

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

Major Metabolic Pathways of Glucose

By

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Metabolic Pathway

Definition

Site:

Cellular (tissue) and Subcellular

Reactions

Rate-limiting enzyme(s)

Regulatory mechanism(s):

**Rapid,
short-term**

**Slow,
long-term**

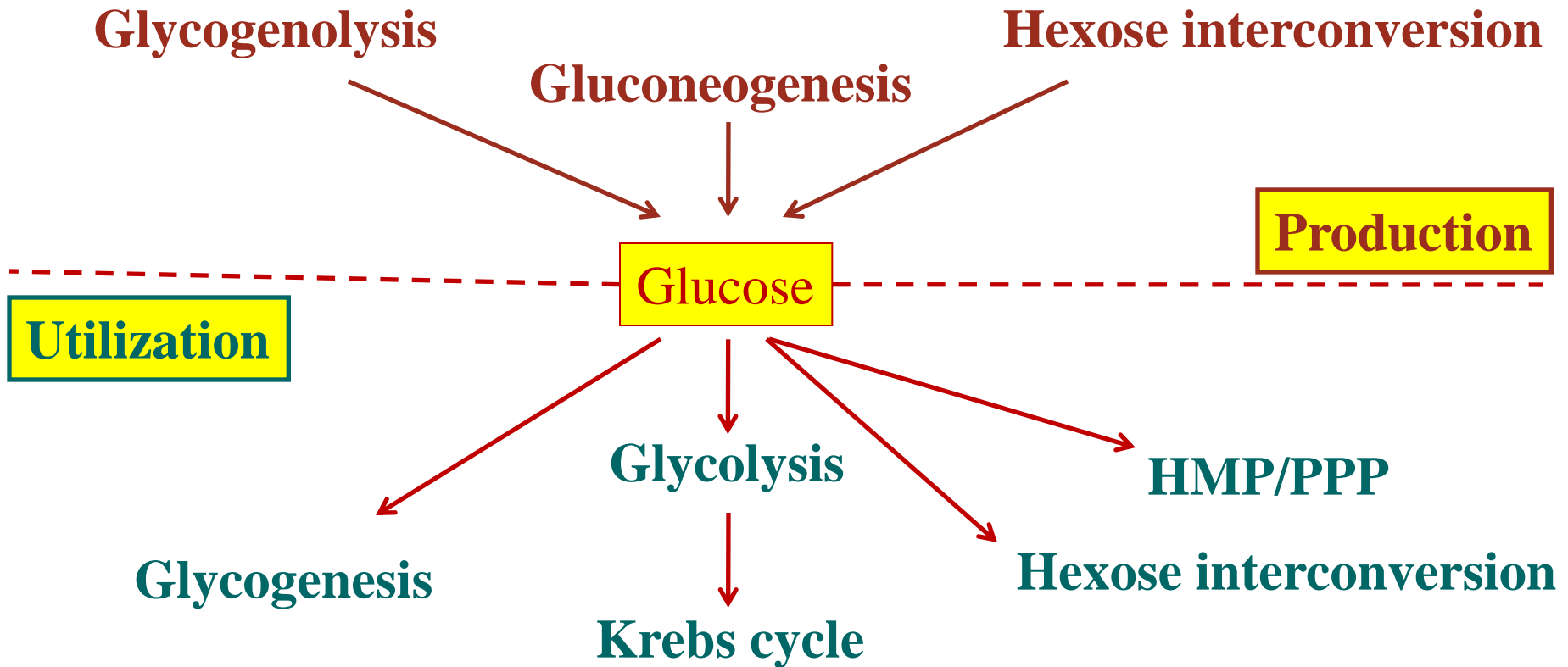
**Covalent
modification**

Allosteric

Induction/repression



Metabolic Pathways of Glucose: Production and Utilization



Metabolic Pathways of Glucose: Catabolic and Anabolic

Catabolic cycles

Glycolysis (Mainly)

Krebs (Mainly)

Glycogenolysis

HMP

Anabolic cycles

Gluconeogenesis

Glycogenesis

Glycogenesis and Glycogenolysis

Glycogenesis:

Synthesis of glycogen from glucose
Mainly liver and muscle, Cytosol

Glycogenolysis

Degradation of glycogen into glucose
Mainly liver and muscle, Cytosol

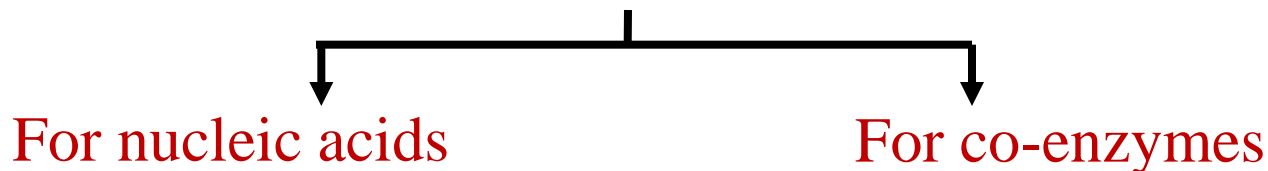
Hexose Monophosphate Pathway (HMP) or Pentose Phosphate Pathway (PPP)

1- Important source for NADPH

Which is used in reductive syntheses

2- Source for metabolically active ribose

Which is used for production of nucleotides:



Glucose Transport

Na⁺-Monosaccharide Cotransporter:

Against concentration gradient

Energy dependent

Carrier-mediated

Coupled to Na⁺ transport

Small intestine, renal tubules & choroid plexus

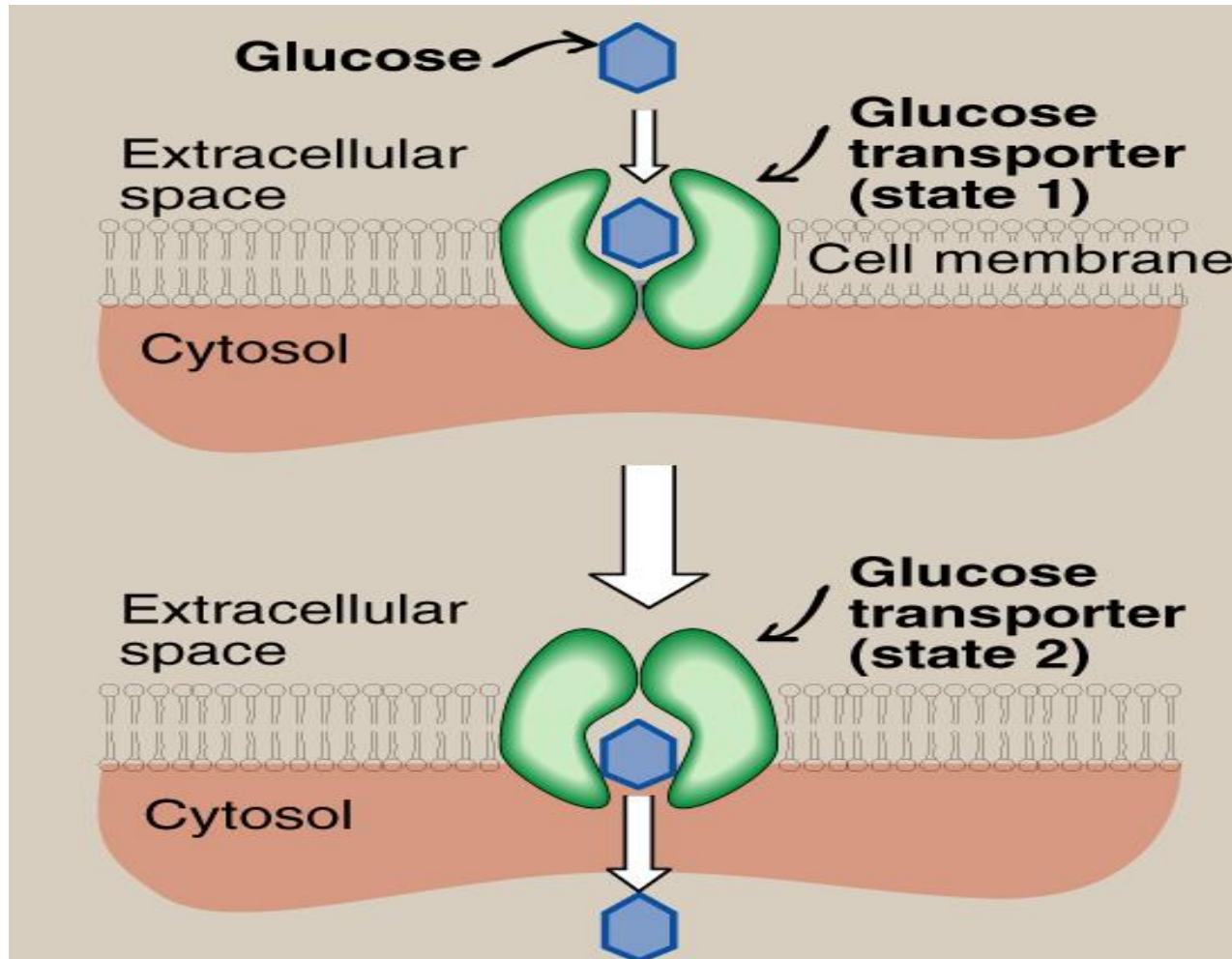
Na⁺-Independent Facilitated Diffusion:

With concentration gradient

Energy Independent

Glucose Transporters (GLUT 1-14)

Glucose Transport: Facilitated Diffusion



Glucose Transporters

- **Tissue-specific expression pattern**

GLUT-1

RBCs and brain

GLUT-2

Liver, kidney & pancreas

GLUT-3

Neurons

GLUT-4

Adipose tissue & skeletal muscle

GLUT-5

Small intestine & testes

GLUT-7

Liver (ER-membrane)

- **Functions:**

GLUT-1, 3 & 4

Glucose uptake from blood

GLUT-2

Blood & cells (either direction)

GLUT-5

Fructose transport

Glycolysis: 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**

Glycolysis: An Overview

- **Glycolysis, the major pathway for glucose oxidation, occurs in the cytosol of all cells.**
- **It is unique, in that it can function either aerobically or anaerobically, depending on the availability of oxygen and intact mitochondria.**
- **It allows tissues to survive in presence or absence of oxygen, e.g., skeletal muscle.**
- **RBCs, which lack mitochondria, are completely reliant on glucose as their metabolic fuel, and metabolizes it by anaerobic glycolysis.**

