Course: Cell Physiology-PHYS-115

ATP AND METABOLISM-I

Glycolysis

Learning Objectives:

- ❖ Define the term "metabolism" and describe it's main two pathways.
- ❖ Describe the structure of ATP and explain how it is used to carry and provide energy to the cell.
- ❖ List the tow main ways of ATP production in the body.
- ❖ List the three main pathways of cellular respiration and mention the site of each process.
- ❖ List the electron acceptor and non-electron acceptor coenzymes and show their related vitamins.
- ❖ Describe BRIEFLY the process of glycolysis: Its main purpose, ATP accounting, and its resulted products.
- ❖ List the three possible fates of pyruvate after it is produced from glycolysis.

Metabolic Pathways:

❖ Cells cannot survive without a source of energy and a source of chemical "***building blocks***' the small molecules from which macro-molecules such as proteins, nucleic acids, and polysaccharides are synthesized.

❖ The chemical reactions used by cells to obtain energy also can provide the various small molecules that cells need for synthesis of macromolecules & other cellular constituents.

❖ When we consider all the chemical reactions that occur within a cell, we are talking about **metabolism** (Greek word = 'to change").

❖ The over all metabolism of a cell consists, in turn, of ***many specific metabolic pathways, each of which accomplishes a particular task.***

❖ From biochemistry perspective, ***life at cellular level*** can be defined as a ***network of integrated & carefully regulated metabolic pathways, each contributing to the sum of activities that a cell must carry out***. During metabolism, substances are constantly built up and torn down.

Metabolic Pathways:

❖Metabolic pathways are of two general types:

- **Anabolic pathways** (Greek "ana" = "up"): These pathways *synthesize cellular components (increase in molecular order) and they are* ***endergonic*** *(energy –requiring).* ***Polymer synthesis & biological reduction of CO2 to sugar are examples of anabolic pathways*** *(always synthesize polymers such as starch & glycogen to store energy for future use).*

- **Catabolic pathways** (Greek "kata"= "down"): *These pathways involve breakdown of cellular constituents (decrease in molecular order) and they are* ***exergonic*** *(energy liberating).* ***They involve hydrolysis of macromolecules or biological oxidations. e.g. the hydrolysis of foods in the digestive tract*** . Catabolic pathways play two roles:

  - ✓ **They release the free energy needed to drive cellular functions**.
  - ✓ **They give rise to small organic molecules (metabolites), that are the building blocks for biosynthesis.**

ATP – *The primary Energy Currency of the Biological World:*

- *Food fuels cannot be used to energize body activities directly*. Instead, ***some of the food energy is captured temporarily in the bonds of a chemical called adenosine triphosphate (ATP)*** . ***Later, ATP's bonds are broken and the stored energy is released as needed to do cellular work.***

- Chemical energy in the form of ATP is the most useful form of energy in living systems because it is used to run almost all functional processes.

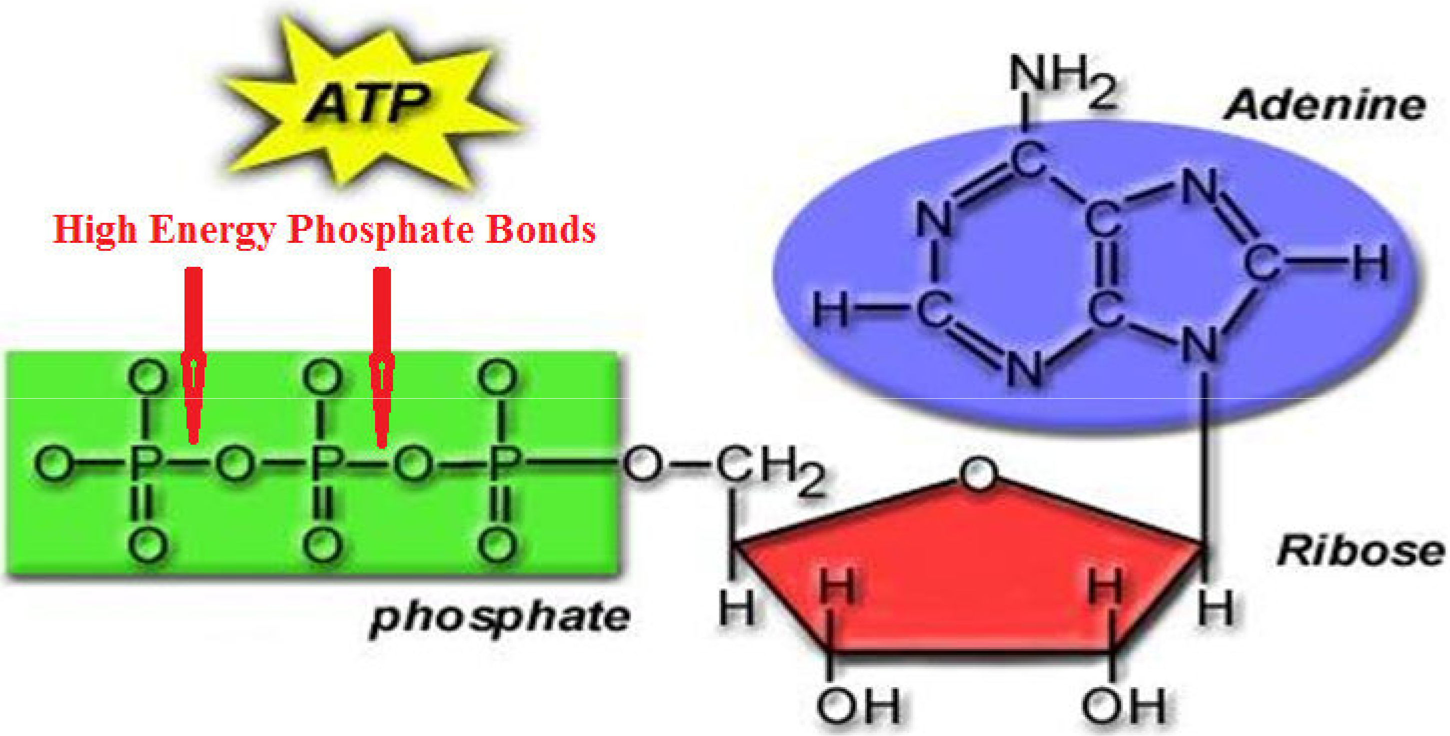
- **Adenosine-triphosphate (ATP)** is a nucleoside triphosphate used in cells as ***a coenzyme***. It is often called the ***"molecular unit of currency "*** of intracellular energy transfer. ATP transports chemical energy within cells for metabolism. It is one of the end products of ***photophosphorylation, cellular respiration, and fermentation*** and used by enzymes and structural proteins in many cellular processes, including biosynthetic reactions, motility, and cell division.

