP so that the cell always maintains a supply of this essential molecule.
- ATP is remarkable for its ability to enter into many coupled reactions, both those to food to extract energy and with the reactions in other physiological processes to provide energy to them.
- In animal systems, the ATP is synthesized in the tiny energy factories called mitochondria.

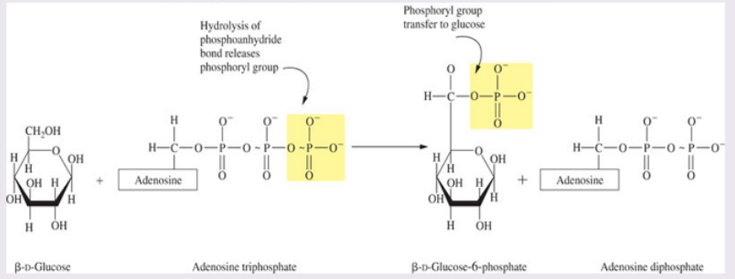
(b) Discuss the structure of ATP in metabolism



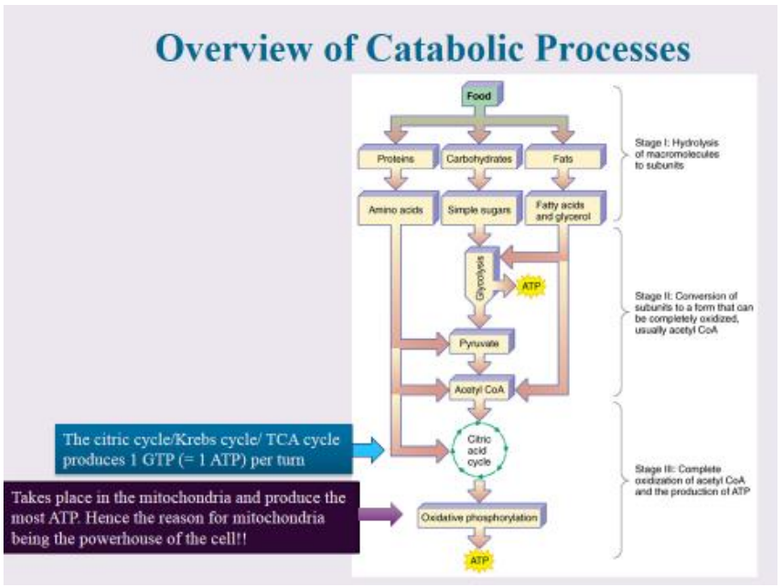
- The structure of ATP has an ordered carbon compound as a backbone, but the part that is really critical is the phosphorous part - the triphosphate.
- Three phosphorous groups are connected by oxygens to each other, and there are also side oxygens connected to the phosphorous atoms.
- Under the normal conditions in the body, each of these oxygens has a negative charge, and as you know, electrons want to be with protons - the negative charges repel each other.
- These bunched up negative charges want to escape - to get away from each other, so there is a lot of potential energy here.

ATP-Coupled reactions

- Using an energetically favorable reaction to drive an energetically unfavorable one.
- E.g. phosphorylation of glucose using ATP → G-6-P
  - Glucose + P_i → G-6-P + H_2O (needs 3 kcal/mol)
  - ATP + H_2O → ADP + P_i (releases 7 kcal/mol)



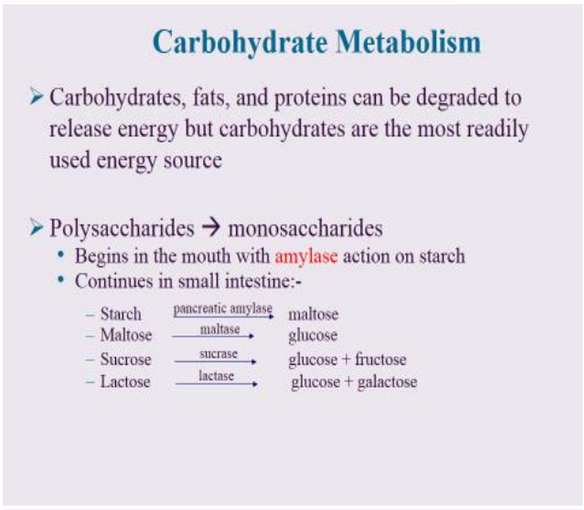
- If you remove just one of these phosphate groups from the end, so that there are just two phosphate groups, the molecule is much happier.
- This conversion from ATP to ADP is an extremely crucial reaction for the supplying of energy for life processes.
- Just the cutting of one bond with the accompanying rearrangement is sufficient to liberate about 7.3 kilocalories per mole = 30.6 kJ/mol. This is about the same as the energy in a single peanut.
- Living things can use ATP like a battery.
- The ATP can power needed reactions by losing one of its phosphorous groups to form ADP, but you can use food energy in the mitochondria to convert the ADP back to ATP so that the energy is again available to do needed work.

