بسم الله الرحمن الرحيم

Glucose Metabolism: Glycolysis

By

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Objectives: Glycolysis

By the end of this lecture, students are expected to:

- **Recognize the major regulatory mechanisms for glycolysis**
- **Discuss the unique nature of glycolysis in RBCs**
- **Assess the ATP production in glycolysis (aerobic/anaerobic)**
- **Define pyruvate kinase deficiency hemolytic anemia**

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**

Summary: Regulation of Glycolysis

Regulatory Enzymes (Irreversible reactions):

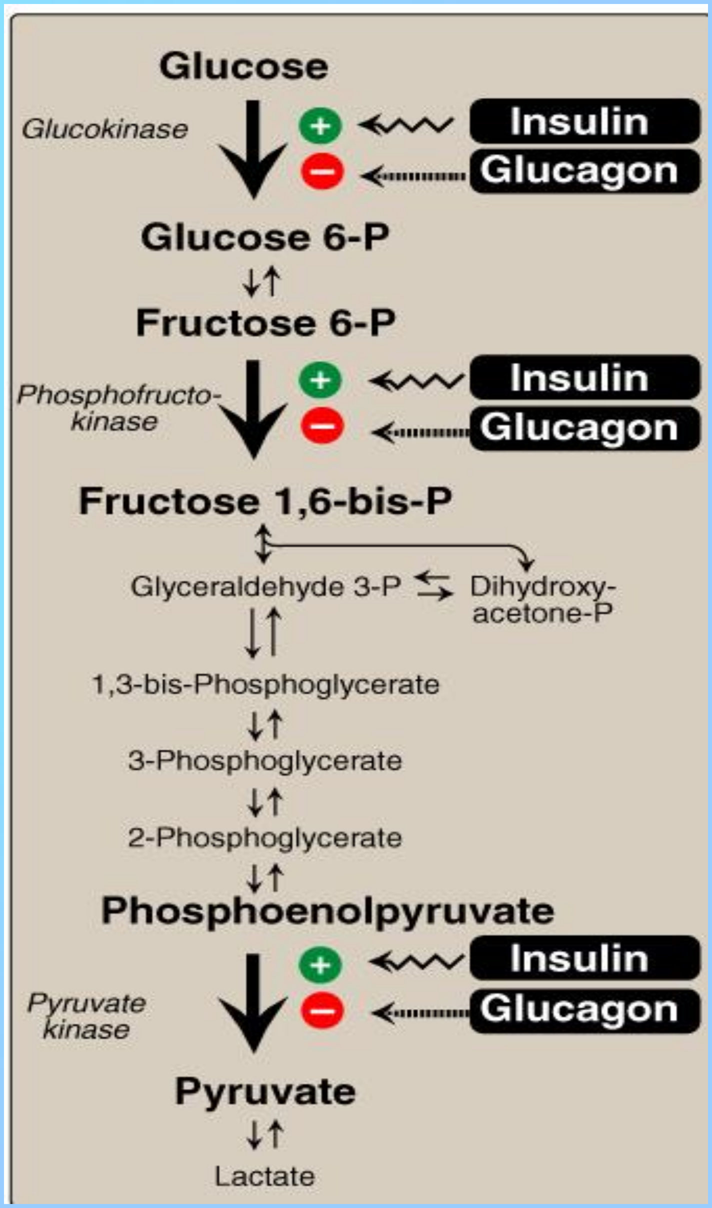
- Glucokinase/hexokinase
- PFK-1
- Pyruvate kinase

