434 Biochemistry Team

Glucose Metabolism: Glycolysis

Foundation block..

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**

Table of contents

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

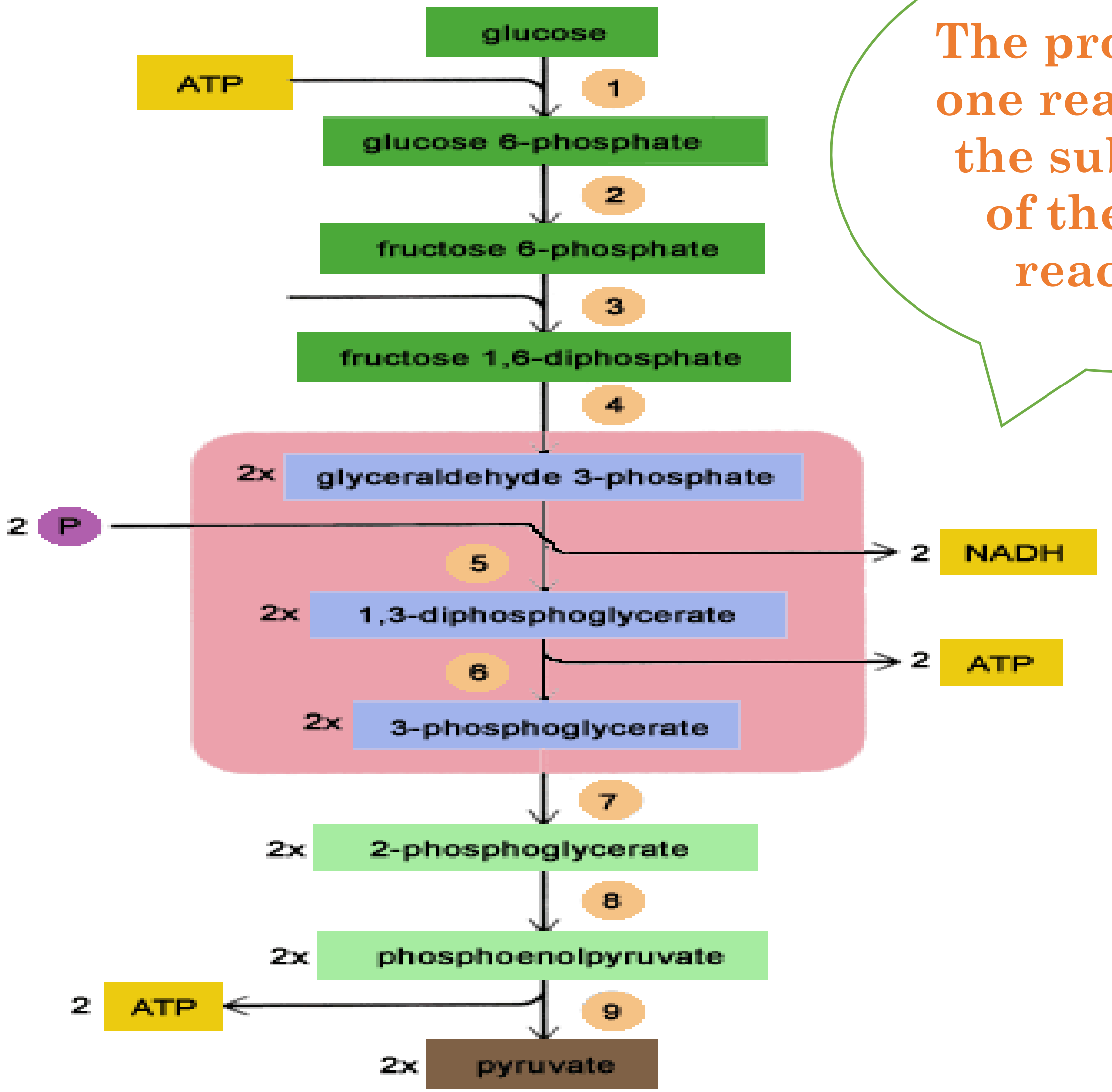
PFK-1 (phosphofructokinase-1)

- Regulatory Mechanisms :