- *Energy is released by breaking the high- energy bonds between the last two phosphates in ATP (hydrolysis) by the action of* ***ATPase enzyme***. *ATP is re made by the reversing the hydrolysis by the action of* ***ATP synthetase enzyme***.

ATP – *The primary Energy Currency of the Biological World:*

- **ATP** consists of ***adenine*** + ***ribose*** + ***3 phosphates***.
- ***Adenine*** + ***ribose*** = ***adenosine.***
- **AMP** = adenosine monophosphate, and *the phosphate is attached by an ester bond without high energy.*
- **ADP** = adenosine diphosphate, and *the second phosphate is attached by a high energy phosphate bond.*
- In **ATP**, *the third phosphate is attached by an even higher energy phosphate bond.*
- The high energy phosphate bonds in ATP are NOT the very highest energy phosphate bonds in the cell; ***they are intermediate on the bioenergetic scale of phosphate bonds.***
- ***This makes A TP a useful energy currency because the third phosphate bond is of sufficiently high energy to carry packets of energy for practical purposes, but it is not so high that we find it difficult to make it.***

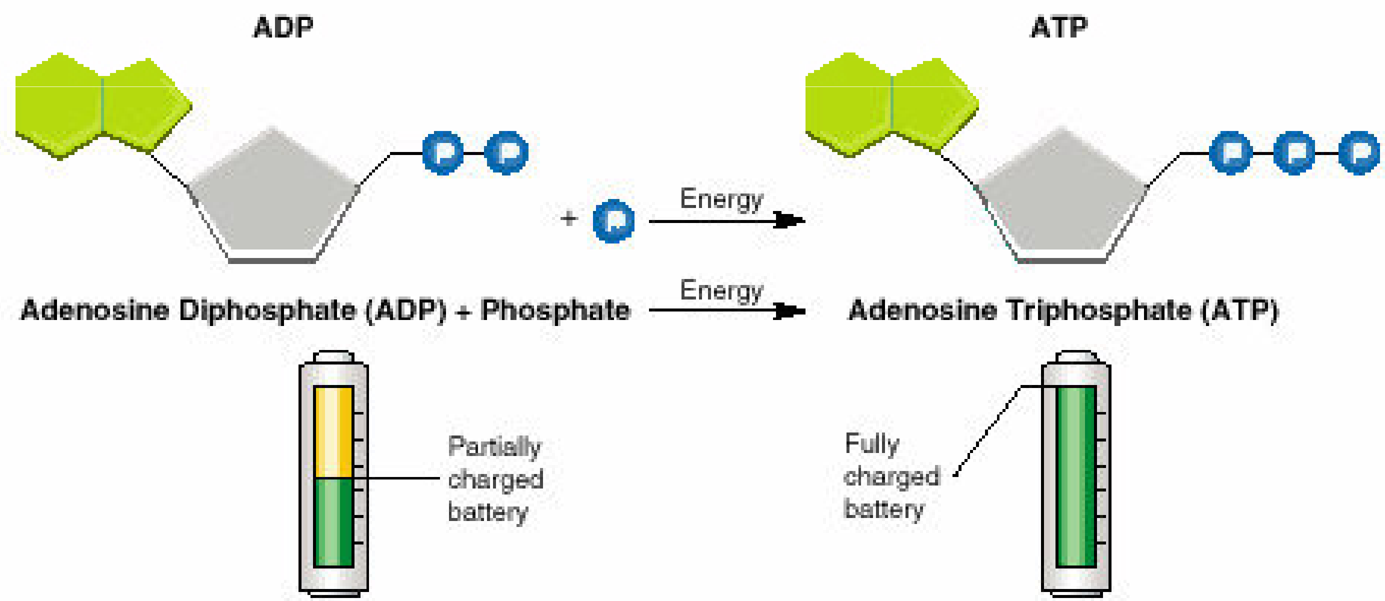
ATP – *Structure:*