Glycolysis: An Overview

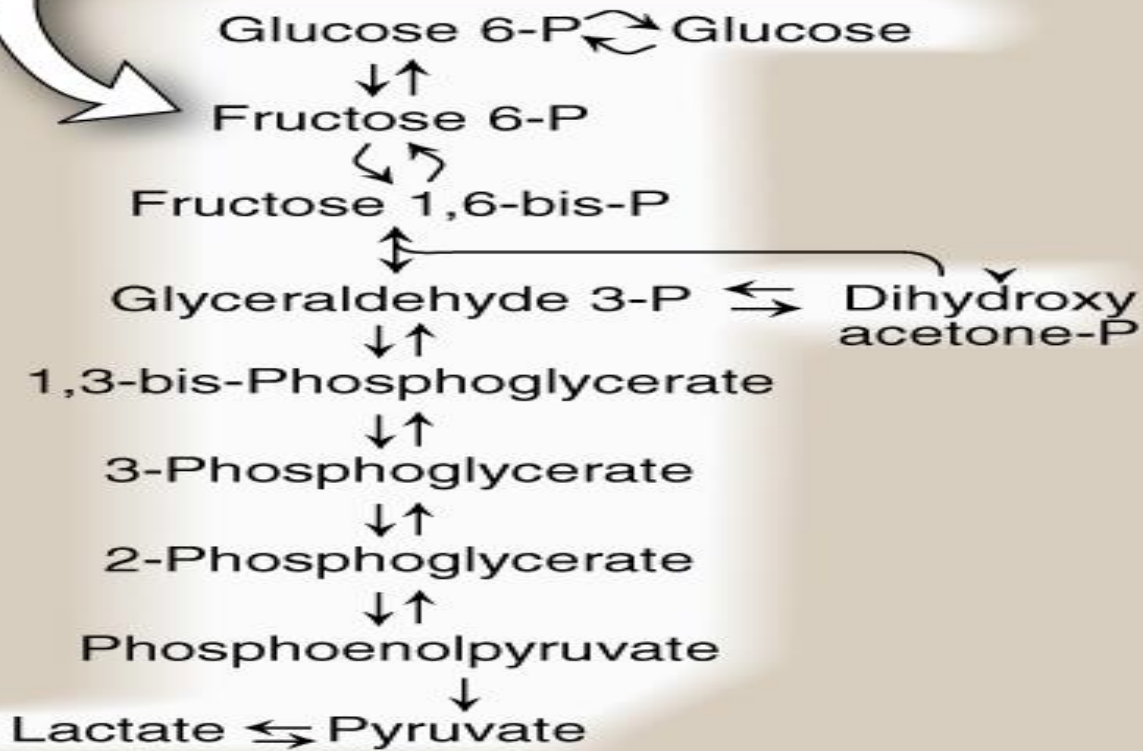
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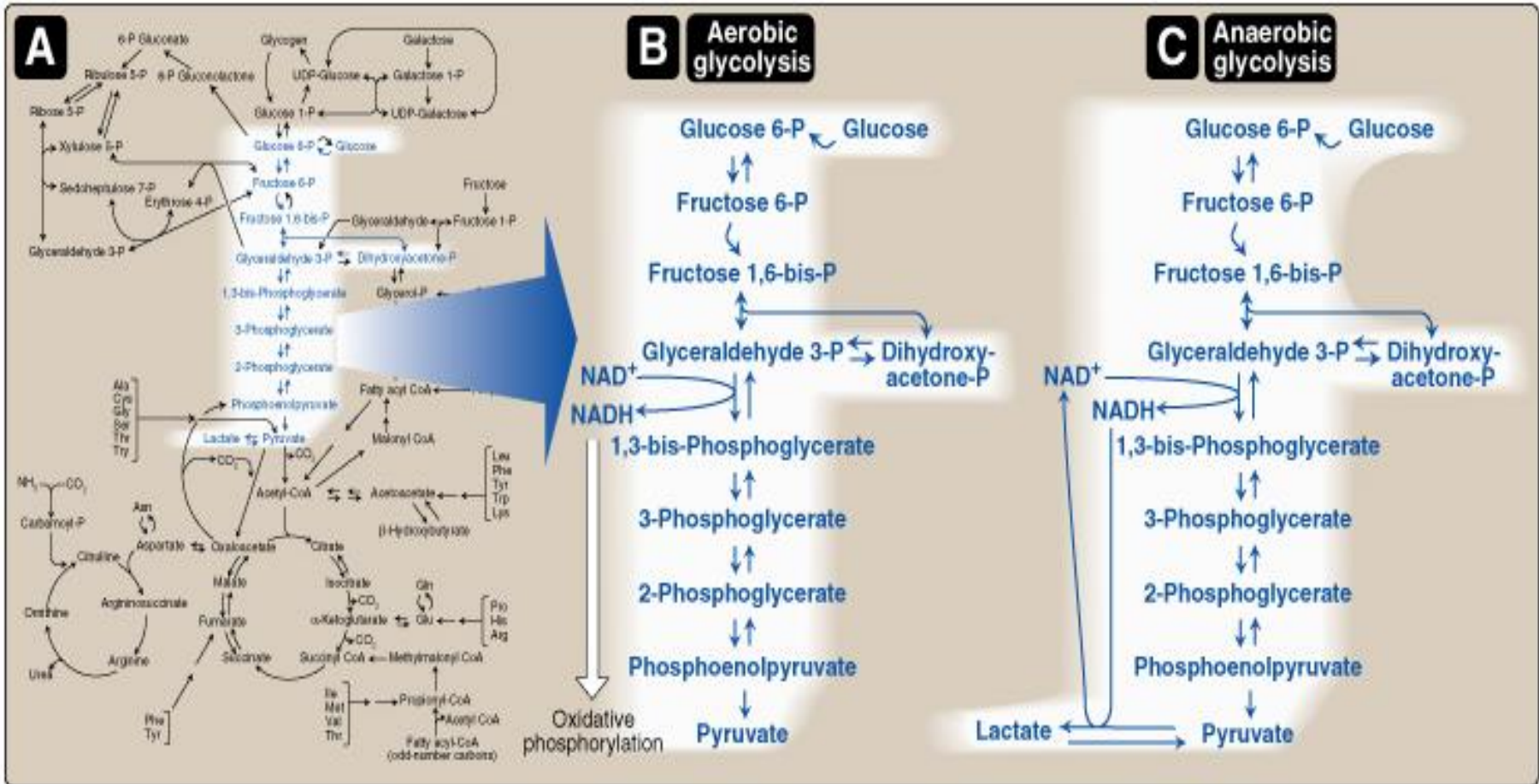
