بسم الله الرحمن الرحيم

Glucose Metabolism: Glycolysis

By

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Glycolysis: Revision

- 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

Substrate-level phosphorylation Vs. Oxidative 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**

Summary: Regulation of Glycolysis

Regulatory Enzymes (Irreversible reactions):

- Glucokinase/hexokinase
- PFK-1
- Pyruvate kinase

Regulatory Mechanisms:

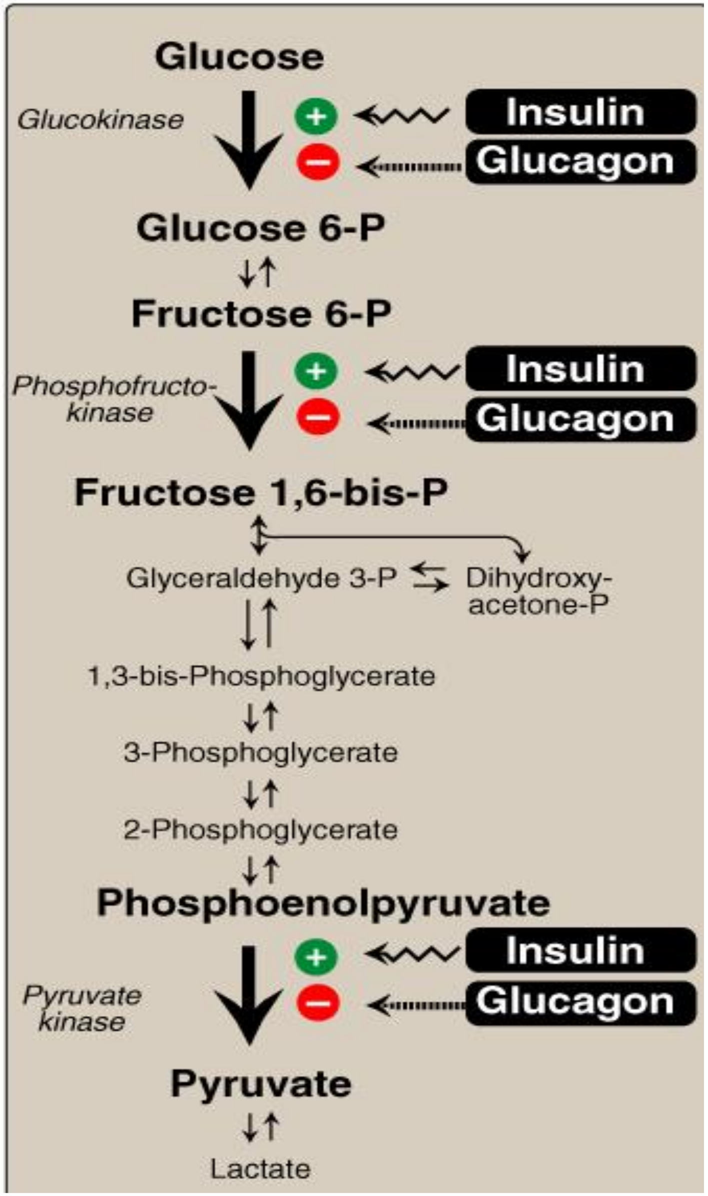
- Rapid, short-term:
  - Allosteric
  - Covalent modifications
- Slow, long-term:
  - Induction/repression