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



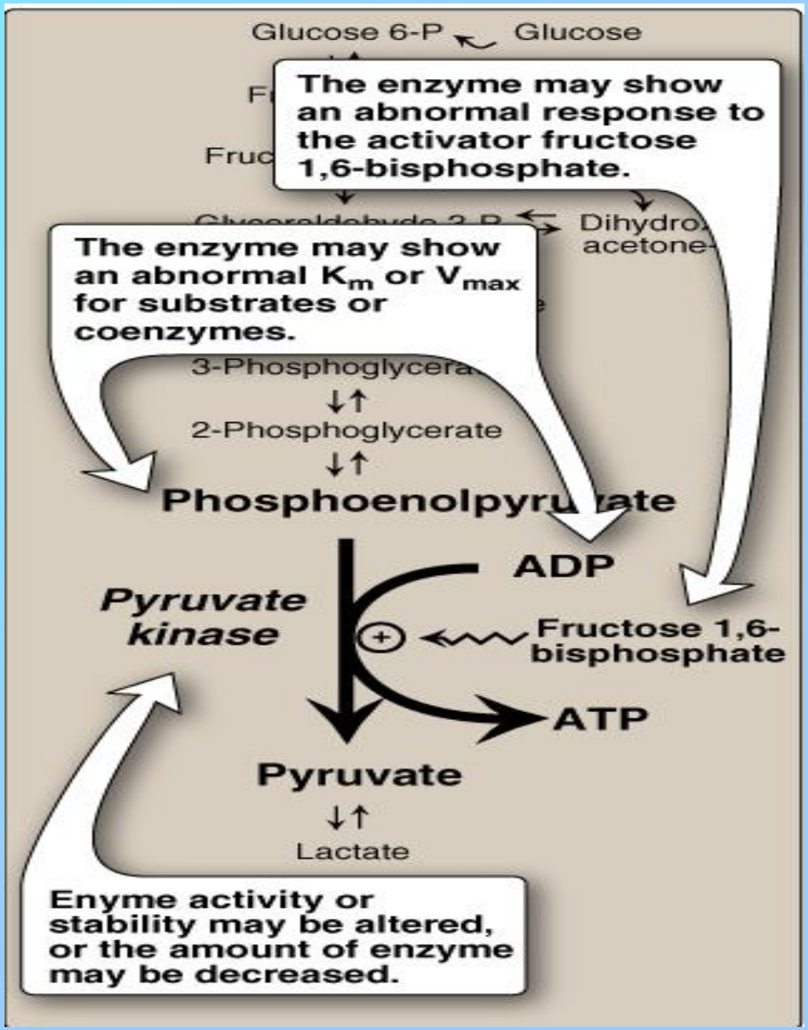
Insulin: Induction

Glucagon: Repression

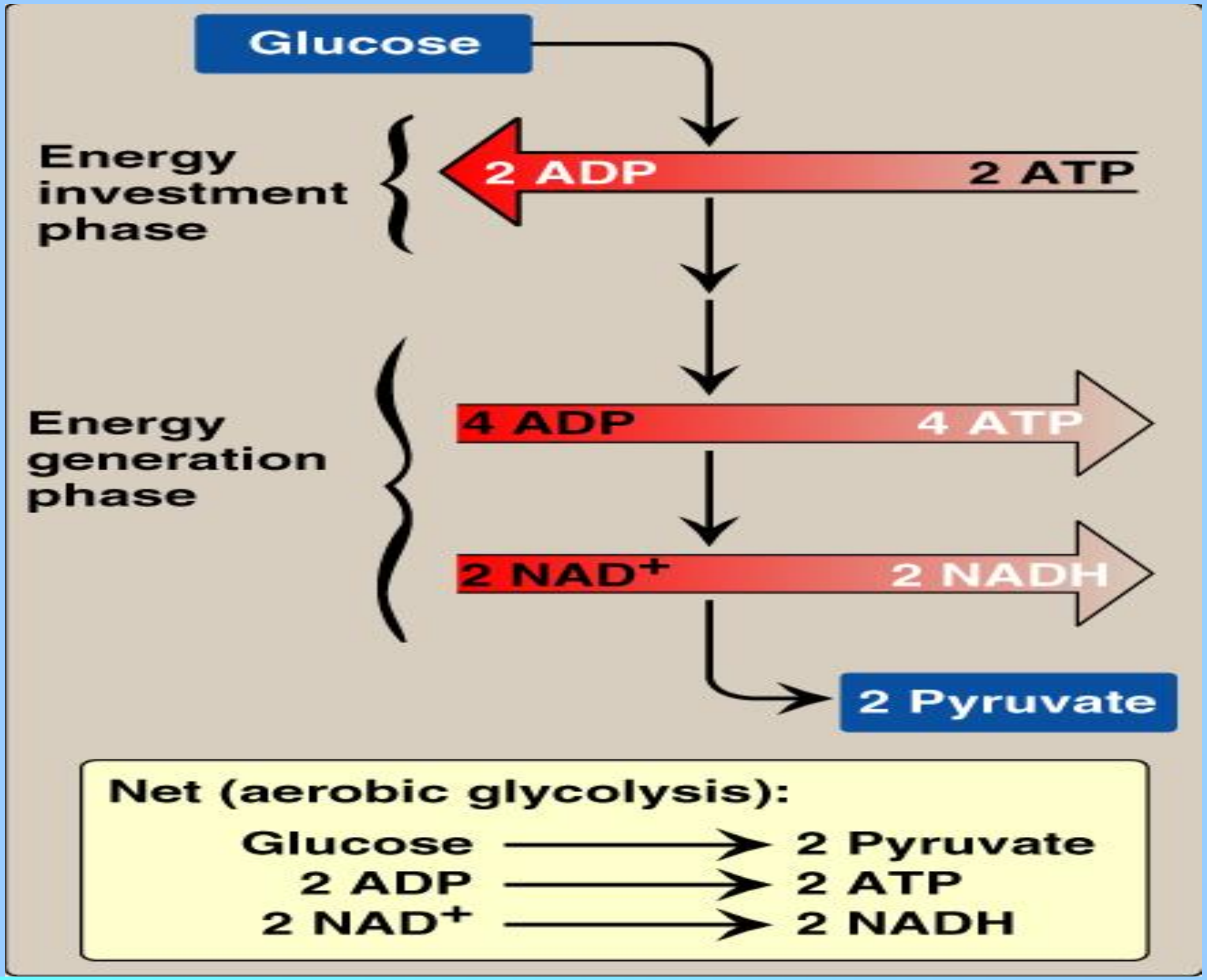
Pyruvate Kinase Deficiency Hemolytic Anemia