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Glycolysis

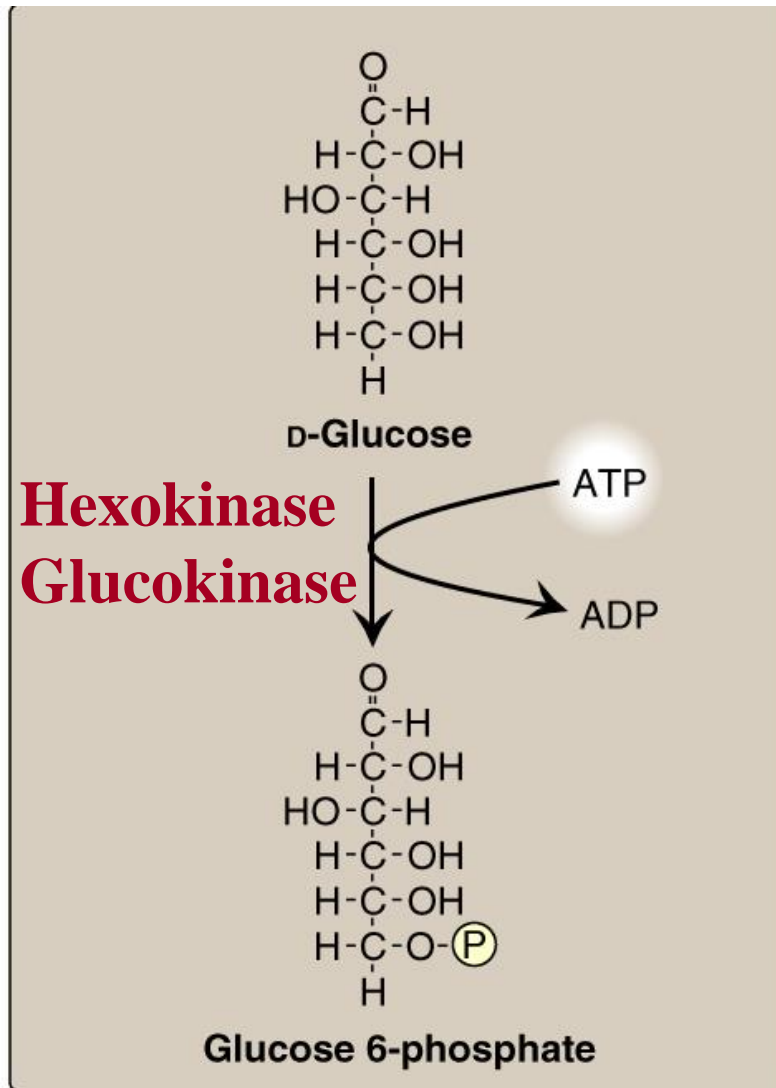
The product of one reaction is the substrate of the subsequent reaction.