Rapid → short term:
Allosteric
Covalent modifications

Slow→ long term:
Allosteric
Induction/repression

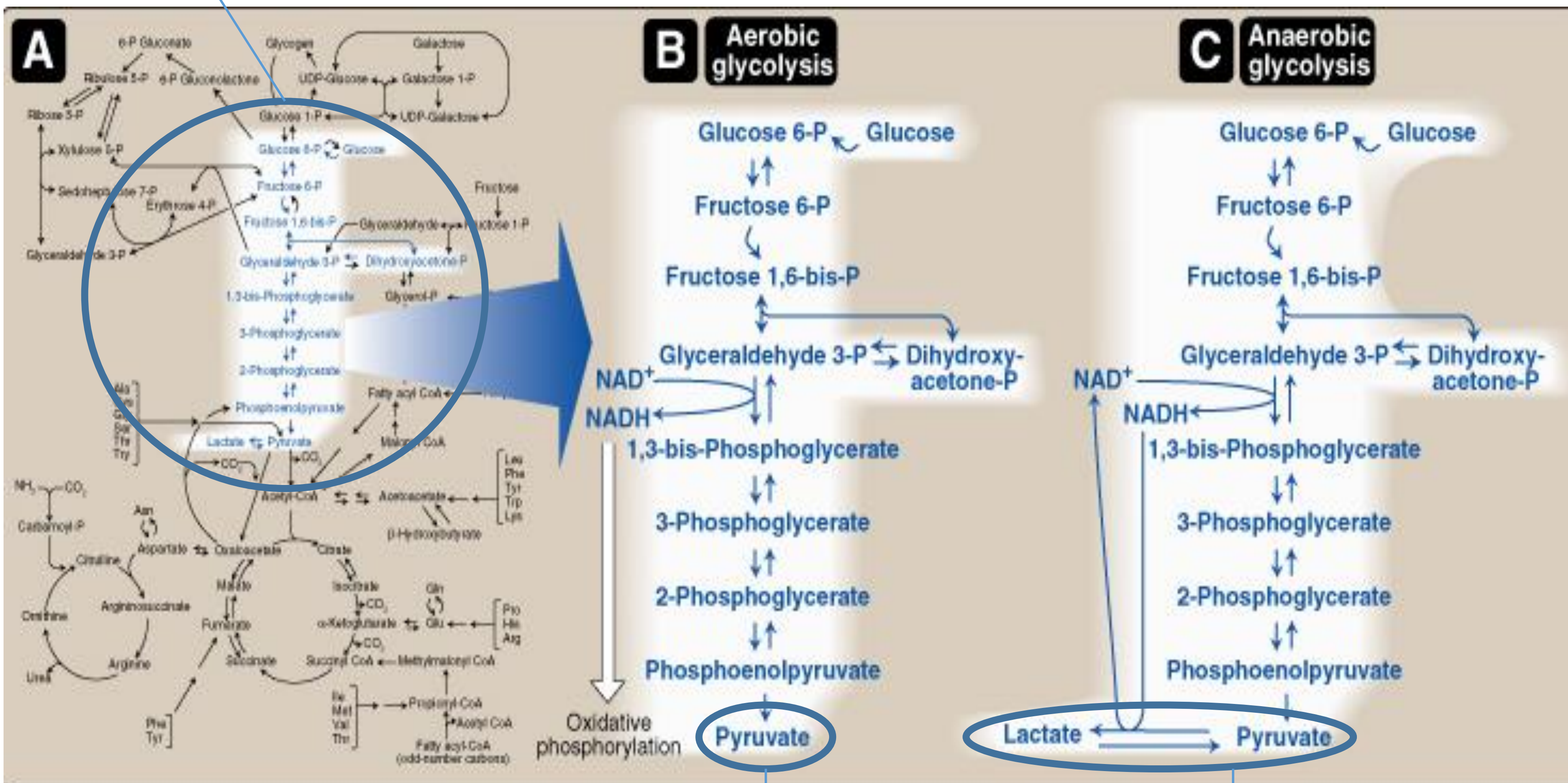
- Glycolysis



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