ATP – *The primary Energy Currency of the Biological World:*

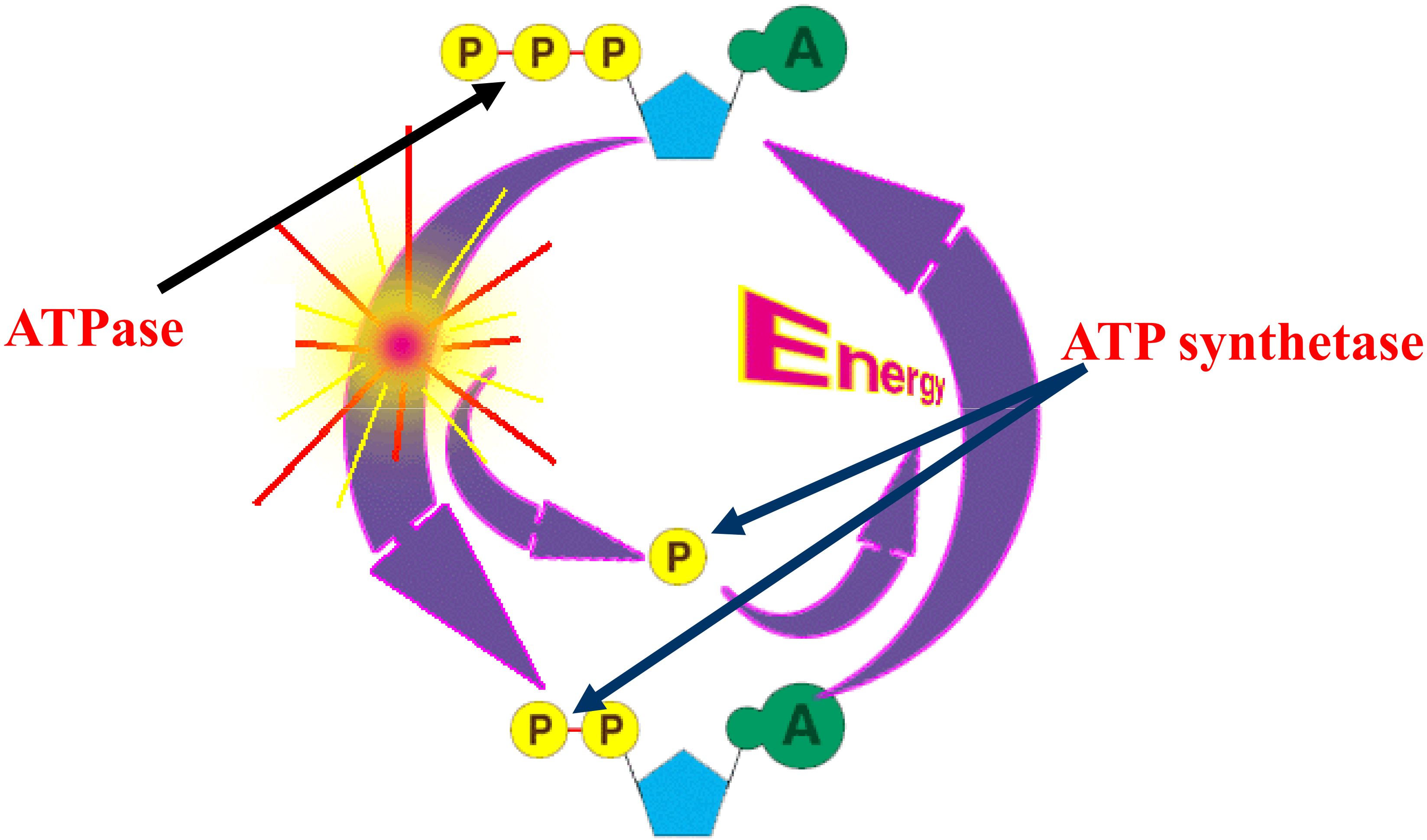
- All energy is stored in the **bonds** of ATP—**breaking** the bond **releases** the energy.

- When the cell has energy available it can store this energy by adding a **phosphate group** to ADP, producing **ATP**



ADP vs. ATP ATP can be compared to a fully charged battery because both contain stored energy, whereas ADP resembles a partially charged battery. **Predicting** *What happens when a phosphate group is removed from ATP?*

ATP – *The primary Energy Currency of the Biological World:*



The ADP-ATP Cycle

ATP Production:

❖ ATP is produced during a process called "***cellular respiration***". The energy comes from glucose, with the overall simplified reaction:

$$6CO_2 + 6H_2O + \text{Energy} \underset{\text{Respiration}}{\overset{\text{Photosynthesis}}{\rightleftharpoons}} C_6H_{12}O_6 + 6O_2$$

❖ The energy which is stored in the whole glucose molecule is approximately100-fold the amount of energy which is stored in a high-energy phosphate bond in 1 ATP molecule.

❖ Therefore, we release the energy from glucose step-wise, releasing tiny packets of energy so that A TP can be synthesized 1 molecule at a time, where possible.