PK Mutation may lead to:

1. Altered Enz. kinetics
2. Altered response to activator
3. Decreased the amount of the Enz. or its stability



Aerobic Glycolysis: Total Vs Net ATP Production



Aerobic Glycolysis: ATP Production

ATP Consumed:

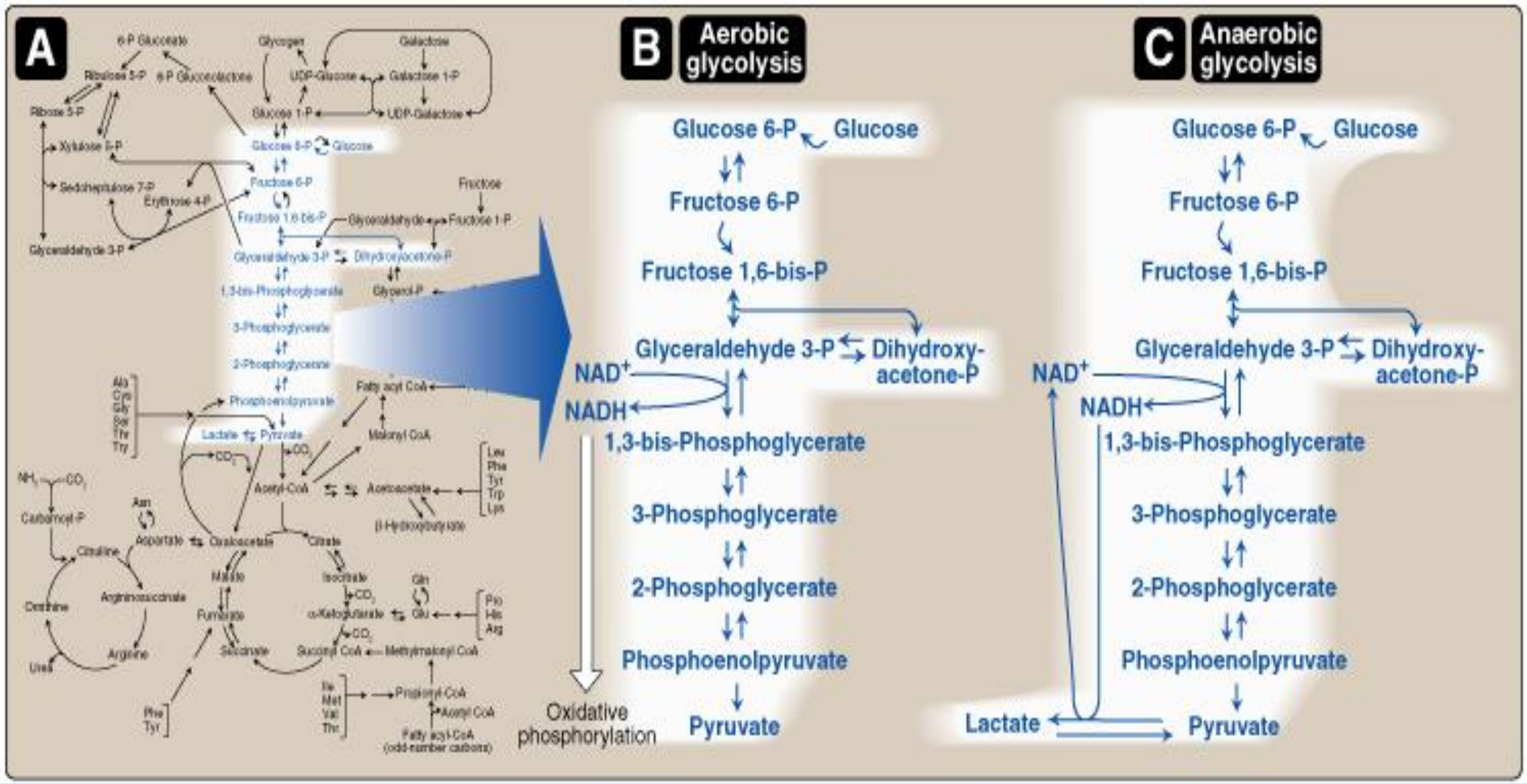
		2	ATP

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

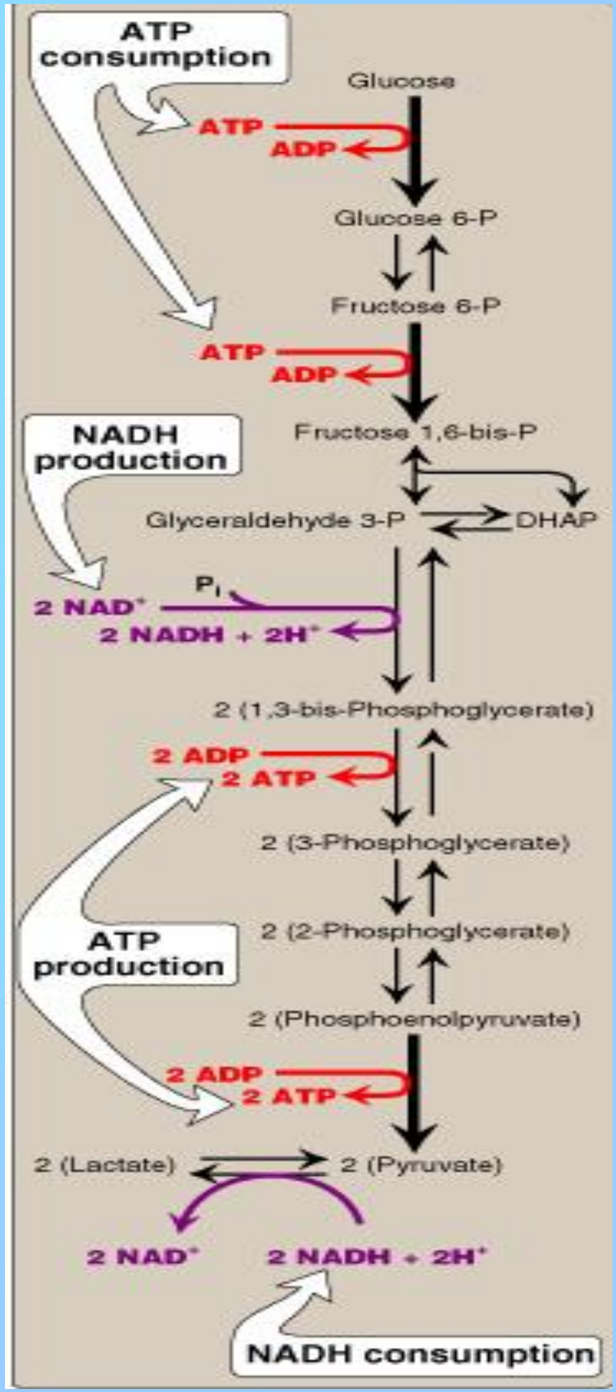
NADH produced cannot be used by ETC for ATP production

(No O_2 and/or No mitochondria)