Apply the above mechanisms for each enzyme where applicable

Long-Term Regulation of Glycolysis

Insulin: Induction

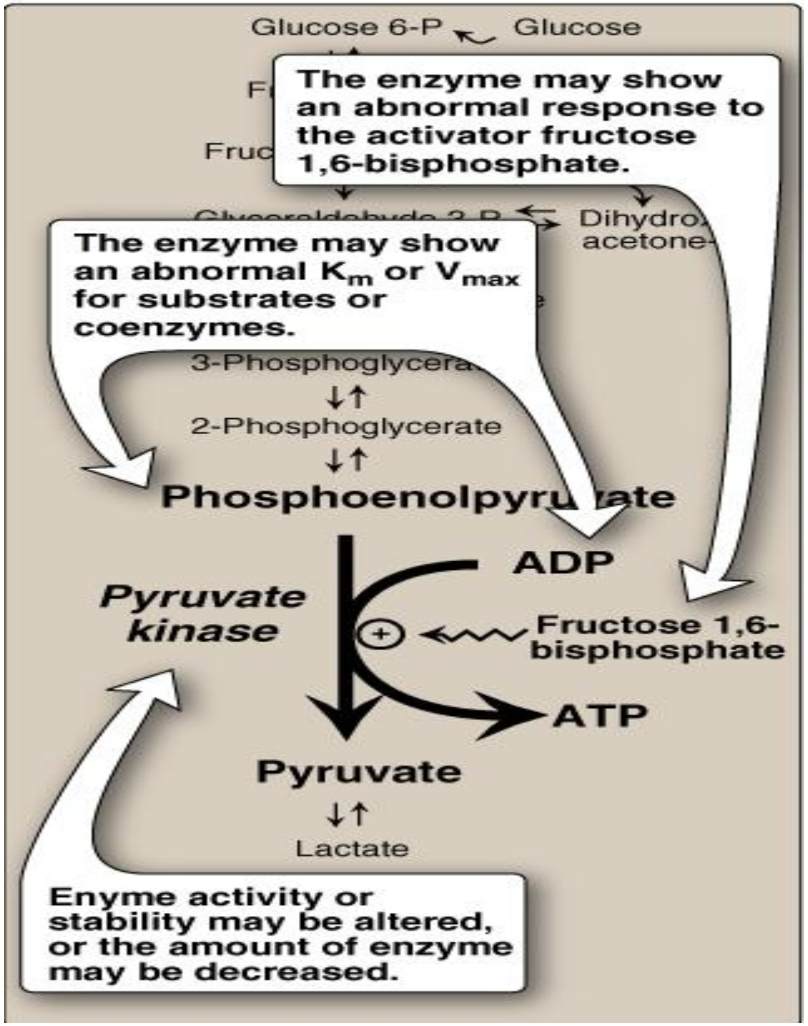
Glucagon: Repression



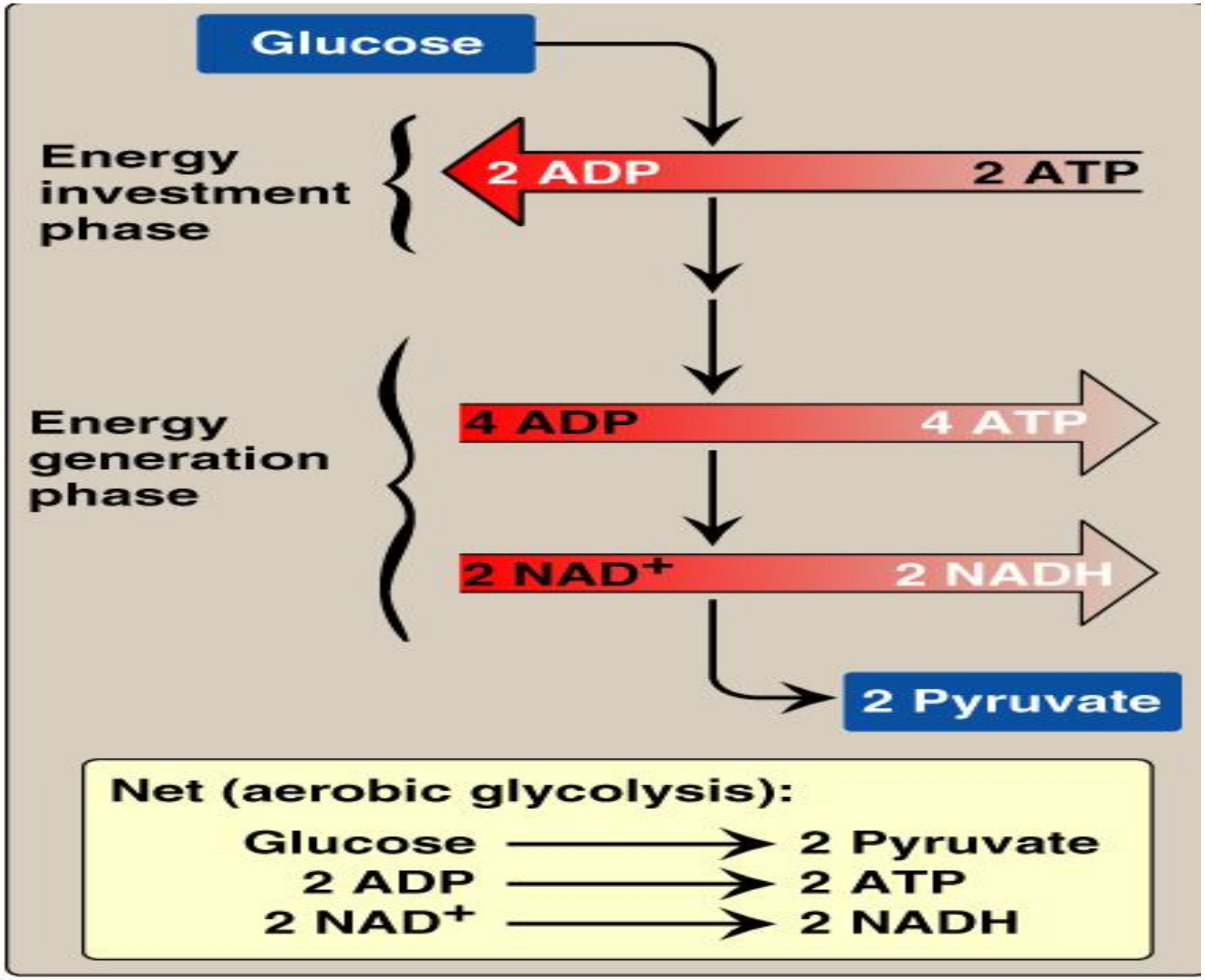
Pyruvate Kinase Deficiency Hemolytic Anemia

PK Mutation may lead to:

1. Altered Enz. kinetics
2. Decreased Enz. stability
3. Altered response to activator



Aerobic Glycolysis:
Total Vs Net ATP Production



Aerobic Glycolysis: ATP Production

ATP Consumed:

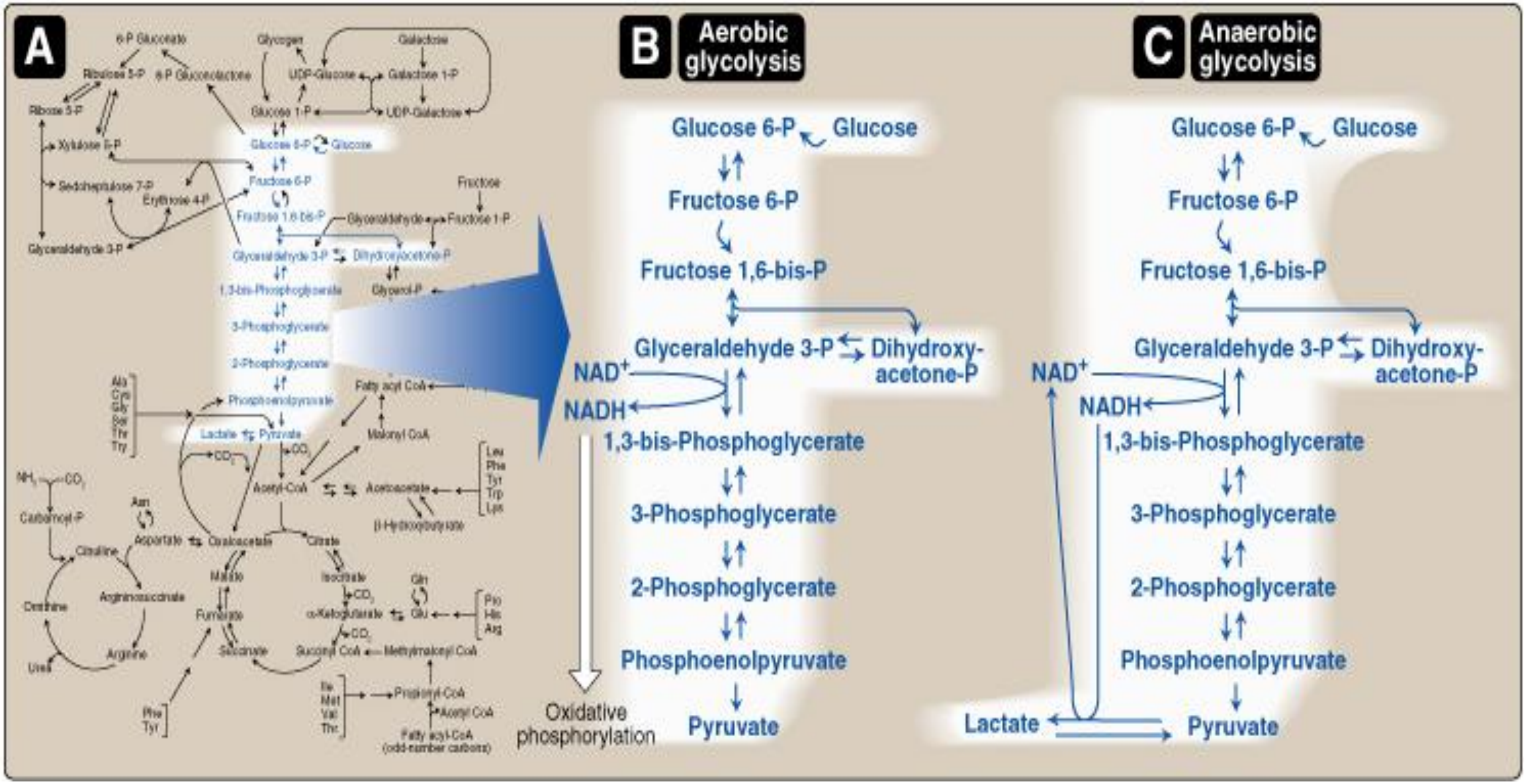
		2	**ATP**

ATP Produced:

Substrate-level	**2 X 2 =**	**4**	**ATP**
Oxidative-level	**2 X 3 =**	**6**	**ATP**
Total		**10**	**ATP**