❖ ATP may be made in 2 ways:

1. **Substrate-level phosphorylation** utilizes the energy of a single exergonic substrate conversion, to directly power the phosphorylation of ADP to make ATP.
2. **Oxidative phosphorylation** utilizes the energy of alternating oxidation and reduction of ***coenzymes*** in the ***electron transport system (ETS)***, to make ATP.

ATP Production:

- Glucose breakdown & ATP production ***(cellular respiration)*** shown in the equation in the previous slide, is complex process and involves ***three main pathways:***

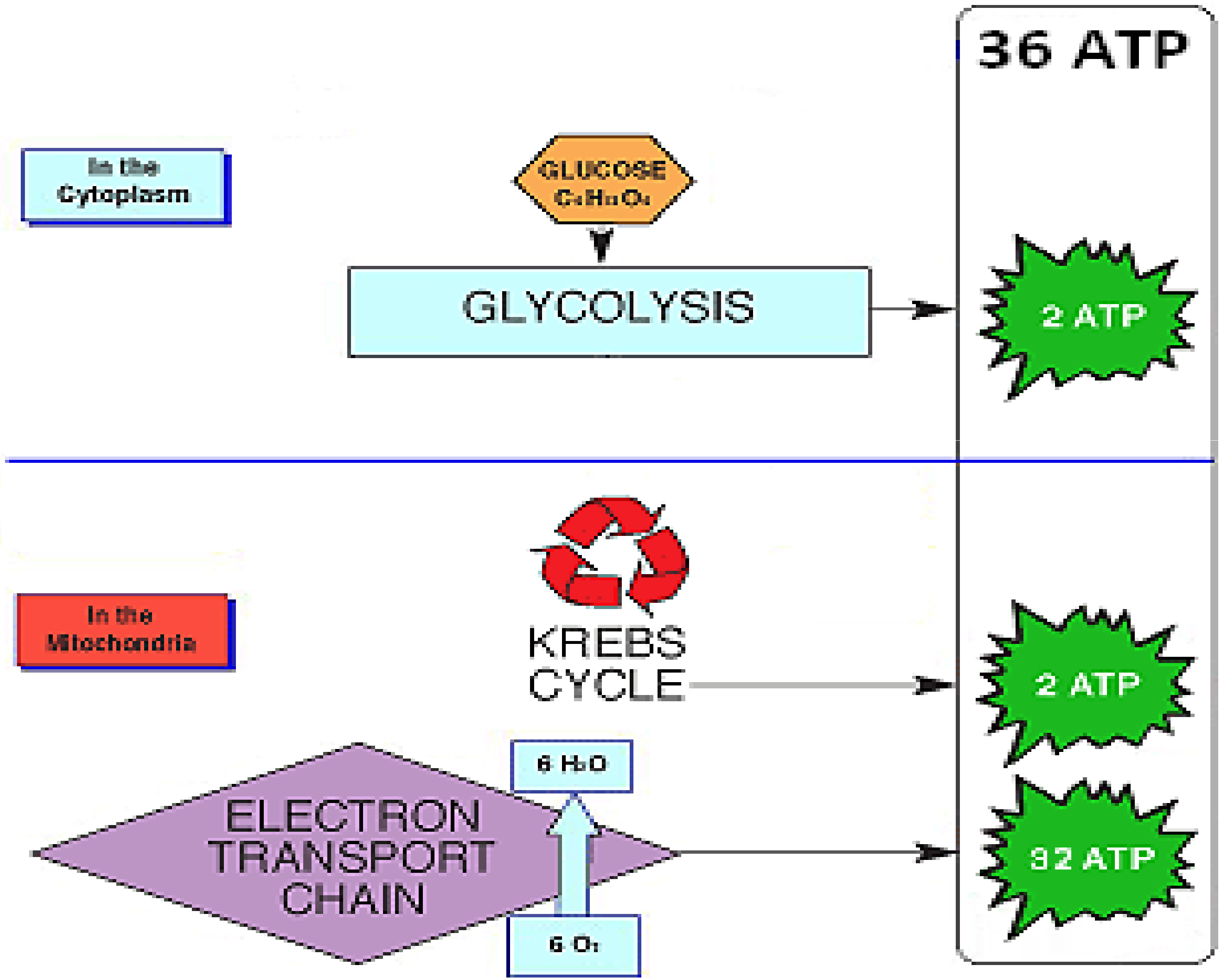
  1. **Glycolysis**, ***occurs in the cell cytoplasm***.
  2. **The Krebs cycle**, ***occurs in the mitochondria***.
  3. **The electron transport chain/system & oxidative phosphrylation*****, also occurs in the mitochondria.***

- So, the cellular respiration occurs in tow sites within the cell, ***the cytoplasm (glycolysis)*** and ***the mitochondria (The Krebs cycle & ETC)***.

- The three pathways will produce a total of **36 ATP molecules** ***(2 from glycolysis, 2 from Krebs cycle, and 32 from ETS) from one glucose.***

- ***These metabolic pathways occur in a definite order***, and we willconsider them sequentially.