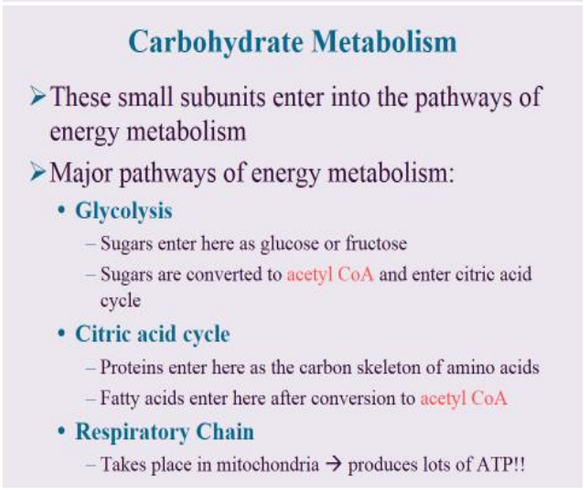


3. Discuss glycolysis in terms of its three major stages:

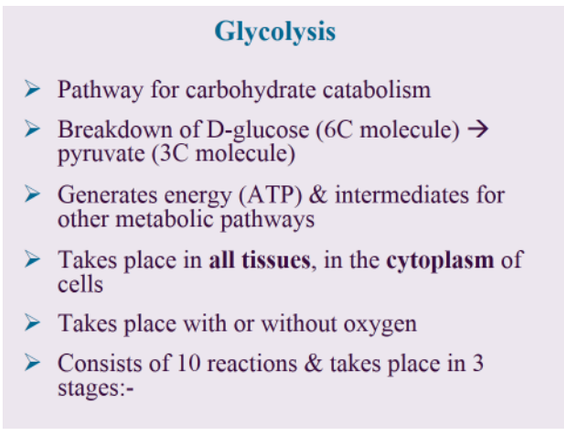
- Activation
- Cleavage
- Harvest

Important Background Information





Glycolysis (can be defined in simple terms as the pathway in which a cell breaks down glucose into energy)



Glycolysis is the metabolic process that serves as the foundation for both aerobic and anaerobic cellular respiration. In glycolysis, glucose is converted into pyruvate. Glucose is a six-memebered ring molecule found in the blood and is usually a result of the breakdown of carbohydrates into sugars. It enters cells through specific transporter proteins that move it from outside the cell into the cell's cytosol. All of the glycolytic enzymes are found in the cytosol.

The overall reaction of glycolysis which occurs in the cytoplasm is represented simply as:

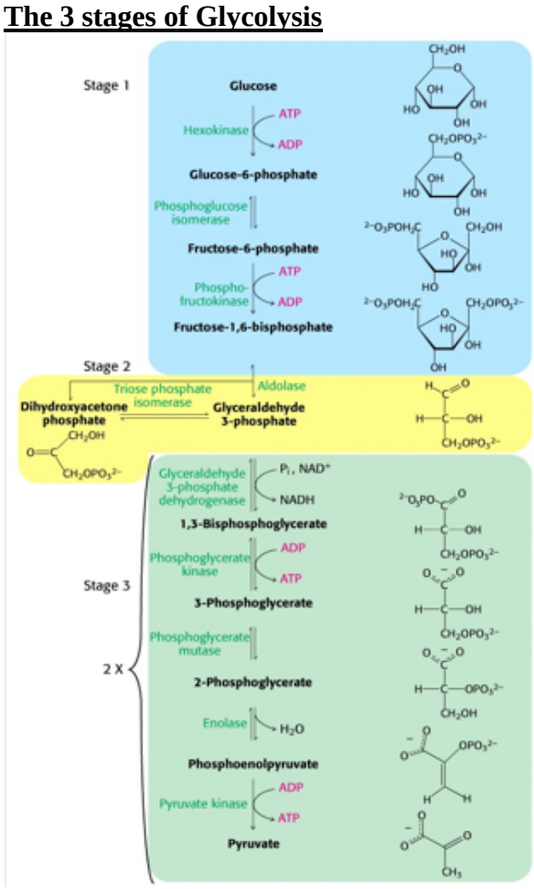
Glycolysis

Reactants (what we need):	End products:
1. One glucose	1. 2 pyruvate
2. NAD^+	2. NADH
3. 2 ATP	3. 4 ATP*

*Remember we used 2 ATP in the process, so we have a **net gain of 2 ATP**

- The Glycolytic pathway describes the oxidation of glucose to pyruvate with the generation of ATP and NADH(ie Nicotinamide adenine dinucleotide)
- Glycolysis is a universal pathway; present in all organisms from yeast to mammals.
- In animals, glycolysis takes place in the cytosol
- Glycolysis is anaerobic; it does not require oxygen
- However as the process continues and in the presence of O_2, pyruvate is further oxidized to CO_2.
- In the absence of O_2, pyruvate can be fermented to lactate or ethanol.

The 3 stages of Glycolysis



Summary of the Glycolysis Reactions

Stage 1: Activation

These reactions correspond to an energy investment; phosphorylated intermediates are formed at expense of 2 ATP molecules

Stage 2: Cleavage

Split into two three-carbon sugars

Stage 3: Harvest

The last 5 reactions is an energy generating phase in which ATP is formed

2 pyruvates, 4ATP and 2NADH produced:

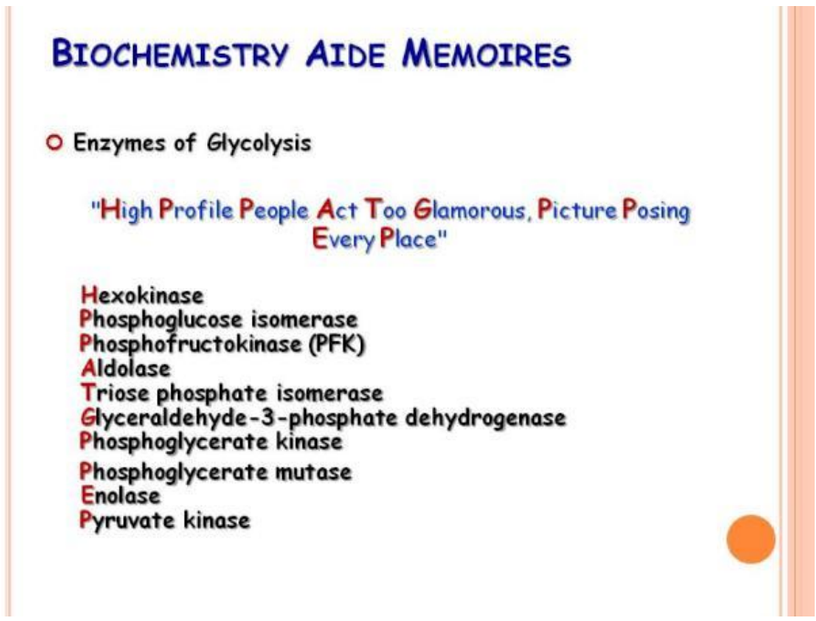
- **Substrate-level phosphorylation** gives 4 ATP → phosphoryl group is transferred to ADP from 1,3-bisphosphoglycerate & phosphoenolpyruvate
- NAD^+ (coenzyme) is reduced →NADH which carries hydride anions with 2 e-s (H^-)
- Pyruvate: the fate depends on cellular conditions

Tips to remember glycolysis reactions.