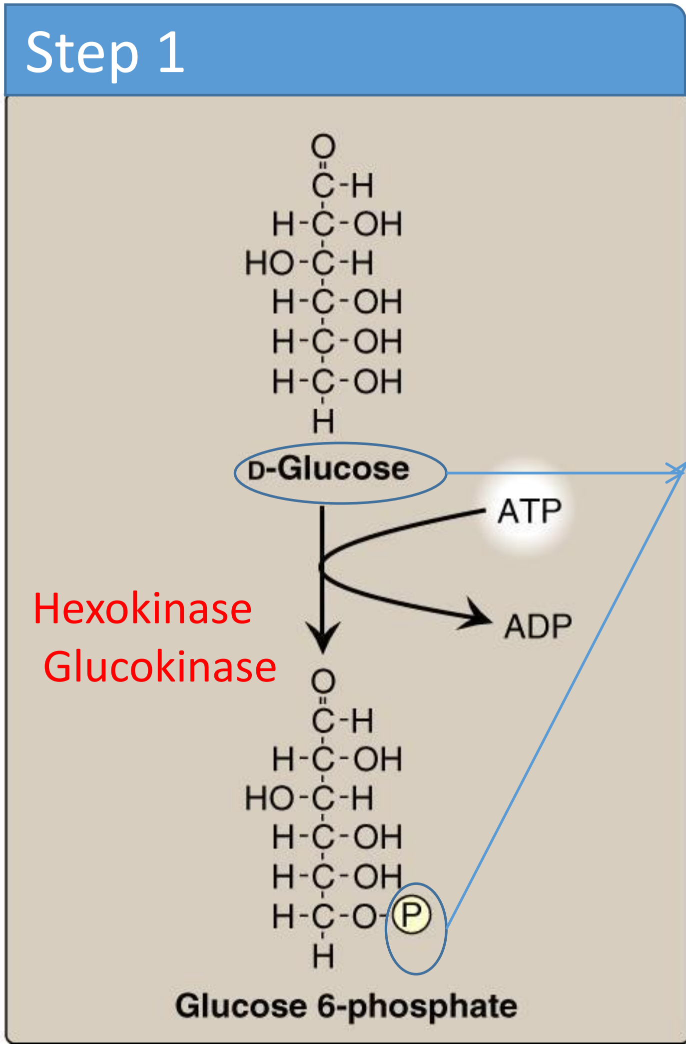
- Aerobic Vs. Anaerobic Glycolysis

This is glycolysis



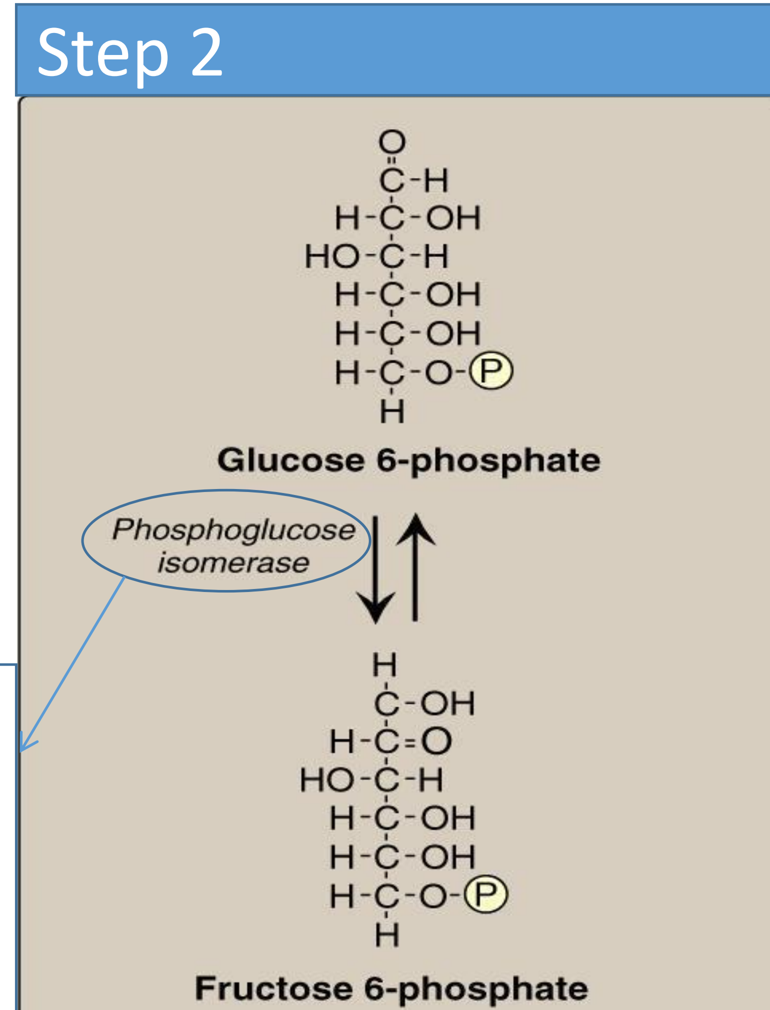
Aeropic ends with pyruvate **Anaeropic ends with lactate**