ATP – *Production:*



ATP – *Production – Coenzymes involved:*

- Many of the reactions involved in ATP production are ***oxidation steps***. Oxidation does not necessarily utilize oxygen immediately; ***some steps are anaerobic***. ***Anaerobic oxidation involves the removal of hydrogen***.

- ***Hydrogen ions are released as protons which acidify the environment, while the electrons from the hydrogen are picked up by an oxidizing agent, or electron acceptor.***

- **Electron acceptors:**
  - **NAD^+** (nicotinamide adenine dinucleotide) is made from nicotinamide or niacin, ***vit amin B3***.
  - **FAD** (flavin adenine dinucleotide) is made from riboflavin, or ***vitamin B2***.
  - **FMN** (flavin mononucleotide) is also made from ***riboflavin***, found in the ETS.
  - **Coenzyme Q** *is not derived from a vitamin*, but is part of the ETS.
  - **Cytochromes** are electron acceptors which contain *iron and copper*, in the ETS.

- **Coenzymes which are not electron acceptors**:

  - **TPP** (thiamine pyrophosphate) is made from thiamine, ***vitamin B1***.
  - **Coenzyme A** is made from pantothenate, ***vitamin B5***.

Glycolysis at A Glance:

- Glycolysis occurs ***in the cytoplasm***, and ***does not require oxygen***.

- Glycolysis starts by ***one glucose (6-carbon sugar)*** and ends up with a product of ***two 3-carbon pyruvate molecules***.

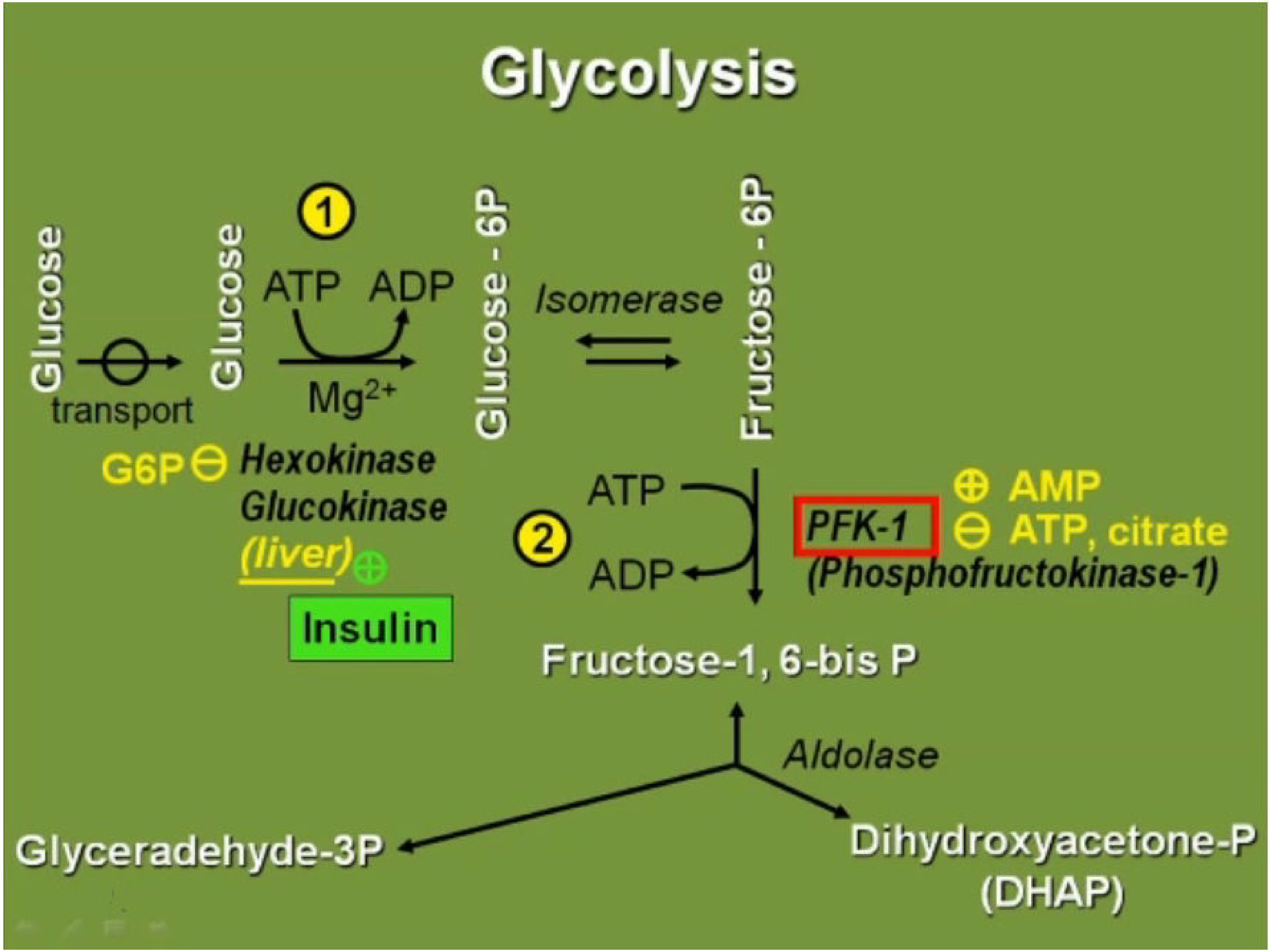
- **ATP accounting:**

  - ***2 molecules of ATP are used up*** in the preparation stages.
  - ***4 molecules of ATP are produced from*** the breakdown of 1 glucose molecule.
  - Therefore, ***the net gain in ATP is just 2 ATP***, for each glucose molecule split.
  - All the ***ATP is made by substrate level phosphrylation.***

