GLUCOSE METABOLISM: GLYCOLYSIS

By:
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Objectives :

- Major oxidative pathway of glucose
- The main reactions of glycolytic pathway
- The rate-limiting enzymes/Regulation
- ATP production (aerobic/anaerobic)
- Pyruvate kinase deficiency hemolytic anemia

HANS KREBS

is a “man of cycle”. Krebs discovered the urea cycle (converting the toxic ammonia to the harmless urea) and citric acid cycle now bears his name—Krebs cycle.

Krebs was a physician by training (his father was a German surgeon). Being a Jewish, he was fired from his medical research job at the University of Freiberg in 1933 when the Nazi took over the government. And this happened even after he achieved the international fame for discovering the urea cycle in 1932. With their policy of expelling all Jewish scientists from German and Austria, Hitler’s Nazi was either too ignorant or too arrogant about them

Phosphorylation

- ✓ **Phosphorylation is the metabolic reaction of introducing a phosphate group into an organic molecule**

Oxidative phosphorylation
The formation of high-energy phosphate bonds by phosphorylation of ADP to ATP coupled to the transfer of electrons from reduced coenzymes to molecular oxygen via the electron transport chain (ETC); it occurs in the mitochondria.

Substrate-level phosphorylation:
The formation of high-energy phosphate bonds by phosphorylation of ADP to ATP (or GDP to GTP) coupled to cleavage of a high-energy metabolic intermediate (substrate). It may occur in cytosol or mitochondria

REGULATION OF GLYCOLYSIS

- **Regulatory Enzymes (Irreversible reactions):**

Glucokinase/hexokinase Pyruvate kinase

PFK-1

- **Regulatory Mechanisms:**

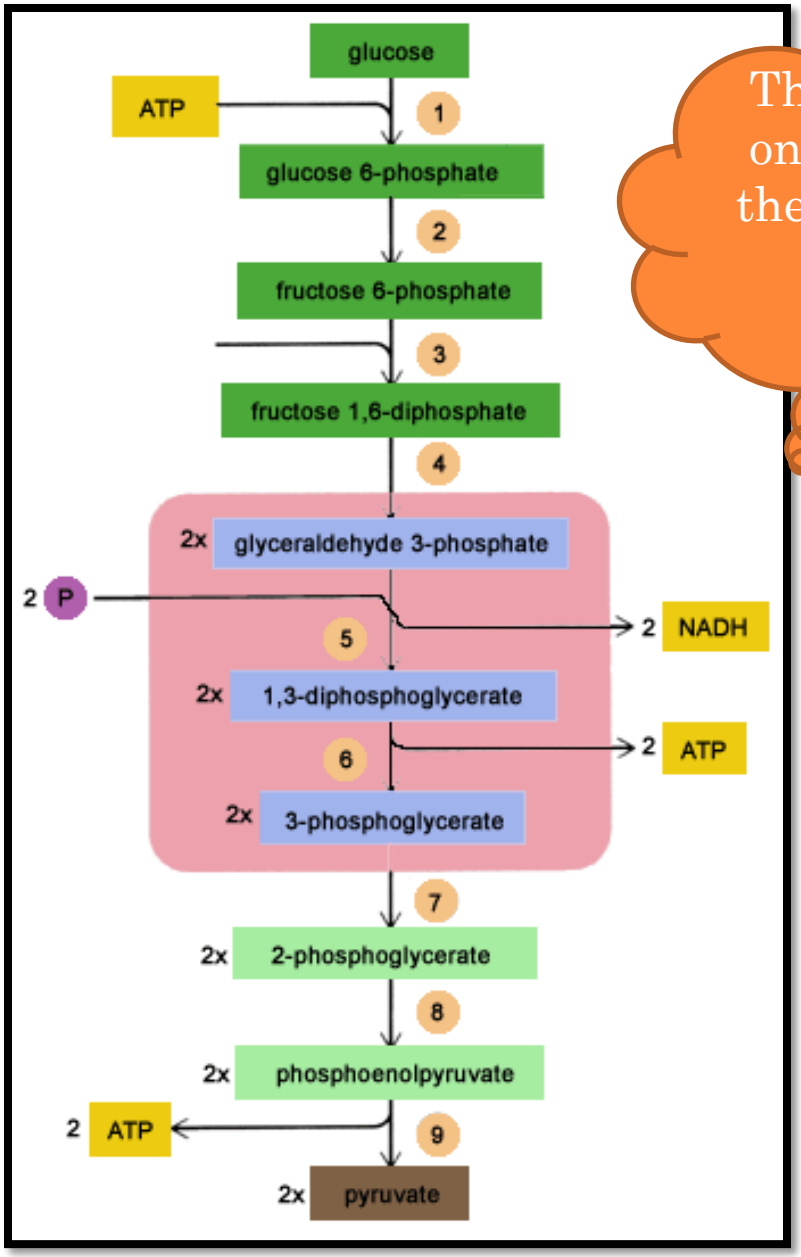
1- Rapid, short-term:

Allosteric
Covalent modifications

2-Slow, long-term:

Induction/repression

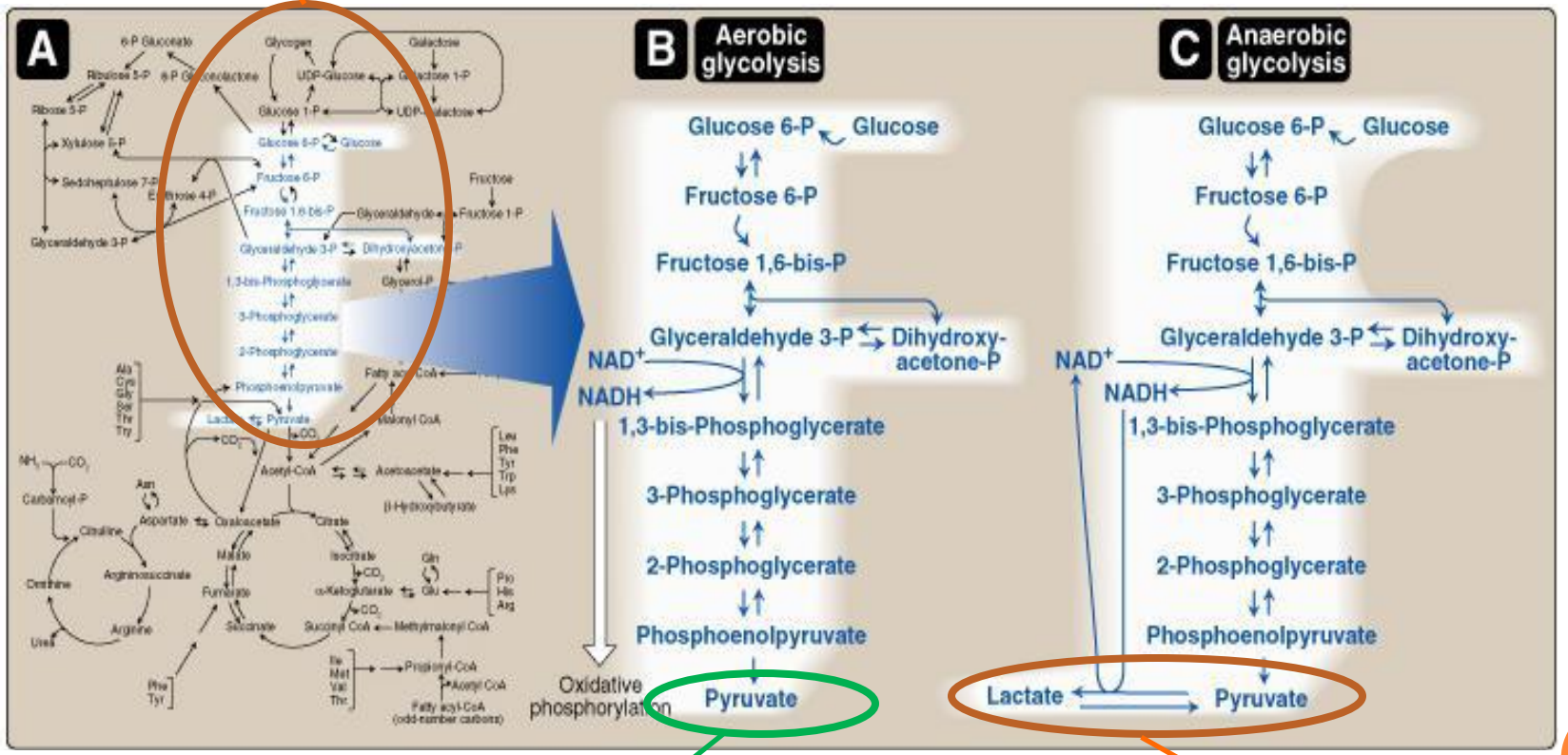
Glycolysis



The product of one reaction is the substrate of the next reaction

Aerobic Vs. Anaerobic Glycolysis

This is Glycolysis