• Aerobic Glycolysis



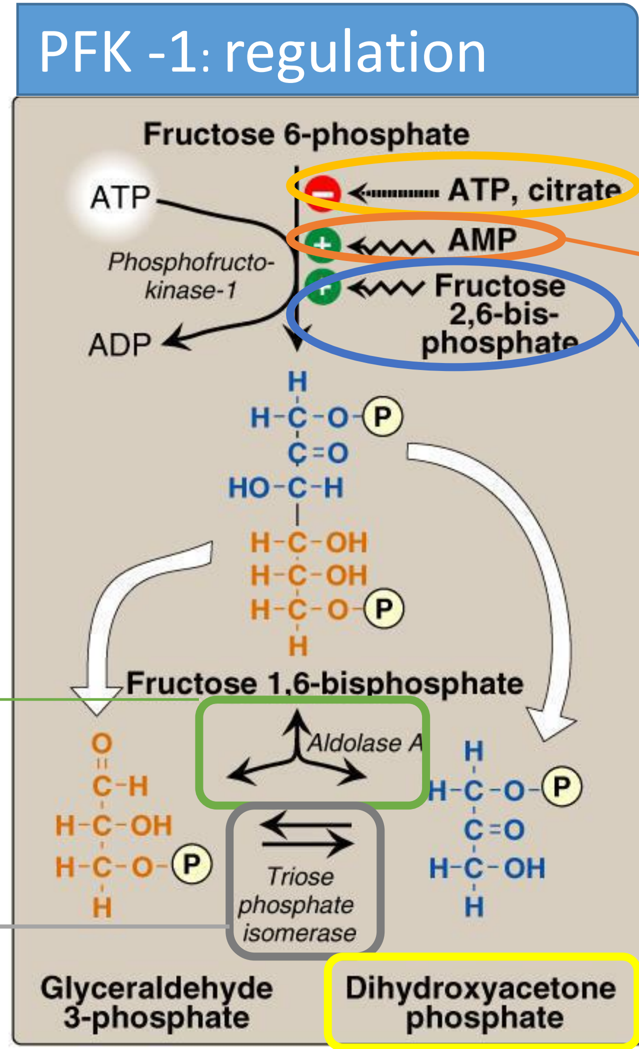
When the glucose inter the pathway , there is a phosphate attached to it to prevent the glucose goes outside

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



- Hexokinase: Most tissues
- Glucokinase: Hepatocytes

Aerobic Glycolysis: 3-5



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

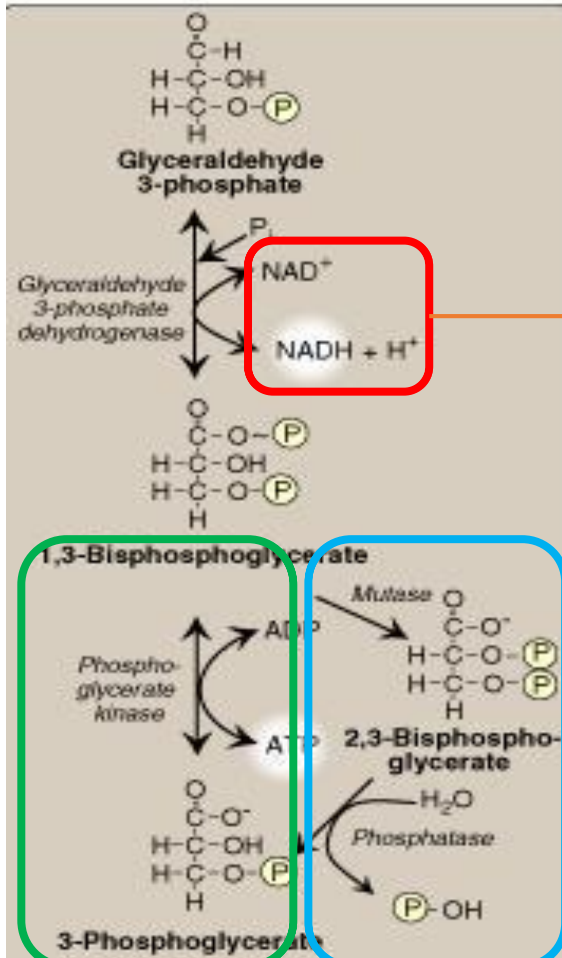
(DHAP)

PFK-1: is the rate-limiting regulatory enzyme

Aerobic Glycolysis: 6 -10

6-7

2x



2x

2x

Substrate-Level Phosphorylation

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

✓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".