Glycolysis

Glycolysis

Goodness (Glucose)
Gracious, (Glucose-6-P)
Father (Fructose-6-P)
Franklin (Fructose-1,6-diP)
Did (Dihydroxyacetone-P)
Go (Glyceraldehyde-P)
By (1,3-Biphosphoglycerate)
Picking (3-phosphoglycerate)
Pumpkins (2-phosphoglycerate)
(to)
PrEPare (Phosphoenolpyruvate [PEP])
Pies (Pyruvate)



- **Stage 1** is the **investment stage**. 2 mols of ATP are consumed for each mol of glucose
- Glucose is converted to fructose-1,6-bisphosphate.
- Glucose is trapped inside the cell and at the same time converted to an unstable form that can be readily **cleaved** into 3-carbon units.
- In **stage 2** fructose-1,6-bisphosphate is cleaved into two (2) 3- carbon units of glycerladehyde-3-phosphate.
- **Stage 3** is the **harvesting stage.** 4 mols of ATP and 2 mols of NADH are gained from each initial mol of glucose.
- This ATP is a result of substrate-level phosphorylation
- Glyceraldehyde-3-phosphate is oxidized to pyruvate

10 Step-wise reactions of glycolysis

Reaction 1: Phosphorylation of glucose to glucose-6 phosphate.

- Here, the glucose ring is phosphorylated. Phosphorylation is the process of adding a phosphate group to a molecule derived from ATP. As a result, at this point in glycolysis, 1 molecule of ATP has been consumed.
- The reaction occurs with the help of the enzyme **hexokinase**, an enzyme that catalyzes the phosphorylation of many six-membered glucose-like ring structures. Atomic magnesium (Mg) is also involved to help shield the negative charges from the phosphate groups on the ATP molecule. The result of this phosphorylation is a molecule called glucose-6-phosphate (G6P), thusly called because the 6′ carbon of the glucose acquires the phosphate group.
- This step is irreversible. So the glucose gets trapped inside the cell.
- (Glucose transporters transport only free glucose, not phosphorylated glucose)

Reaction 2: Isomerization of glucose-6-phosphate to fructose 6- phosphate. The aldose sugar is converted into the keto isoform.

- The second step of glycolysis involves the conversion of glucose-6-phosphate to fructose-6-phosphate (F6P). This reaction occurs with the help of the enzyme **phosphoglucose isomerase (PI)**. As the name of the enzyme suggests, this reaction involves an isomerization reaction.
- The reaction involves the rearrangement of the carbon-oxygen bond to transform the six-membered ring into a five-membered ring. To rearrangement takes place when the six-membered ring opens and then closes in such a way that the first carbon becomes now external to the ring.
- This is a reversible reaction.
- The fructose-6-phosphate is quickly consumed and the forward reaction is favored.

Reaction 3: is another kinase reaction. Phosphorylation of the hydroxyl group on C1 forming fructose-1,6- bisphosphate.

- In the third step of glycolysis, fructose-6-phosphate is converted to fructose- 1,6-bisphosphate (FBP). Similar to the reaction that occurs in step 1 of glycolysis, a second molecule of ATP provides the phosphate group that is added on to the F6P molecule.
- The enzyme that catalyzes this reaction is **phosphofructokinase (PFK)**. As in step 1, a magnesium atom is involved to help shield negative charges.
- The PFK enzyme regulates the pace of glycolysis.
- Reaction is coupled to the hydrolysis of an ATP to ADP and Pi.
- This is the second irreversible reaction of the glycolytic pathway.

Reaction 4: fructose-1,6-bisphosphate is split into two (2) 3-carbon molecules, one aldehyde and one ketone.

- This step utilizes the enzyme **aldolase**, which catalyzes the cleavage of FBP to yield two 3-carbon molecules. One of these molecules is called glyceraldehyde-3-phosphate (GAP) and the other is called dihydroxyacetone phosphate (DHAP).

Reaction 5: DHAP and GAP are isomers of each other and can readily inter-convert by the action of the enzyme triose-phosphate isomerase.