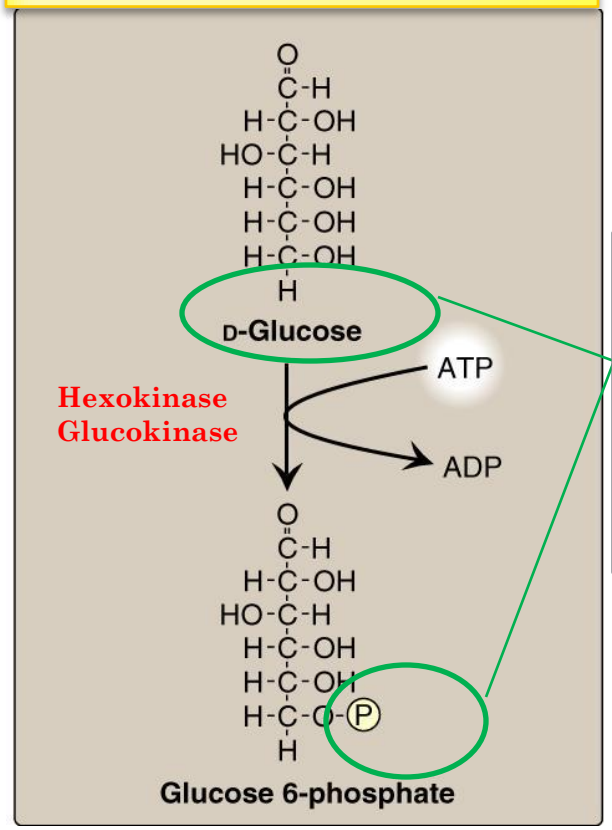


Aerobic ends with pyruvate

Anaerobic ends with lactate

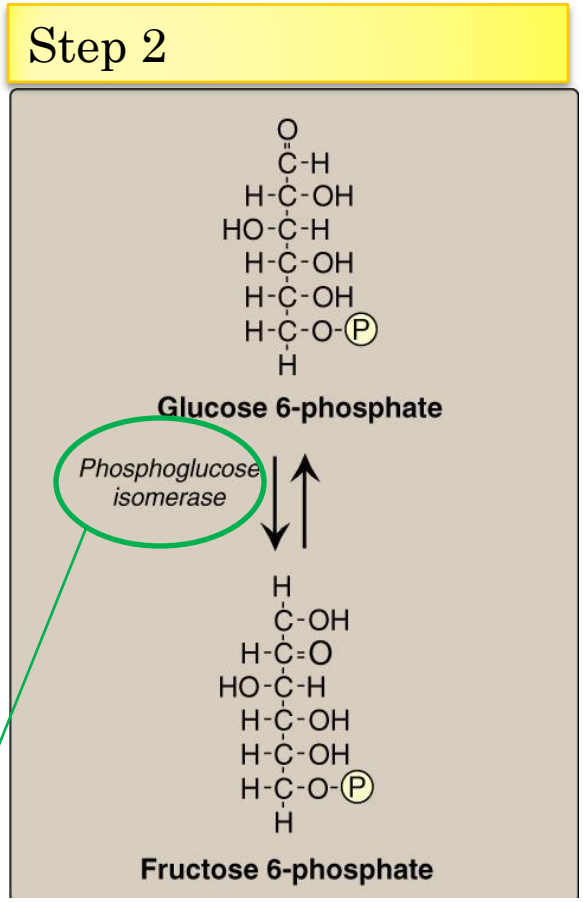
Aerobic Glycolysis

Step 1



When the glucose inter the pathway , there is a phosphate attached to it to prevent the glucose goes outside