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

Aerobic Glycolysis: 6 -10

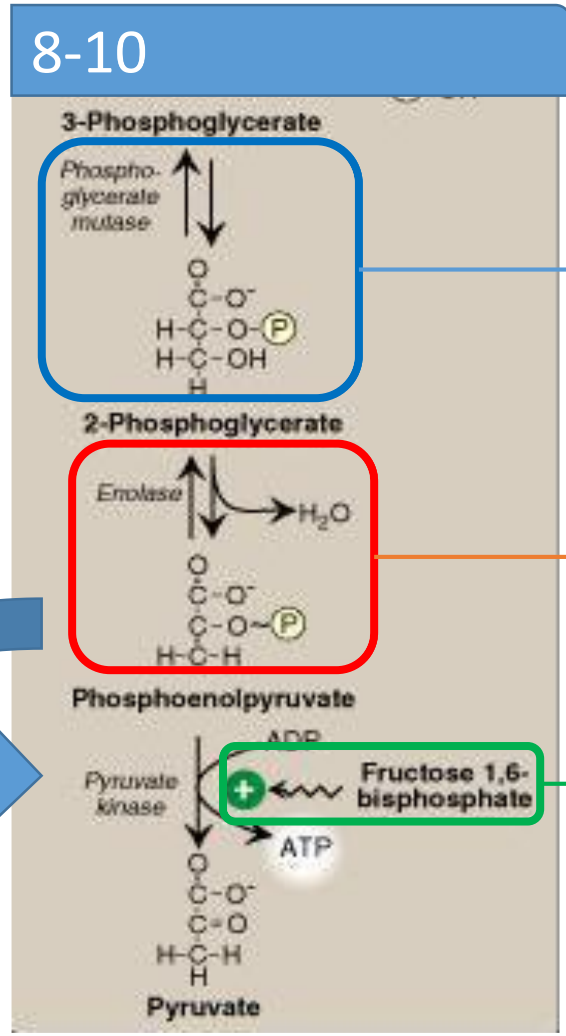
2x

2x

2x

2x

Substrate-Level Phosphorylation

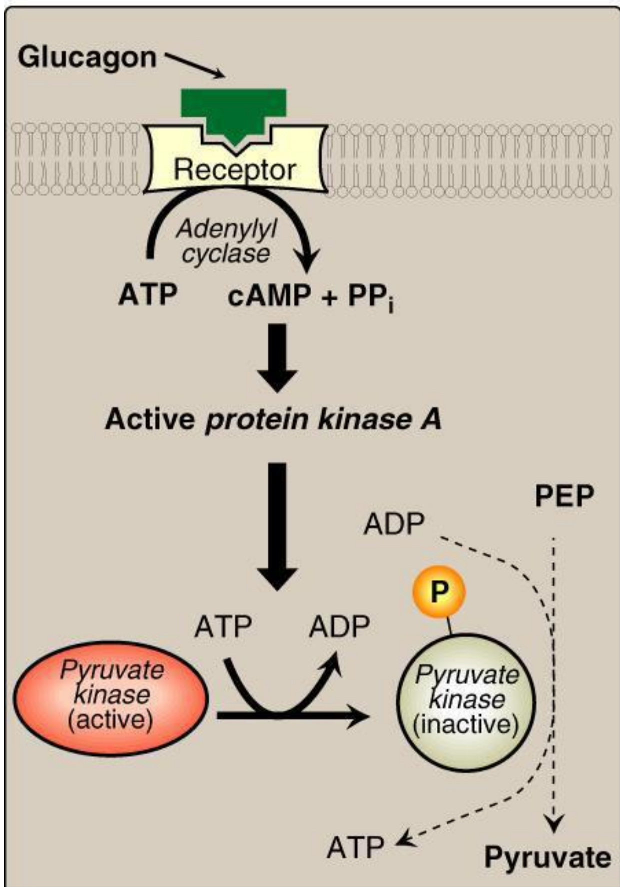


This reaction is to change the position of P group (3 to 2 position)

Formation of high energy phosphate bind in phosphoenolpyruvate.