- **Oxidation:**

  - There is just ***1 oxidation step in glycolysis***, applied to each 3-carbon compound.
  - ***2 molecules of NAD^+ are reduced*** to **$NADH + H^+$**

Glycolysis in Details:



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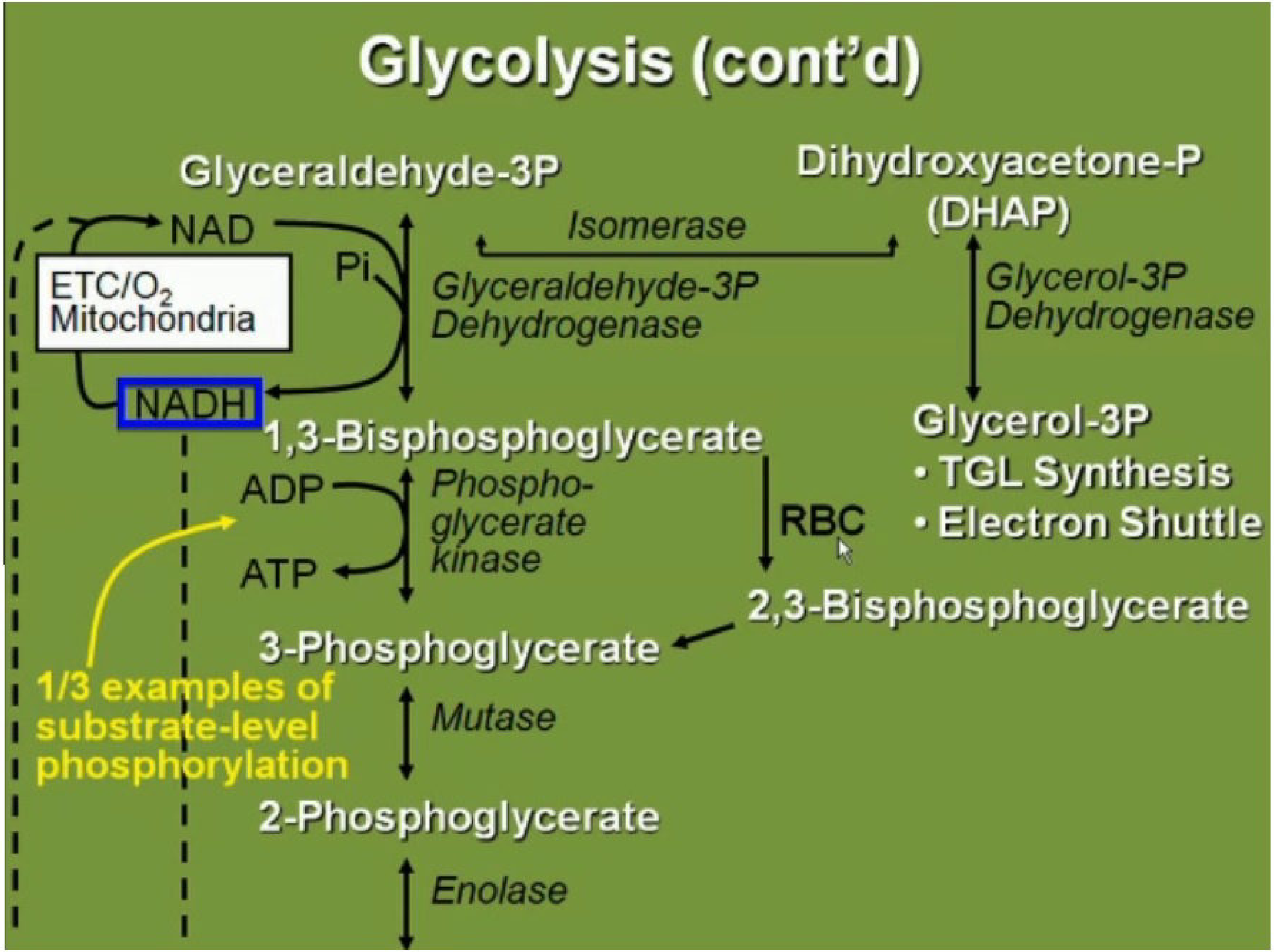