Step 2

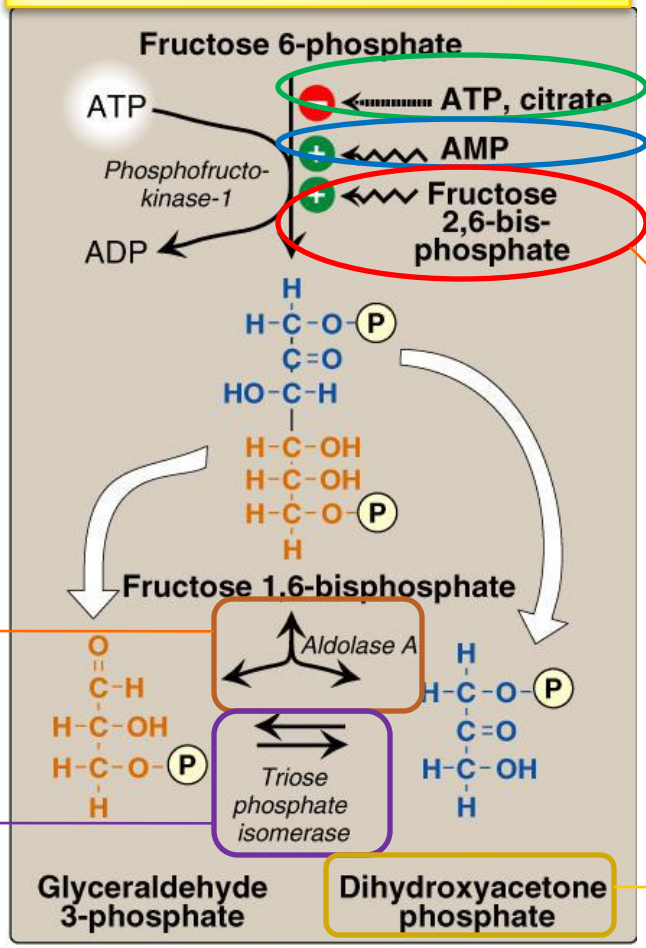


This enzyme change glucose (aldos) to fructose (ketose)

- **Hexokinase: Most tissues**
- **Glucokinase: Hepatocytes**

Aerobic Glycolysis: 3-5

PFK -1: regulation



Inhibit glycolysis because the cell have energy

(Adenosine monophosphate) stimulate glycolysis

- Stimulate glycolysis
- Inhibit gluconeogenesis in the most important step

Breaking down the fructose 1,6-bisphosphate to 3 carbons molecules.

It is a reversible reaction but usually it goes in this side ← to produce Glyceraldehyde 3-phosphate

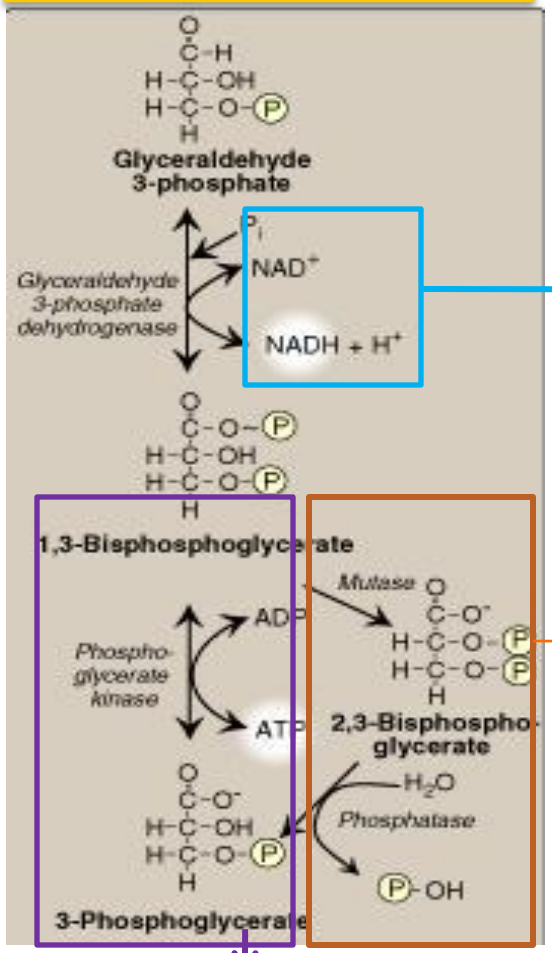
(DHAP)