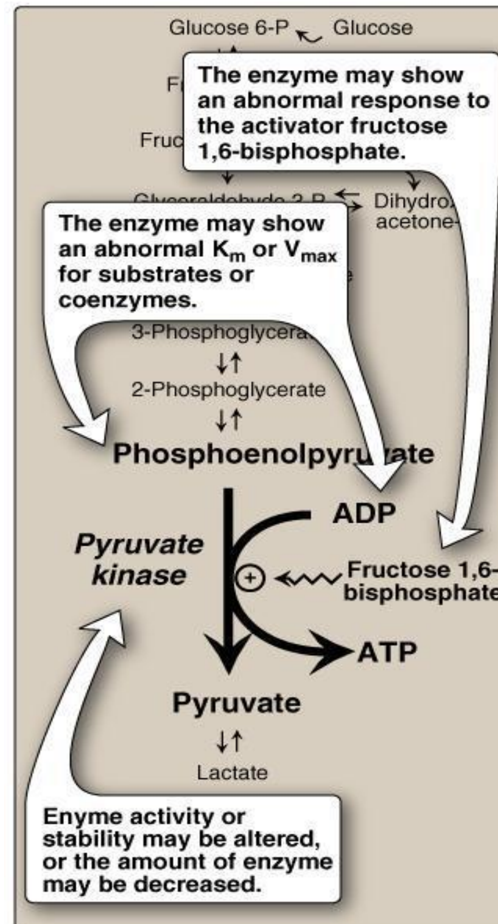
Fructose 1,6-bisphosphate formed in 3rd step , it will go to the last step (it is Allosteric)

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 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

Remember:

Glycolysis

- the major oxidative pathway for glucose
- and it happens in cytosol
- Glycolysis is mainly a catabolic pathway for ATP production, But it has some anabolic features (amphibolic)
- is employed by all tissues
- is a tightly-regulated pathway

Aerobic Glycolysis

Hexokinase / Most tissues
★ Glucokinase / Hepatocyte

Glucose 6-P ⟷ Glucose "-1 ATP"

Phosphoglucose isomerase ⇕

Fructose 6-P

Phosphofructokinase 1 ★ ↓ "-1 ATP"

Fructose 1.6-bisP

↑ Aldoase A

(2x) Glyceraldehyde 3-P ⟷ Dihydroxyacetone P (x2)

Trios P isomerase

⇕ Glyceraldehyde 3-P dehydrogenase "+2 NADH"

(2x) 1,3-BisPhosphoglycerate

⇕ Phosphoglycerate kinase "+2 ATP"

(2x) 3-Phosphoglycerate

⇕

(2x) 2-Phosphoglycerate

⇕

(2x) Phosphoenolpyruvate

↓ Pyruvate kinase ★ "+2 ATP"

(2x) Pyruvate

ATP Consumed		2
ATP Prodused		
	Substrate-level	4
	Oxidative -level	6
Net		8

★ Irreversible

Useful Links:

OVERVIEW:

REACTIONS:

FULL EXPLANATION:

QUIZ:

Quiz

Anaerobic Glycolysis:

- NADH can not go with ETC because there is no O2 and/or no mitochondria.
- Anaerobic glycolysis less ATP production than aerobic.
- The end product of anaerobic glycolysis is lactate. (why?)

Because NADH Needs lactate to be NAD+ for continues process.