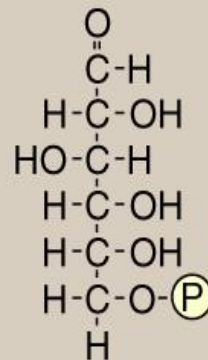
Aerobic Vs Anaerobic Glycolysis



Aerobic Glycolysis-1

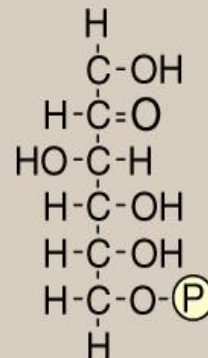


Aerobic Glycolysis-2



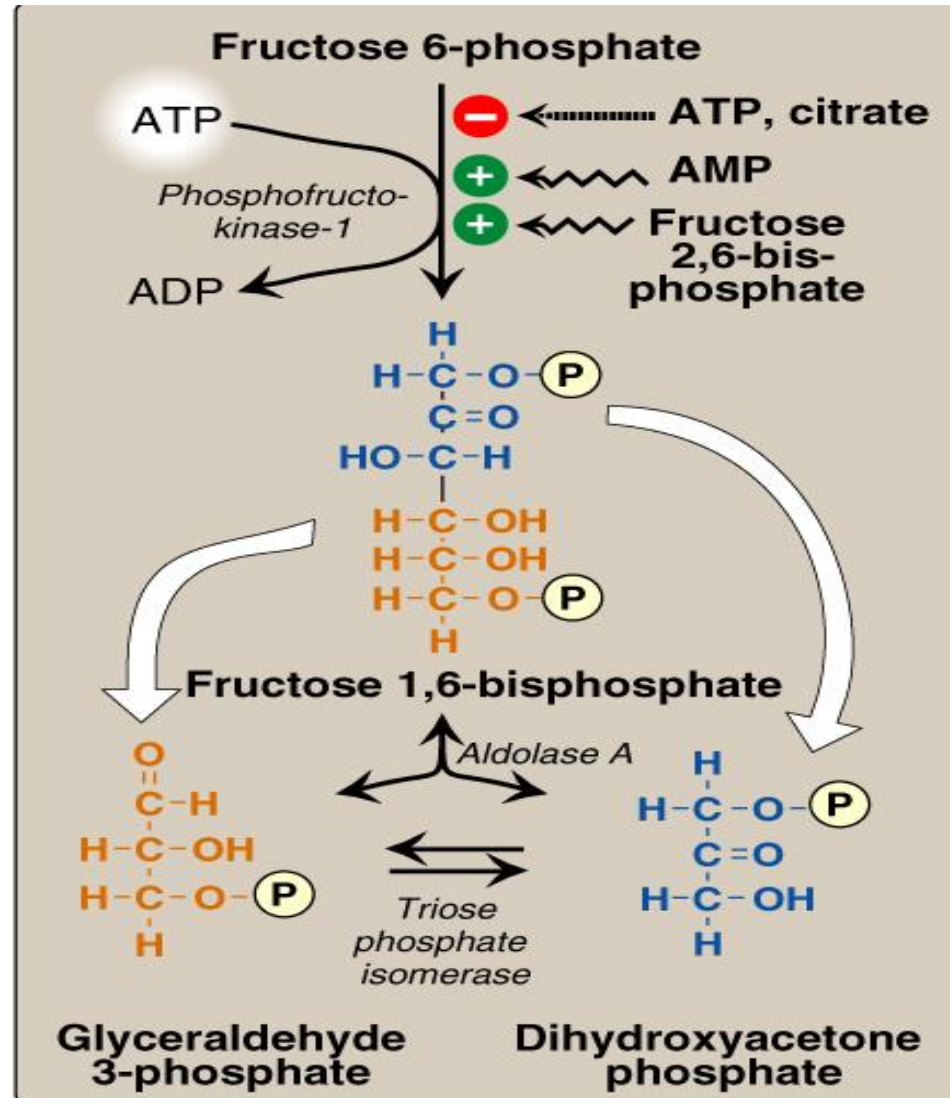
Glucose 6-phosphate

*Phosphoglucose
isomerase*

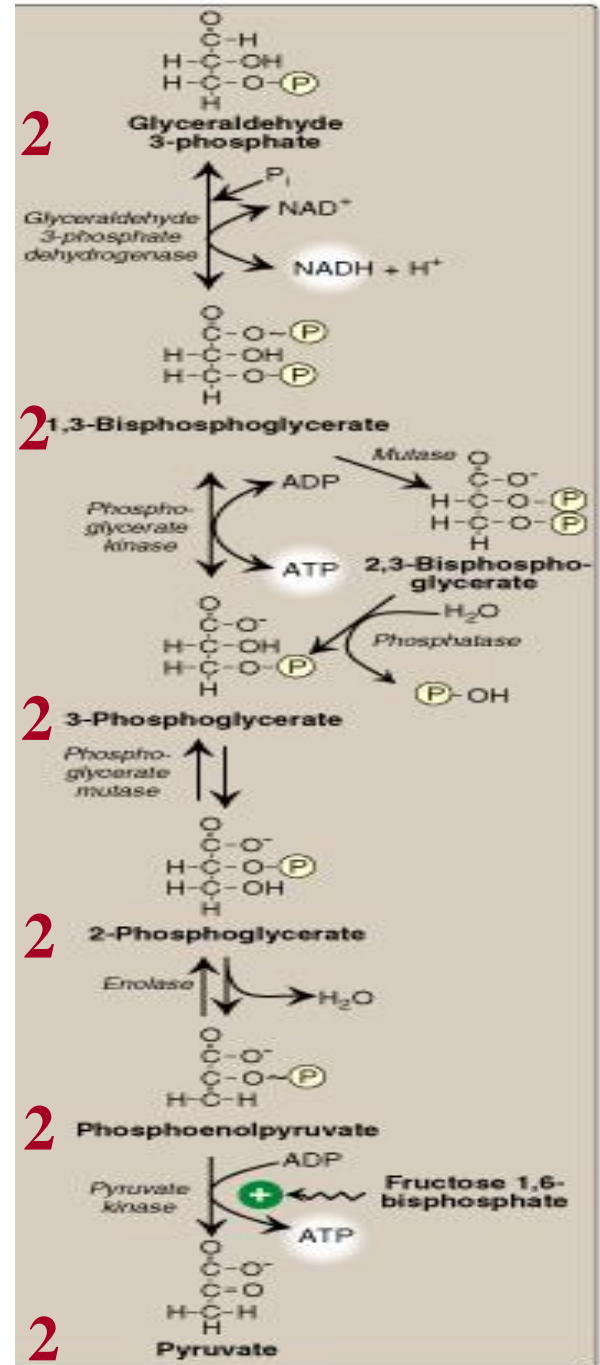