Net:	**10 – 2 =**	**8**	**ATP**

Aerobic Vs Anaerobic Glycolysis

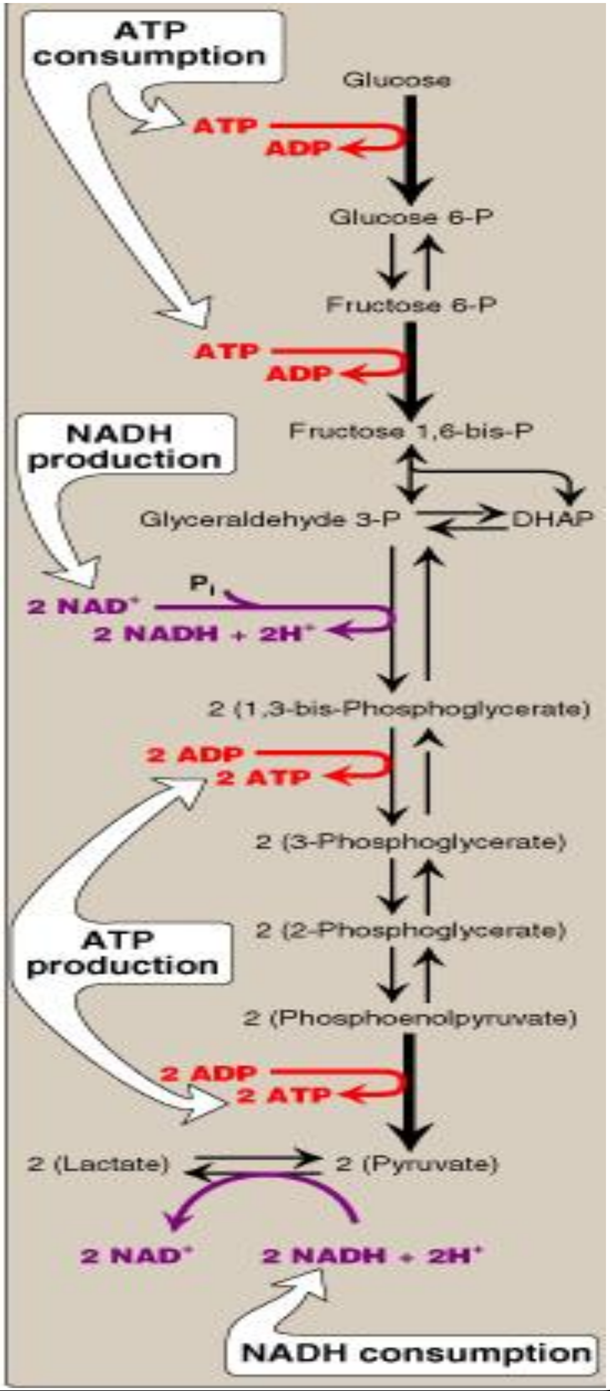


Anaerobic Glycolysis

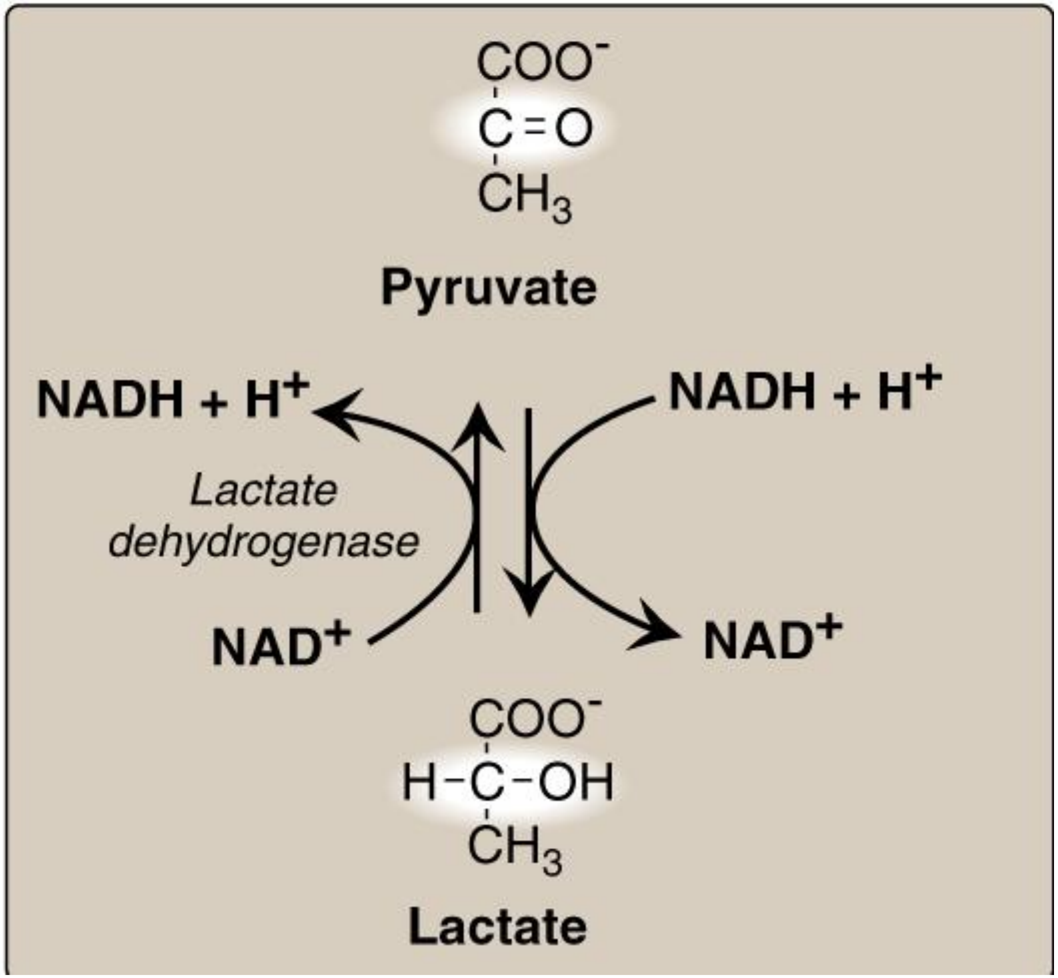
NADH produced cannot used by ETC for ATP production
(No O_2 and/or No mitochondria)