PFK-1: is the rate-limiting regulatory enzyme

Aerobic Glycolysis: 6 -10

6-7

2x



Oxidation to the molecule (the oxidation reaction is used to add P group to the molecule)
Each NADH 3ATP
So, 2NADH → give 6ATP in ETC in mitochondria

2x

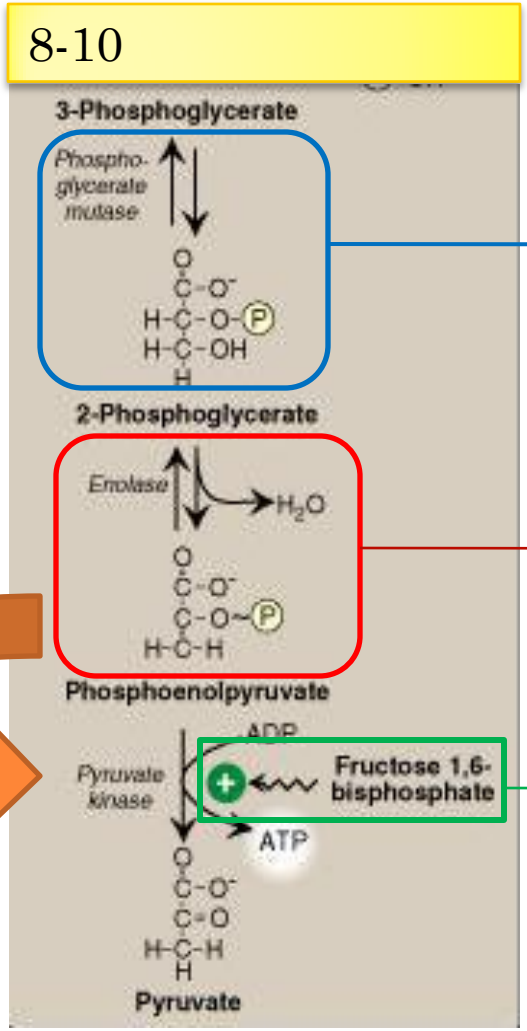
✓1,3BPG → 2,3 BPG (Isomers)
✓2,3BPG → 3BPG (hydrolytic removal of P group)
"this exception is for RBCs to regulate the affinity between O2 and Hb".

Substrate-Level Phosphorylation

2x

It may goes directly to form 3-phosphoglycerate and produce energy (ADP to ATP)