- GAP is the only molecule that continues in the glycolytic pathway. As a result, all of the DHAP molecules produced are further acted on by the enzyme **triphoshpate isomerase** (TIM), which reorganizes the DHAP into GAP so it can continue in glycolysis. At this point in the glycolytic pathway, we have two 3-carbon molecules, but have not yet fully converted glucose into pyruvate.GAP is a substrate for the next step in glycolysis so all of the DHAP is eventually depleted.
- So, 2 molecules of GAP are formed from each molecule of glucose
- Upto this step, 2 molecules of ATP were required for each molecule of glucose being oxidized
- The remaining steps release enough energy to shift the balance sheet to the positive side.
- This part of the glycolytic pathway is called as the **payoff** or **harvest stage.**
- Since there are 2 GAP molecules generated from each glucose, each of the remaining reactions occur twice for each glucose molecule being oxidized.

Reaction 6: GAP is dehydrogenated by the enzyme glyceraldehyde 3-phosphate dehydrogenase (GAPDH).

- In this step, two main events take place: 1) glyceraldehyde-3-phosphate is oxidized by the coenzyme nicotinamide adenine dinucleotide (NAD); 2) the molecule is phosphorylated by the addition of a free phosphate group. The enzyme that catalyzes this reaction is **glyceraldehyde-3-phosphate dehydrogenase (GAPDH)**.
- The enzyme GAPDH contains appropriate structures and holds the molecule in a conformation such that it allows the NAD molecule to pull a hydrogen off the GAP, converting the NAD to NADH. The phosphate group then attacks the GAP molecule and releases it from the enzyme to yield 1,3 bisphoglycerate, NADH, and a hydrogen atom.In the process, NAD^+ is reduced to NADH + H^+ from NAD.
- Oxidation is coupled to the phosphorylation of the C1 carbon.
- The product is 1,3-bisphosphoglycerate.(BPG)

Reaction 7: BPG has a mixed anhydride, a high energy bond, at C1. This high energy bond is hydrolyzed to a carboxylic acid and the energy released is used to generate ATP from ADP. Product: 3-phosphoglycerate.

- Enzyme: **phosphoglycerate kinase**.

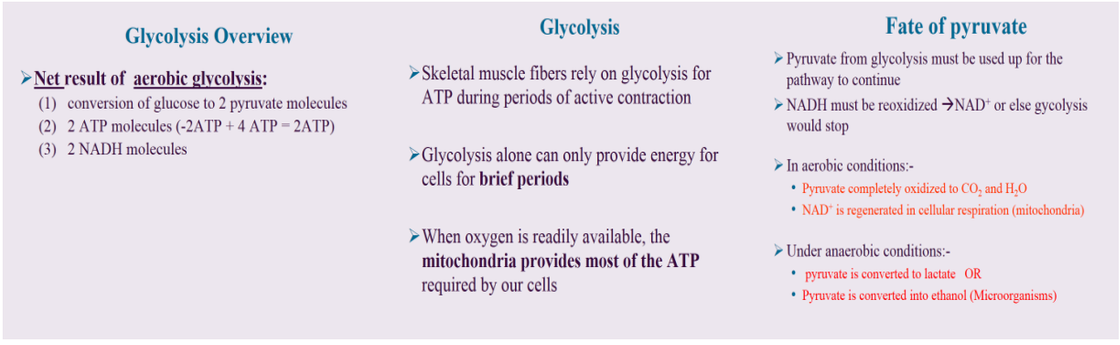
Reaction 8: The phosphate shifts from C3 to C2 to form 2- phosphoglycerate.

- Enzyme: **phosphoglycerate mutase**.

Reaction 9: Dehydration catalyzed by **enolase (a lyase)**. A water molecule is removed to form phosphoenolpyruvate which has a double bond between C2 and C3.

Reaction 10: Enolphosphate is a high energy bond. It is hydrolyzed to form the enolic form of pyruvate with the synthesis of ATP.

- The irreversible reaction is catalyzed by the enzyme **pyruvate kinase**.
- Enol pyruvate quickly changes to keto pyruvate which is far more stable.