Fructose 6-phosphate

Aerobic Glycolysis: 3-5



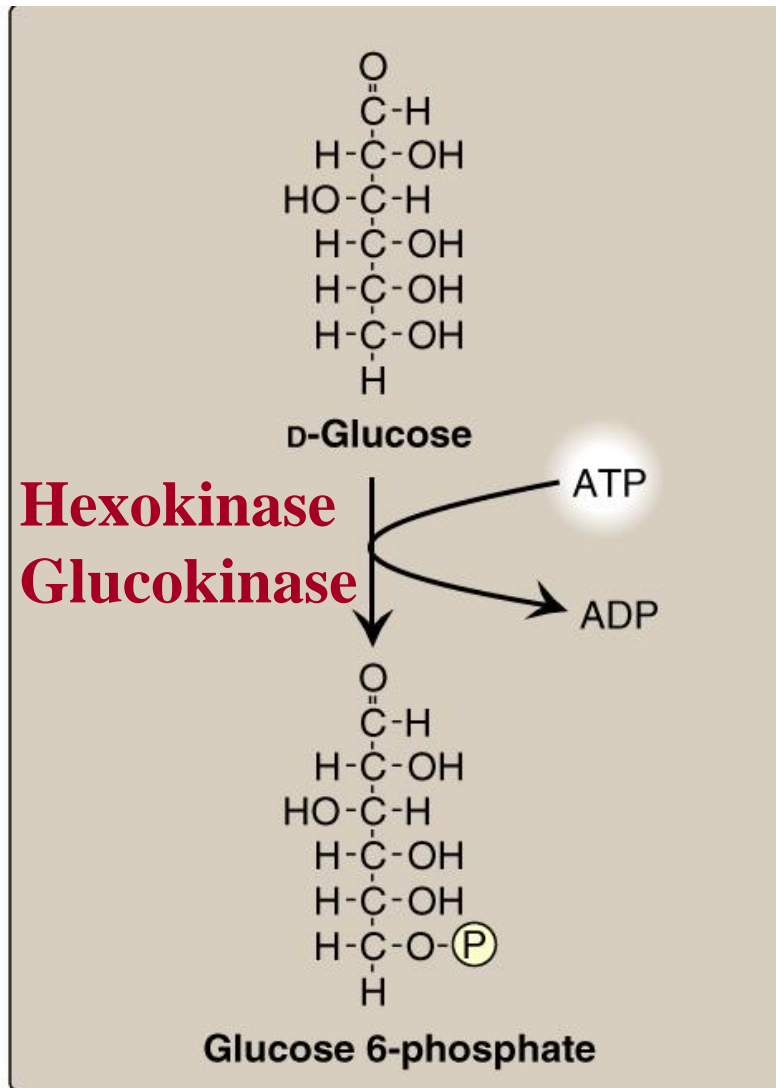
Aerobic Glycolysis: 6-10



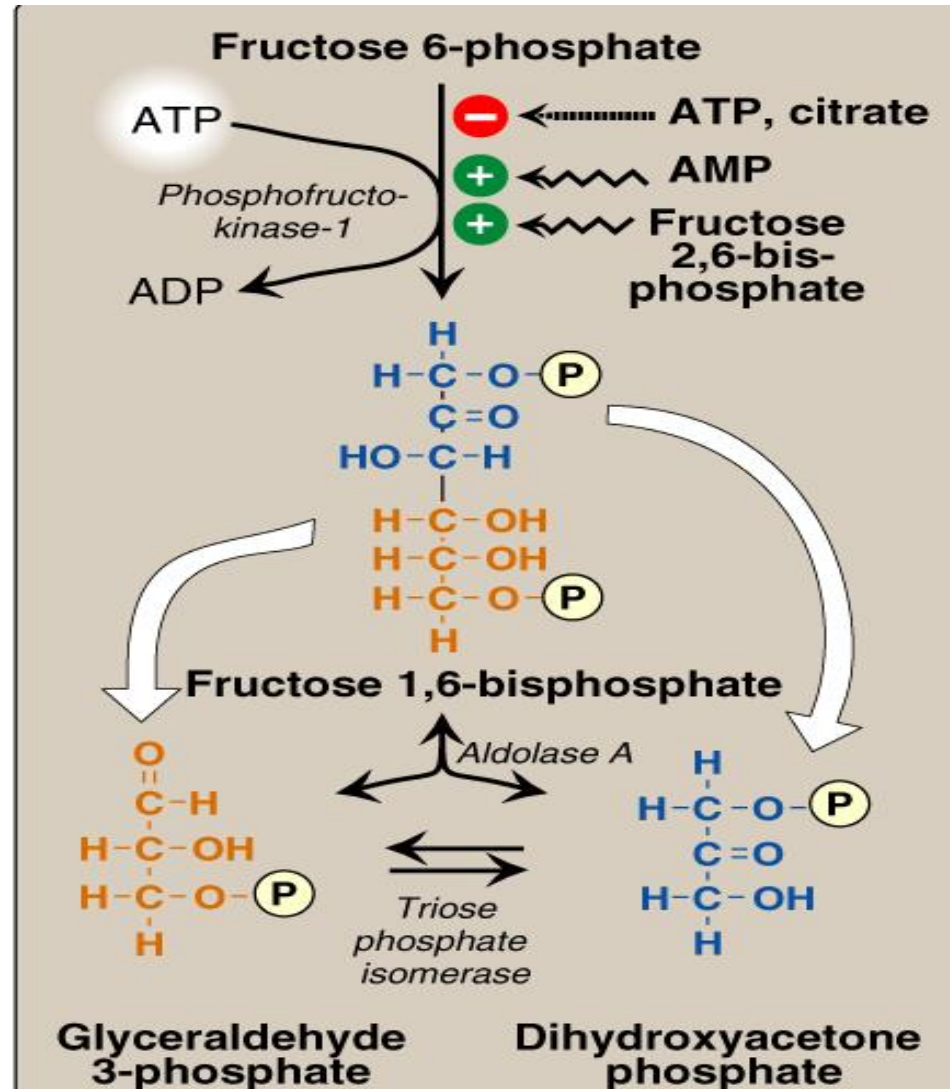
Aerobic Glycolysis-1

Hexokinase:
Most tissues

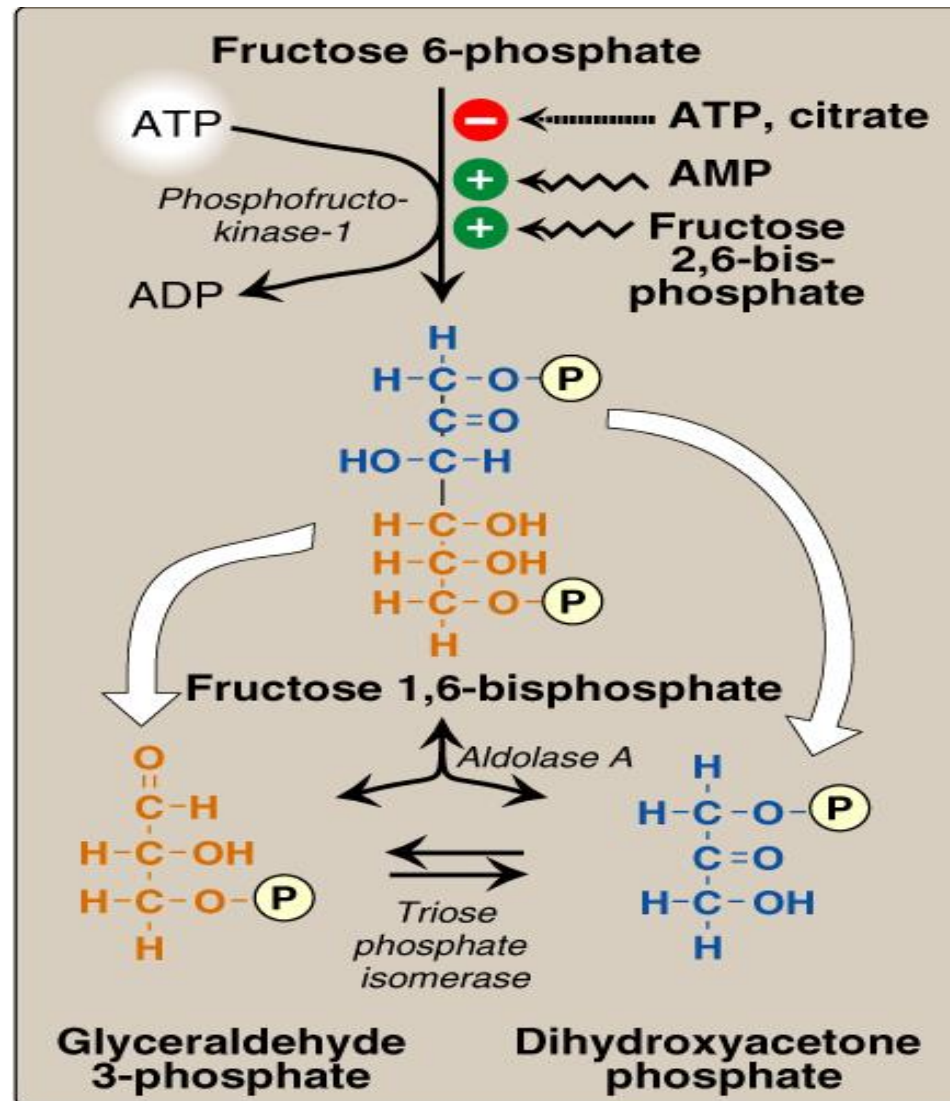
Glucokinase:
Hepatocytes



PFK-1: Regulation

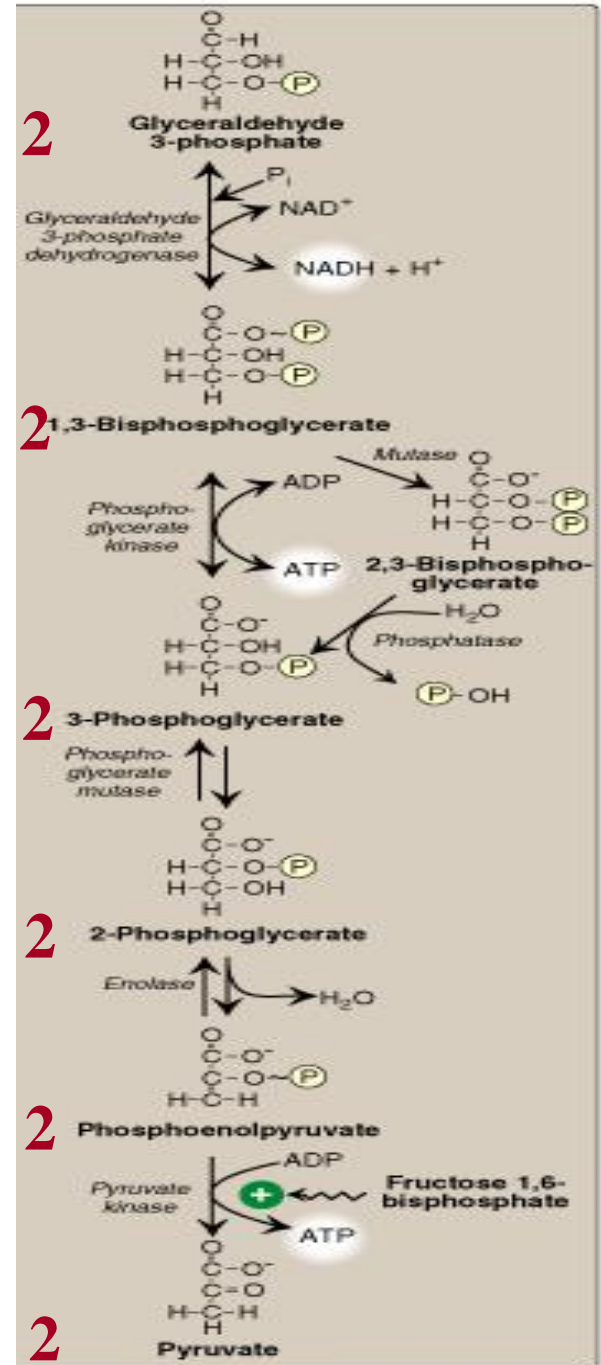


Aldolase and Triose Isomerase

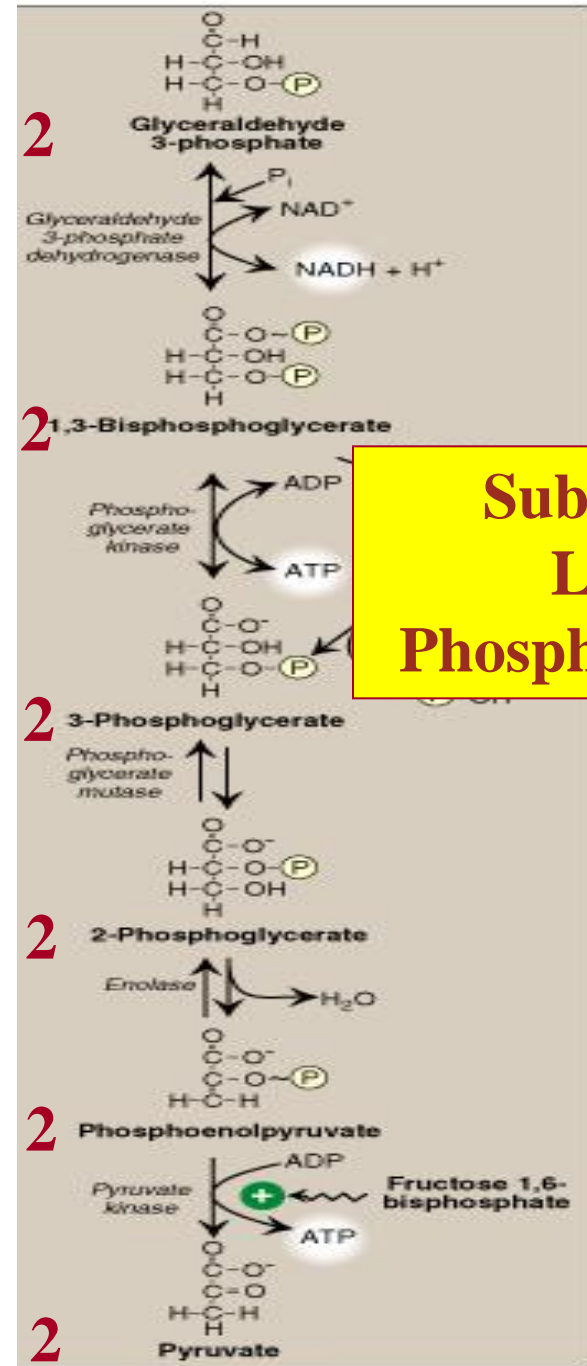


Glyceraldehyde 3-Phosphate Dehydrogenase

For each NADH, 3 ATP will
be produced by ETC
in the mitochondria
i.e., 6 ATP are produced