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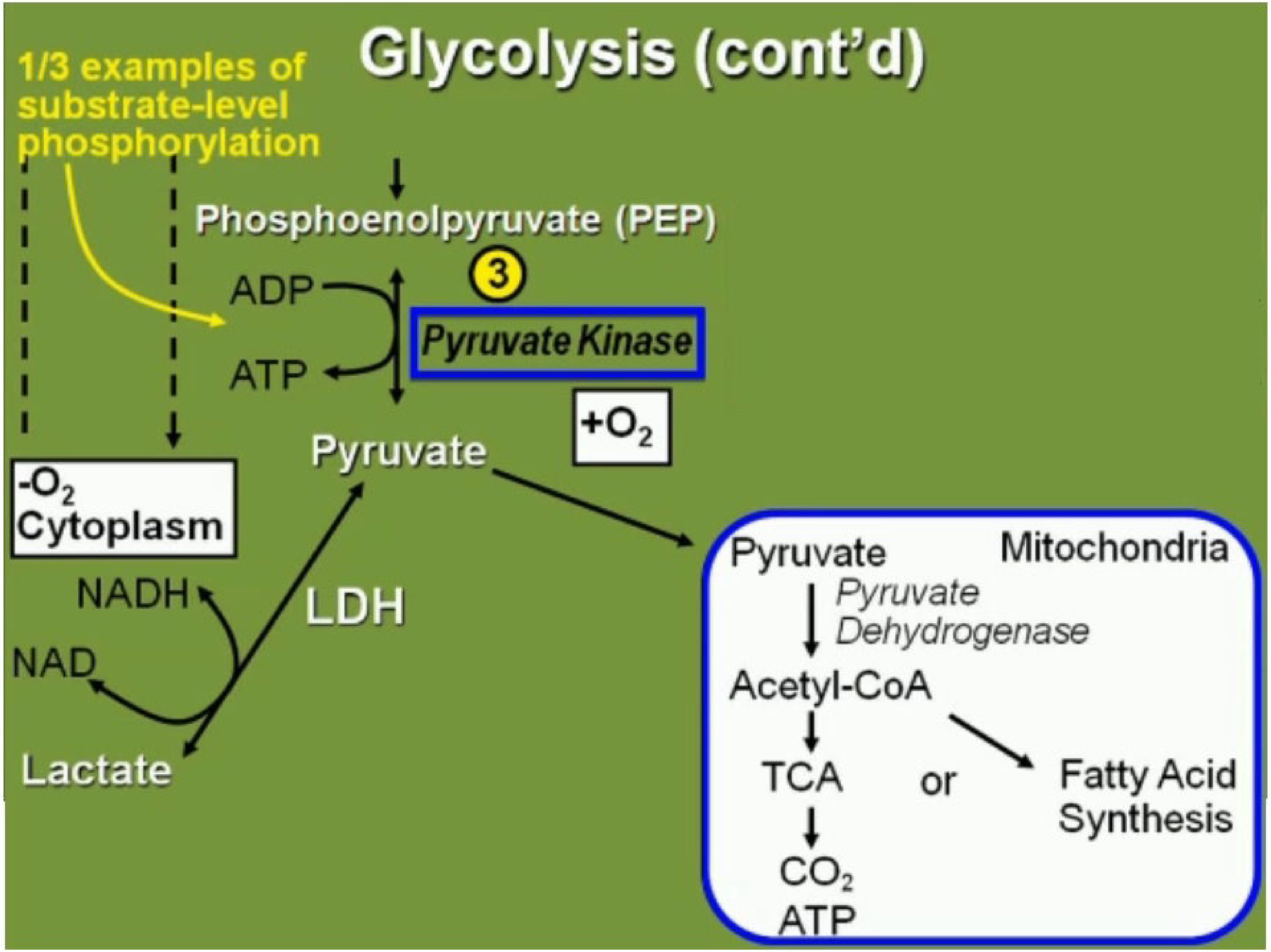


Glycolysis (Simplified Version):

- **Reactions 1-3, preparation**: Glucose is phosphorylated to make **fructose 1,6-bisphosphate.** ***Two molecules of ATP are used up in this process***.

- **Reactions 4-5, cleavage**: Fructose 1,6-bisphosphate is split into two molecules, which at first are slightly different from each other. One of them undergoes an isomerization to make them the same, so we end up with ***2 identical molecules of glyceraldehyde-3-phosphate***. ***From this point, the process is in duplicate if we think on a "per glucose" basis.***