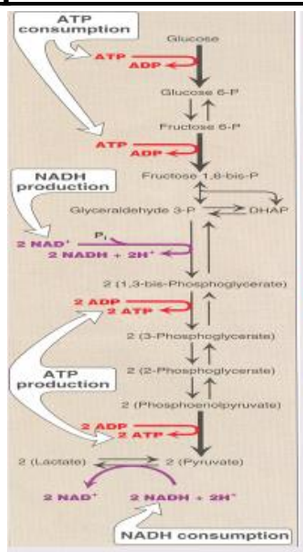
4. Write an equation for the overall reaction of aerobic glycolysis

- In aerobic respiration, the pyruvate from glycolysis is completely oxidized to carbon dioxide and water USING OXYGEN.
- You will learn about KREBS CYCLE AND RESPIRATORY CHAIN IN LECTURE 4
- OVERALL REACTION of aerobic glycolysis is :

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O + 38ATP$$

- Thus 38 molecules of ATP are produced for every glucose molecule oxidized in aerobic respiration.

5. Discuss the practical and metabolic role of anaerobic glycolysis



Anaerobic glycolysis – Lactate formation

- The irreversible reactions of glycolysis are shown with thick arrow.
- DHAP = dihydroxyacetone phosphate
- Occurs in exercising muscle & cells with no mitochondria e.g. RBCs

NET RESULT OF ANAEROBIC GLYCOLYSIS:

(1) conversion of 1 glucose to 2 lactate molecules
(2) 2 ATP molecules (-2ATP + 4 ATP = 2ATP)
(3) 0 NADH

- Anaerobic respiration is often referred to as fermentation
- Anaerobic respiration occurs in a variety of microorganisms, as well as, in the muscle tissues of animals
- A variety of microorganisms use anaerobic respiration as their major source of ATP
- In **anaerobic respiration involving microorganisms**, ethanol is the alcohol that is produced.
- This alcohol is found in alcoholic beverages
- This process is called alcoholic fermentation and its occurrence in yeast is made use of in the manufacture of beer, wine and other alcoholic drinks
- Production of carbon dioxide by yeast is used in bread making, to make dough rise
- Ethanol is a waste product that still contains a lot of energy (for example, it is used to make gasohol, a fuel that is used for cars in Brazil)
- In **anaerobic respiration involving animals,** no carbon dioxide is produced
- Also alcohol is NOT made
- Instead the product is lactate (lactic acid) whose build- up in muscles contributes to the sensation of fatigue and can contribute to cramp
- Recall – build-up of oxygen debt during vigorous exercise
- Lactate still contains a LOT of energy

6. Give the main products of anaerobic glycolysis

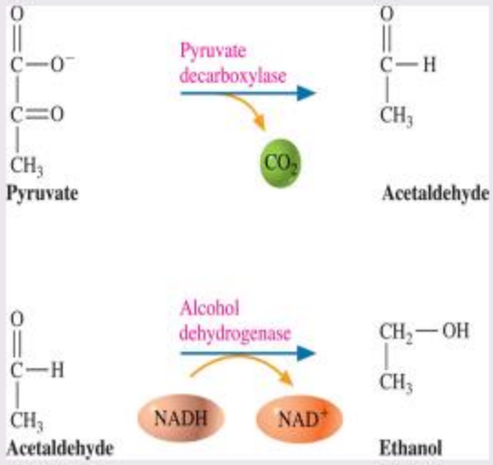
If you are dealing with **ANIMALS**, then the main products of glucose undergoing anaerobic respiration (anaerobic glycolysis) is:

- Lactate (lactic acid)
- ATP

If you are dealing with **FUNGI (example yeast)**, then the main products of glucose undergoing anaerobic respiration (anaerobic glycolysis) is:

- Ethanol
- Carbon Dioxide
- ATP

Anaerobic glycolysis- Alcohol fermentation



- Yeast ferment sugars of fruit and grains anaerobically, using pyruvate from glycolysis
  - *Pyruvate decarboxylase* removes CO_2 from the pyruvate producing acetaldehyde
  - *Alcohol dehydrogenase* catalyzes reduction of acetaldehyde to ethanol, releasing NAD^+ in the process
  - Regeneration of NAD^+ allows glycolysis to continue
  - Thus, products of alcohol fermentation are ethanol & CO_2