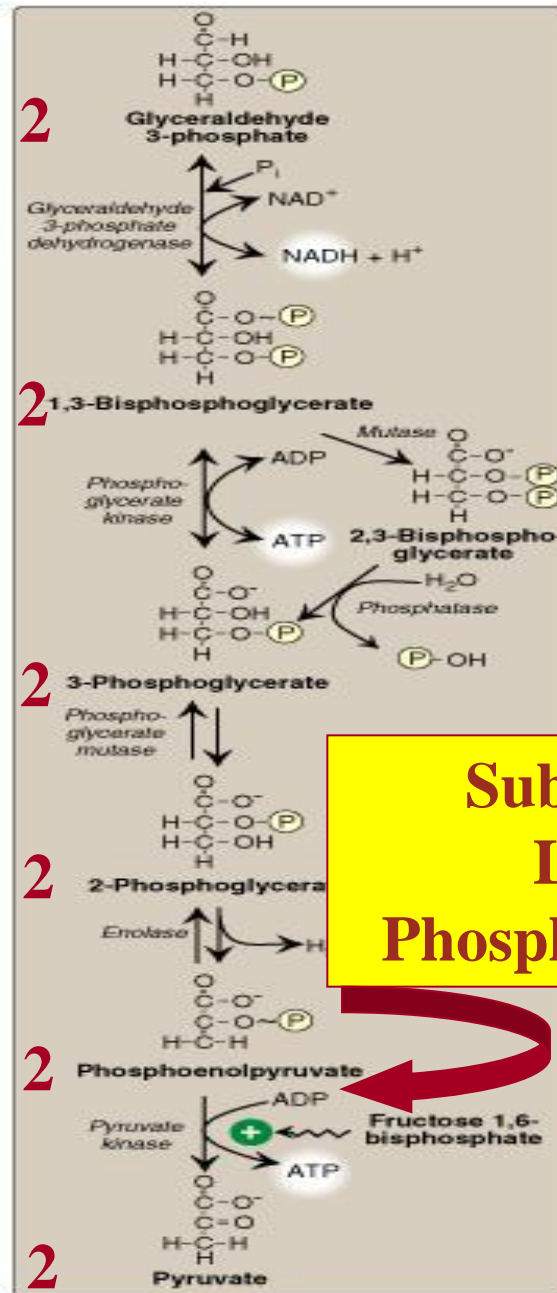


Phospho-glycerate Kinase



Substrate-Level Phosphorylation

Pyruvate Kinase

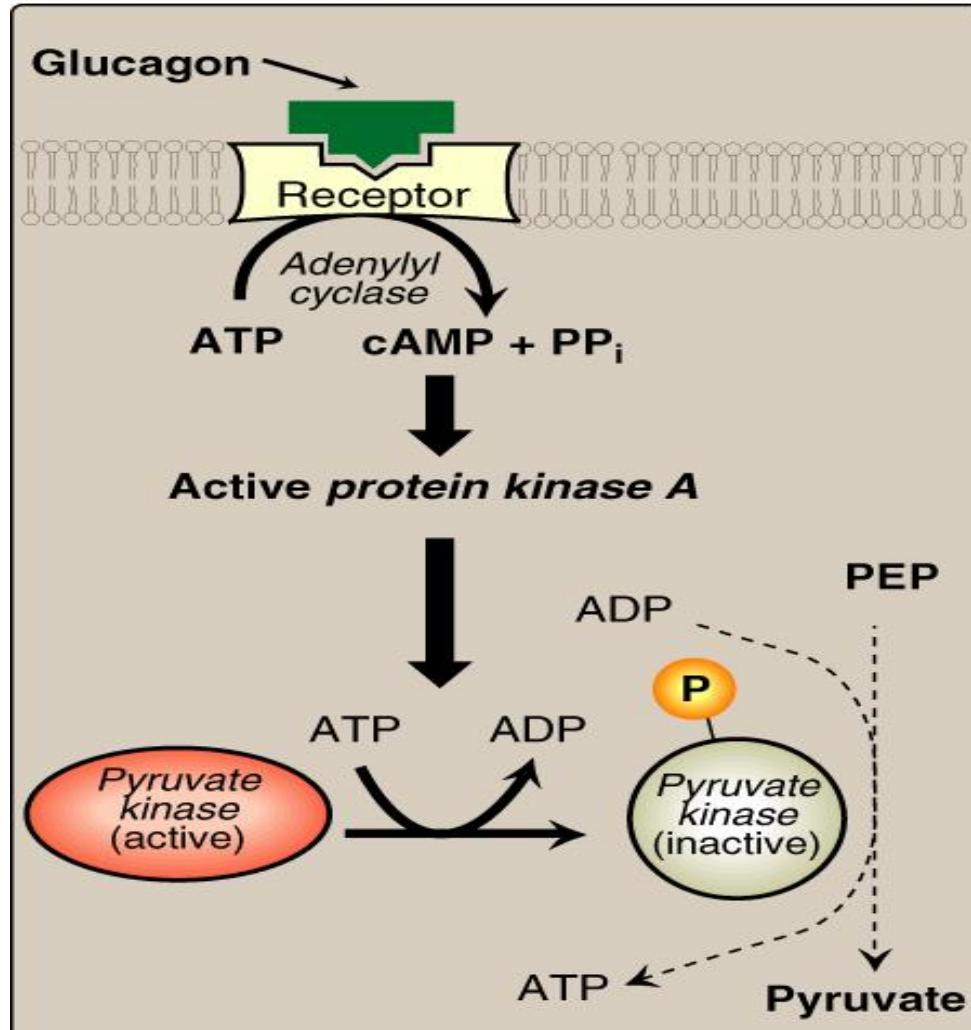


Substrate-Level Phosphorylation

Substrate-level phosphorylation Vs. Oxidative phosphorylation

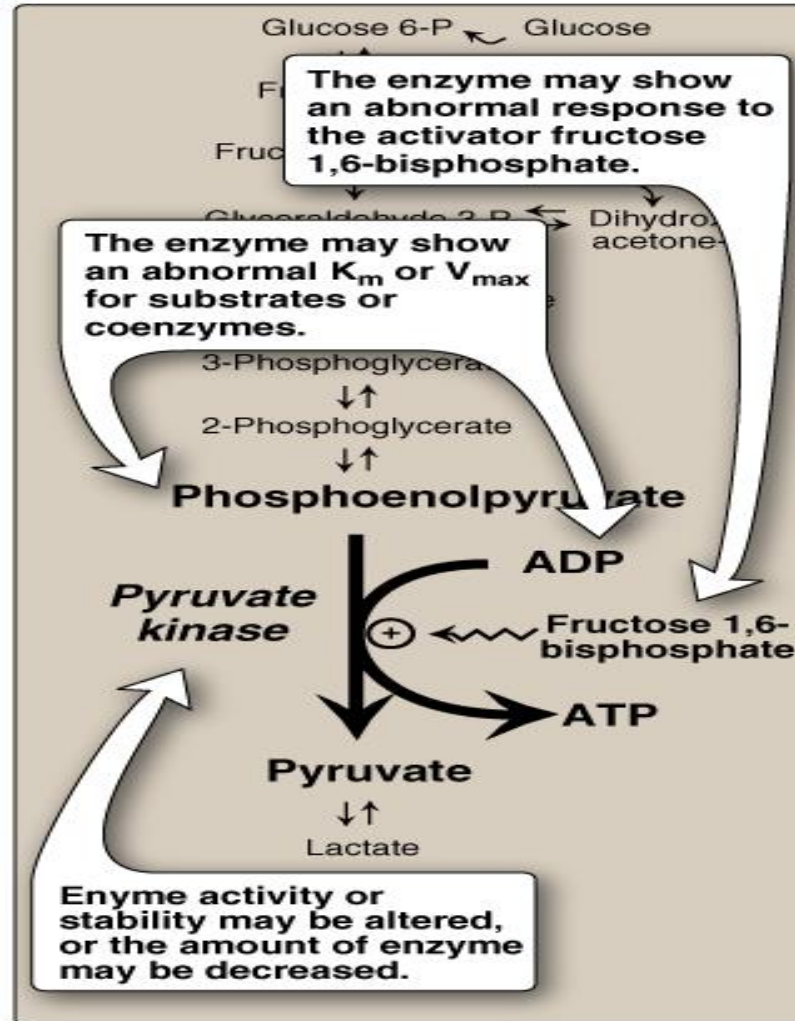
- **Phosphorylation** is the metabolic reaction of introducing a phosphate group into an organic molecule.
- **Oxidative phosphorylation:** The formation of high-energy phosphate bonds by phosphorylation of ADP to ATP coupled to the transfer of electrons from reduced coenzymes to molecular oxygen via 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

Pyruvate Kinase Covalent Modification



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

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

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 pathway for ATP production, **But** it has some anabolic features (amphibolic)
- Pyruvate kinase deficiency in RBCs results in hemolytic anemia

THANK YOU