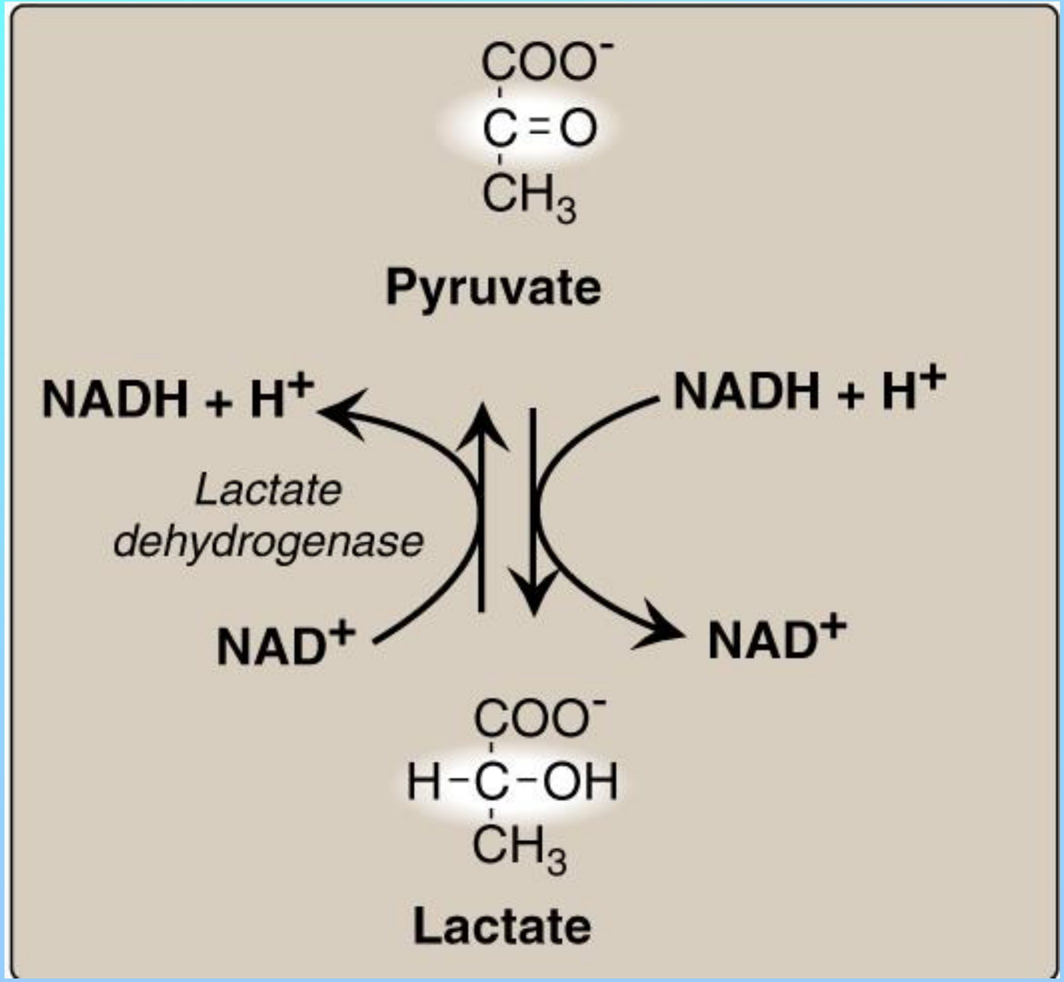
Less ATP production, as compared to aerobic glycolysis

Lactate is an obligatory end product, Why?

Because if not formed, All cellular NAD+ will be converted to NADH, with no means to replenish the cellular NAD → Glycolysis stops→ death of the cell



Lactate Dehydrogenase



Anaerobic Glycolysis: ATP Production

ATP Consumed:

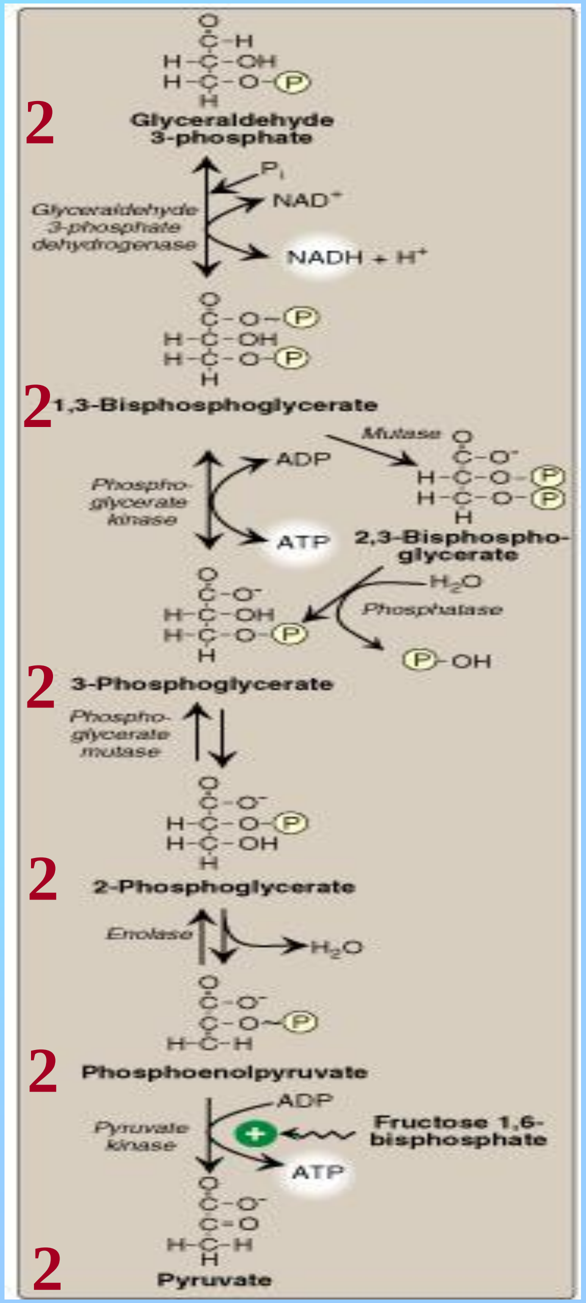
		2	ATP

ATP Produced:

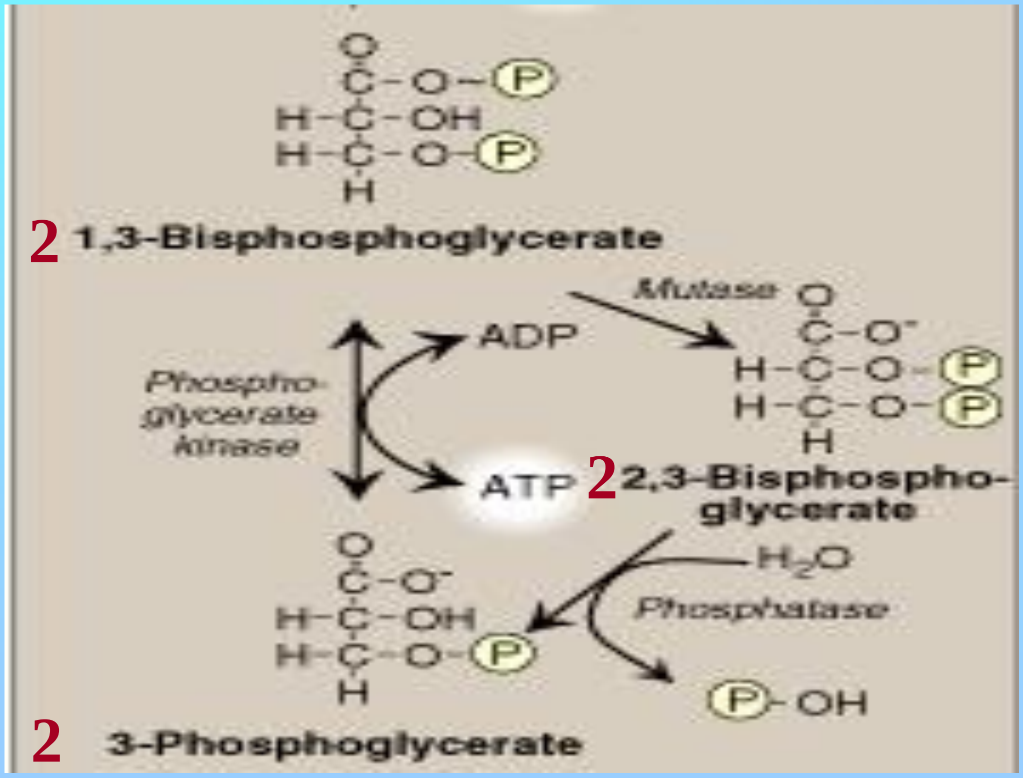
Substrate-level	2 X 2 =	4	ATP
~~Oxidative-level~~	~~2 X 3 =~~	~~6~~	~~ATP~~
Total		4	ATP

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 a tightly-regulated pathway**
- **PFK-1 is the rate-limiting regulatory enzyme**
- **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**

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**