Less ATP production, as compared to aerobic glycolysis

Lactate is an obligatory end product, Why?



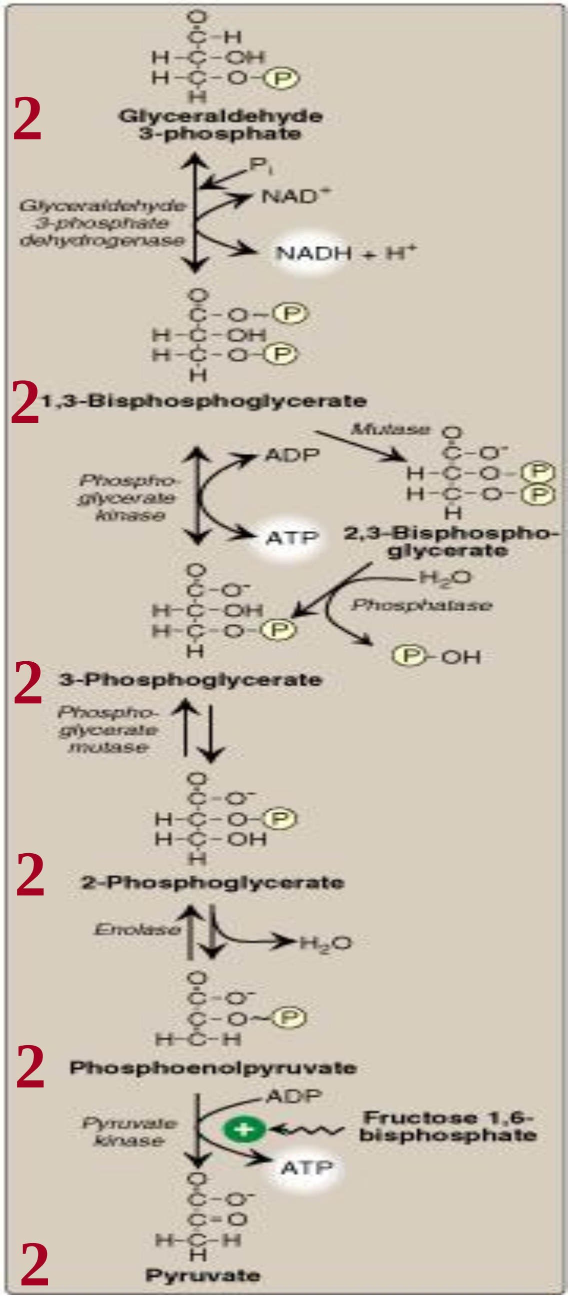
Lactate Dehydrogenase



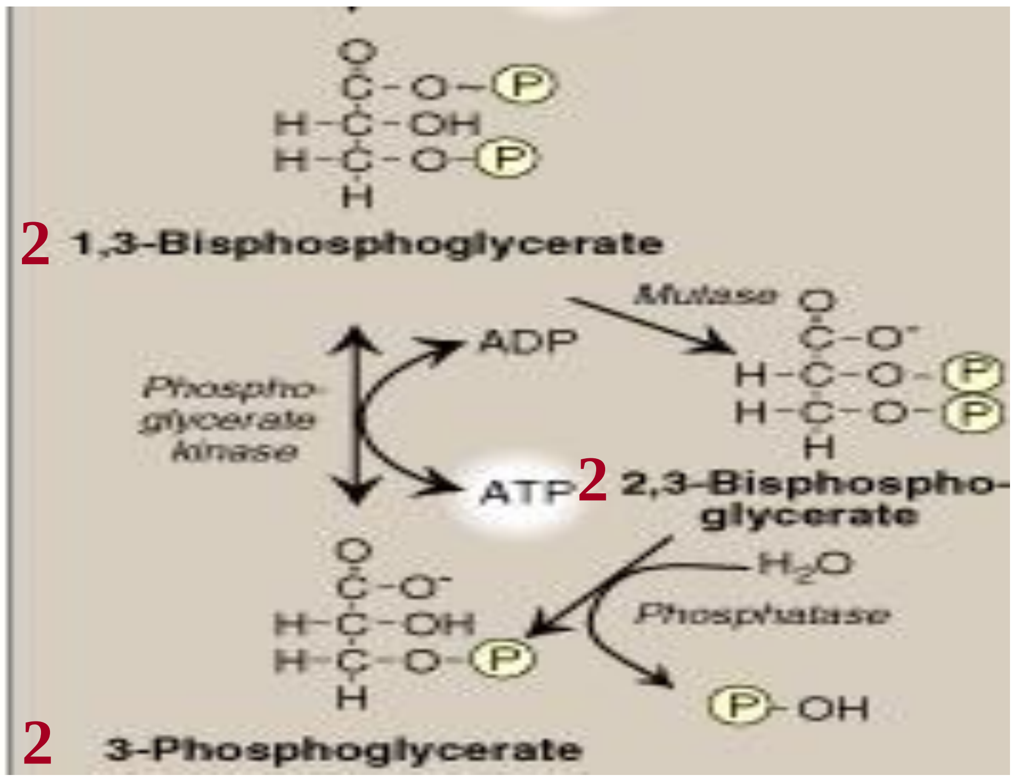
Anaerobic Glycolysis: ATP Production

ATP Consumed:			
		2	**ATP**
ATP Produced:			
Substrate-level	**2 X 2 =**	**4**	**ATP**
~~**Oxidative-level**~~	~~**2 X 3 =**~~	~~**6**~~	~~**ATP**~~
Total		**4**	**ATP**
Net:	**4 – 2 =**	**2**	**ATP**

Anaerobic Glycolysis in RBCs: 2,3-BPG Shunt



Anaerobic Glycolysis in RBCs: 2,3-BPG Shunt



Glycolysis in RBCs: ATP Production

ATP Consumed:				
			2	**ATP**
ATP Produced:				
Substrate-level	**OR**	**2 X 2 =**	**4**	**ATP**
		1 X 2 =	**2**	**ATP**
~~**Oxidative-level**~~		~~**2 X 3 =**~~	~~**6**~~	~~**ATP**~~
Total			**4 OR 2**	**ATP**
Net:	**OR**	**4 – 2 =**	**2**	**ATP**
		2 – 2 =	**0**	**ATP**

Glycolysis in RBCs: Summary

End product:

- Lactate
- No net production or consumption of NADH

Energy yield:

- If no 2,3-BPG is formed: 2 ATP
- If 2,3-BPG shunt occurs: 0 ATP

PK Deficiency hemolytic anemia depends on:

- Degree of PK Deficiency
- Compensation by 2,3-BPG

Take Home Message

- **Glycolysis is the major oxidative pathway for glucose**
- **Glycolysis is employed by all tissues**
- **Glycolysis is a tightly-regulated pathway**
- **PFK-1 is the rate-limiting regulatory enzyme**

Take Home Message

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

- Pyruvate kinase deficiency in RBCs results in hemolytic anemia

Take Home Message

- **Net energy produced in:**
  - **Aerobic glycolysis: 8 ATP**
  - **Anaerobic glycolysis: 2 ATP**

- **Net energy produced in glycolysis in RBCs:**
  - **Without 2,3 BPG synthesis: 2 ATP**
  - **With 2,3 BPG synthesis: 0 ATP**