- **Pyruvate convert to Lactate by Lactate dehydrogenase enzyme.**

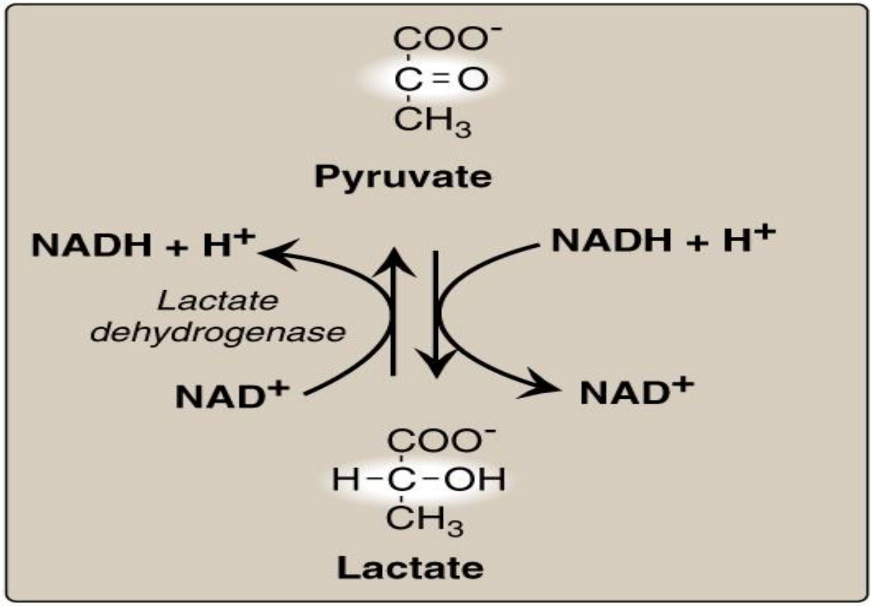
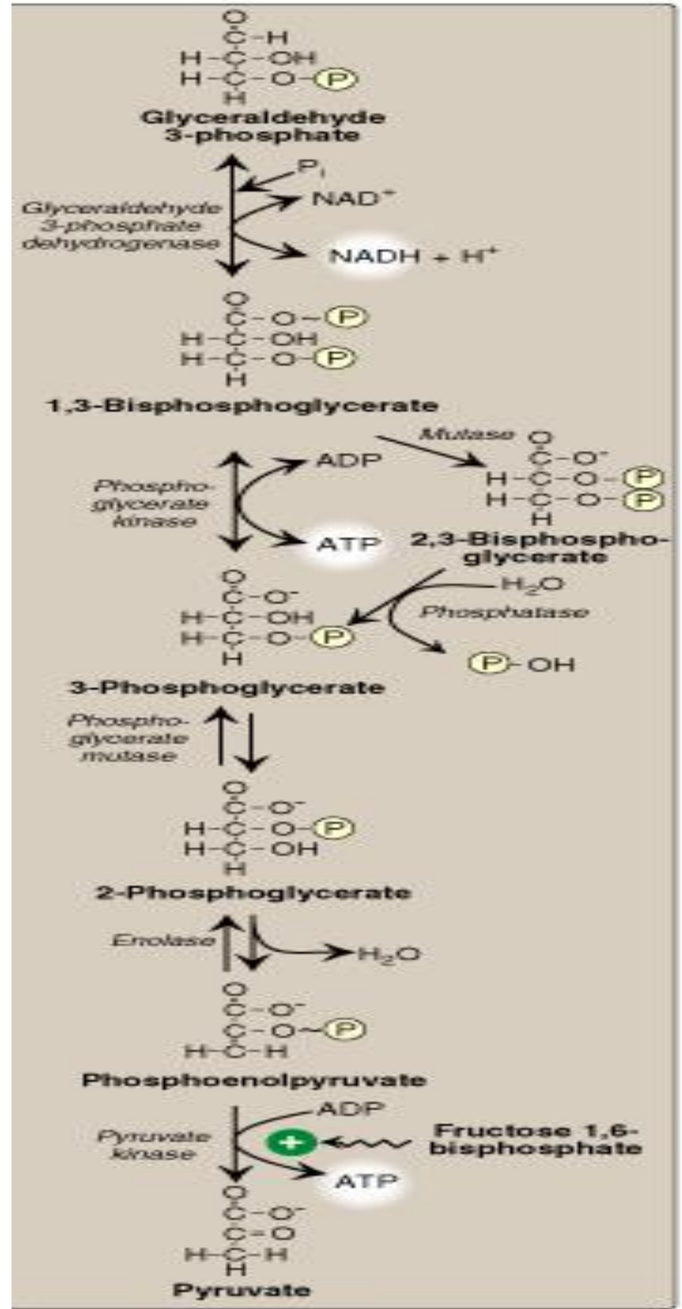