Aerobic Glycolysis: 6 -10



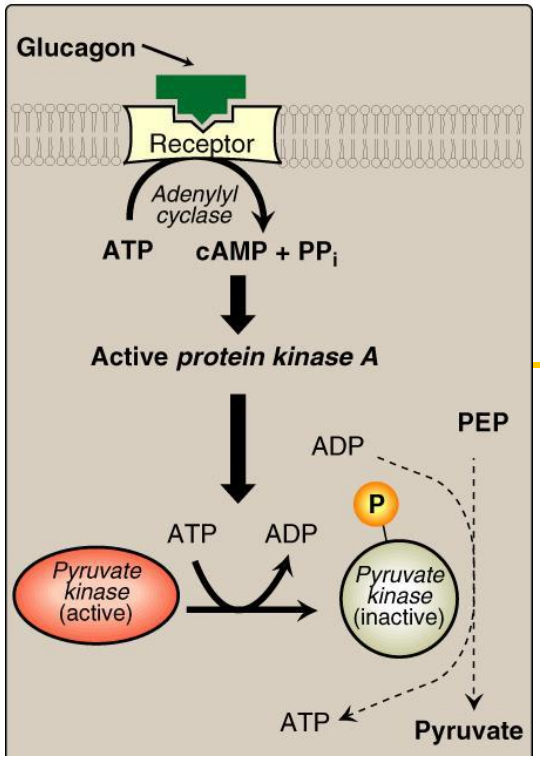
Substrate-Level Phosphorylation

This reaction is to change the position of P group (3 to 2 position)

Formation of high energy phosphate bind in phosphoenolpyruvate.

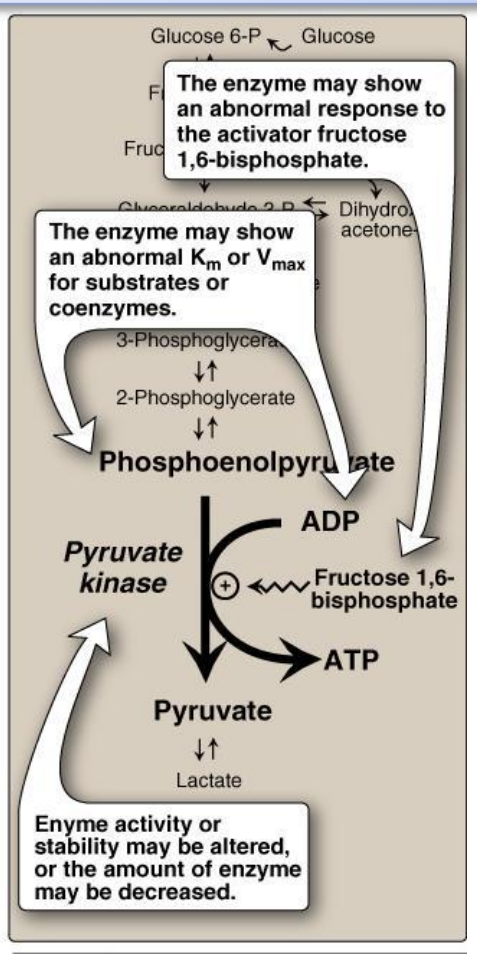
Fructose 1,6-bisphosphate formed in 3rd step , it will go to the last step (it is **Allosteric**)

Pyruvate Kinase



Pyruvate kinase when it phospholrates it becomes inactive

Pyruvate Kinase Deficiency Hemolytic Anemia



Pyruvate kinase deficiency is genetic disease
"it makes a deficiency for one enzyme"

Aerobic Glycolysis: ATP Production ATP

ATP Consumed:

2 ATP

ATP Produced:

Substrate-level

2 X 2 = 4 ATP

Oxidative-level

2 X 3 = 6 ATP

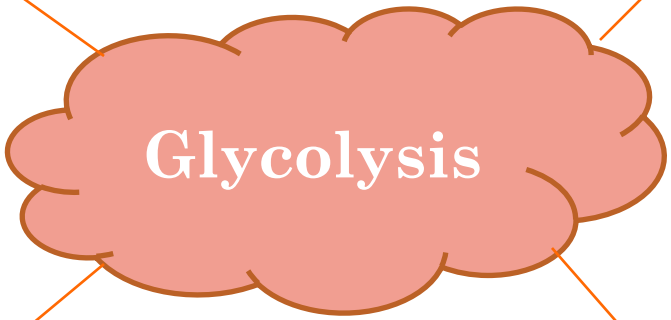
Total 10

ATP Net:

10–2=8 ATP

the major oxidative pathway for glucose

is employed by all tissues and it happens in cytosol



is a tightly-regulated pathway

Glycolysis is mainly a catabolic pathway for ATP production, But it has some anabolic features (amphibolic)

KEEP CALM AND STUDY BIOCHEMISTRY

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