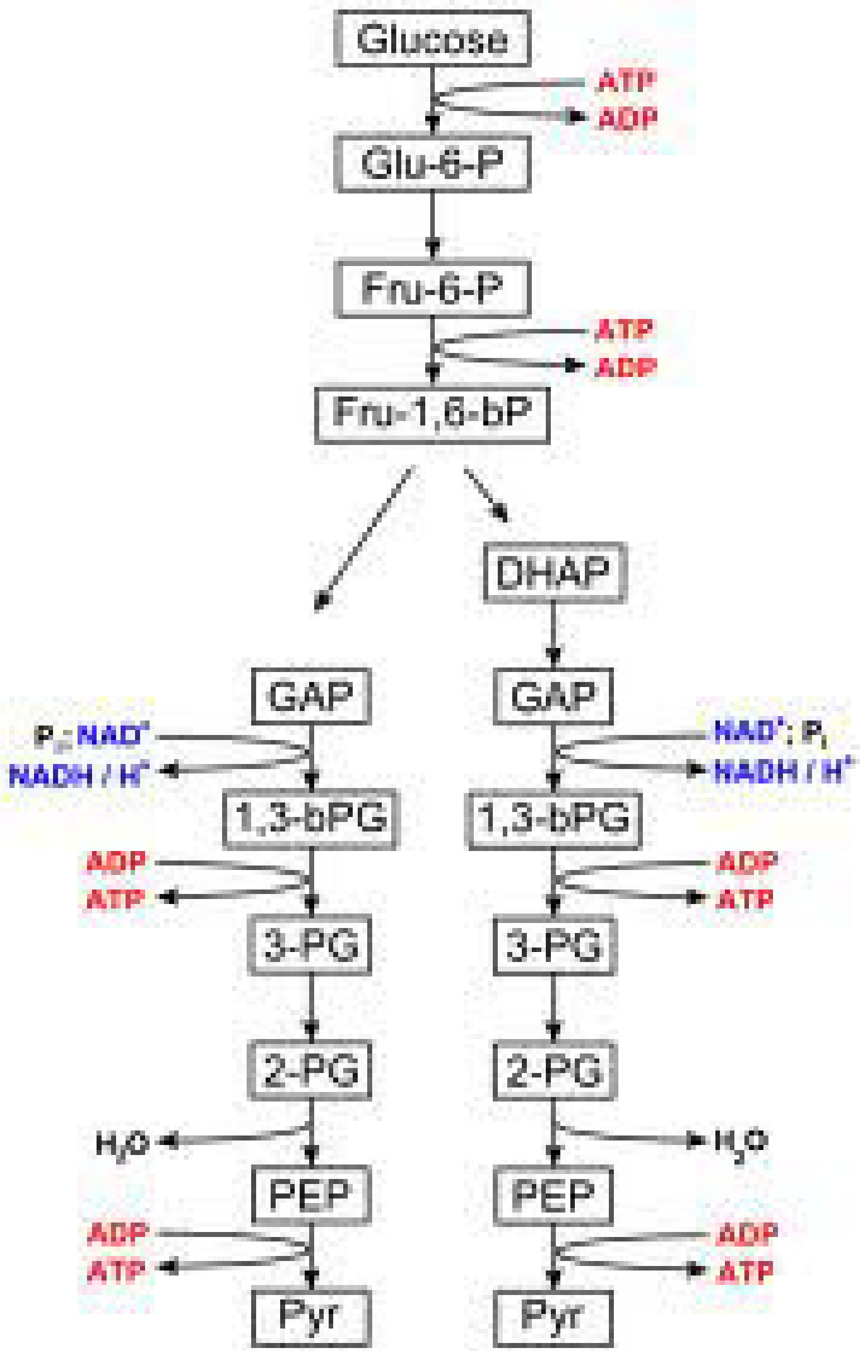
- **Reactions 6-7, oxidation & ATP production**: Glyceraldehyde-3-phosphate is oxidized to ***3-phosphoglycerate.*** (Note that this reaction oxidizes an aldehyde to a carboxylic acid). ***This is an oxidation***, so it requires an ***electron acceptor***, which is $\mathbf{NAD^+ \longrightarrow NADH + H^+}$. ***ATP is produced through substrate-level phosphrylation.***

- **Reactions 8-10, molecular rearrangement & ATP production**: 3-phosphoglycerate undergoes 3 rearrangements, and then its energy is in the right place for it to be used for ***substrate-level phosphrylation to make more ATP***. ***The final product is pyruvate.***

Glycolysis (Simplified Version):

- ❖ Produces: ***2 NADH, 2 water molecules , 4 ATP , 2 pyruvate molecules.***

- ❖ ***2 ATP Used*** **&** ***4 Produced*** **so** ***overall 2 ATP molecules gained from glycolysis.***



Glycolysis (Simplified Version):

❖ Pyruvate to Acetyl COA Conversion (Essential for Krebs Cycle):

- Pyruvate easily enters mitochondria passively before this step occurs.
- Involves the *pyruvate* ***dehydrogenase complex***, which consists of 4 enzymes.
- ***This is an oxidation reaction***, which reduces **NAD^+**. **No ATP is made**.
- Other coenzymes involved are ***FAD, TPP and CoA.***
- ***1 molecule of CO_2 is given off for each molecule of pyruvate*** (2 per glucose mol).
- As 2 pyruvate are made from each glucose, ***2 acetyl CoA are also made per glucose.***

Alternative Fates of Pyruvate:

1. **Conversion to acetyl CoA for use in Krebs cycle:** ***This reaction is irreversible***, and, unlike all the glycolysis reactions, there is no way for acetyl CoA to be converted back into any glycolysis intermediate. No ATP is made, but 1 molecule of NAD is reduced for each pyruvate. ***The acetyl CoA has great potential for ATP production via Krebs cycle and ETS.***

2. **Conversion of pyruvate to lactate (Fermentation):** In active muscles, ***the CO_2 may build up, and oxygen may not be available for the ETS. Pyruvate is reduced to lactate, and this converts NADH back to NAD***. By this means, we can keep glycolysis going, by making NAD always available. ***This is a reversible reaction . As soon as the respiratory gases are back in balance, lactate is converted back to pyruvate, and then the NADH is available for the ETS, and then the pyruvate can go back to #1 above.***

3. **Micro-organisms:** ***Pyruvate is converted to ethyl alcohol and CO_2***: ***This is also a reduction reaction which is carried out to keep the NAD available.*** This is the end stage of carbohydrate metabolism for many organisms. ***The sum total of their ATP production capability is therefore only 2 ATP per glucose in such organsims.***

Glycolysis (Simplified Version):