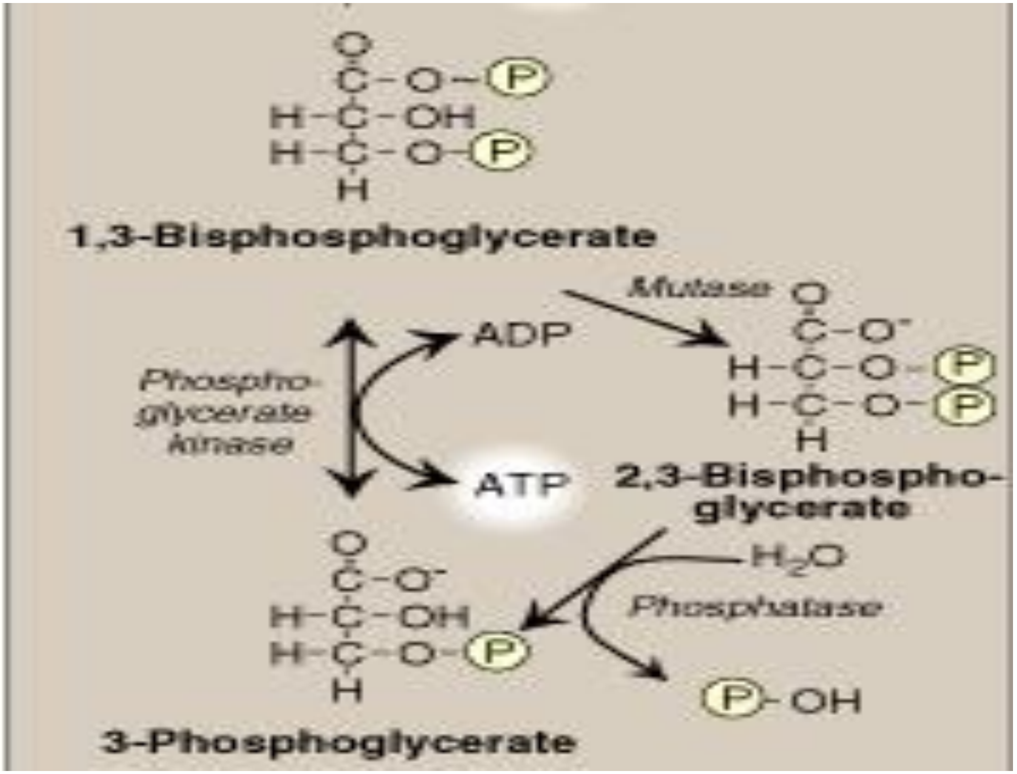
Figure 8.21
Interconversion of pyruvate and lactate.

- All the steps are the same with other anaerobic glycolysis except “2,3-BPG Shunt” in sometimes.



Mutase enzyme

- It is important for association and dissociation between O2 and hemoglobin.
- Increase in “2,3-BPG” will help to loss of association between O2 and hemoglobin and will release more O2.
- It usually occurs with people who live in high altitude.



- No production of ATP in formation of “2,3-BPG”.
- “2,3-bpg” comes back to “3-Phosphoglycerate” by Phosphatase enzyme.

Summary of RBCs

- The end product is Lactate.
- No net production or consumption of NADH

- Energy yield (net):
- No 2,3-BPG 2 ATP
- 2,3-BPG shunt 0 ATP

- Severity of PKD (Pyruvate Kinase Deficiency) hemolytic anemia depends on:

1- Degree of PKD:

if it is less active the anemia will be severe.

2- Compensation by 2,3-BPG:

– Increase in "2,3-BPG" lead to increase in release of O_2 and less dangerous anemia.

– If there is no enough compensation the anemia will be more severe.

ATP Produced:

- Substrate-level:
2 X 2 = 4 ATP and two ATP will consumed

Net = 2

There is no oxidative level.

Anaerobic Glycolysis in RBCs:
- substrate level:
2 X 2=4 ATP → without shunt.
Net= 4-2=2

or

- 2X1=2 ATP → with shunt reaction in RBCs
Net= 2-2= 0

Aerobic Glycolysis

ATP Produced:

– Substrate level:

2x2=4 ATB

– Oxidative level:

3x2=6 ATB

10 ATP production and 2 ATP of them consumed.

Net= 8 ATP

Remember

- ✓ **Glycolysis is the major oxidative pathway for glucose.**
- ✓ **Glycolysis is employed by all tissues.**
- ✓ **Glycolysis is mainly a catabolic pathway for ATP production but it has some anabolic features (Amphibolic).**
- ✓ **Pyruvate kinase deficiency in RBCs results in hemolytic anemia.**

Useful Links:

- Videos can help :

- Quiz your self

Quiz

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جمانة فطاني
اميرة بن زعير

- Thank you ☺