بسم الله الرحمن الرحيم

Glucose Metabolism: Gluconeogenesis

By

Reem M. Sallam, *MD, PhD*

Assistant Prof. , Clinical Chemistry Unit,
Pathology Dept., College of Medicine, KSU

Objectives

- The importance of gluconeogenesis as an important pathway for glucose production
- The main reactions of gluconeogenesis
- The rate-limiting enzymes of gluconeogenesis
- Gluconeogensis is an energy-consuming, anabolic pathway

Gluconeogenesis: An Overview

- Liver (mainly) and Kidneys
- Both mitochondria and Cytosol are involved

  Exception: if the substrate is Glycerol: only cytosol

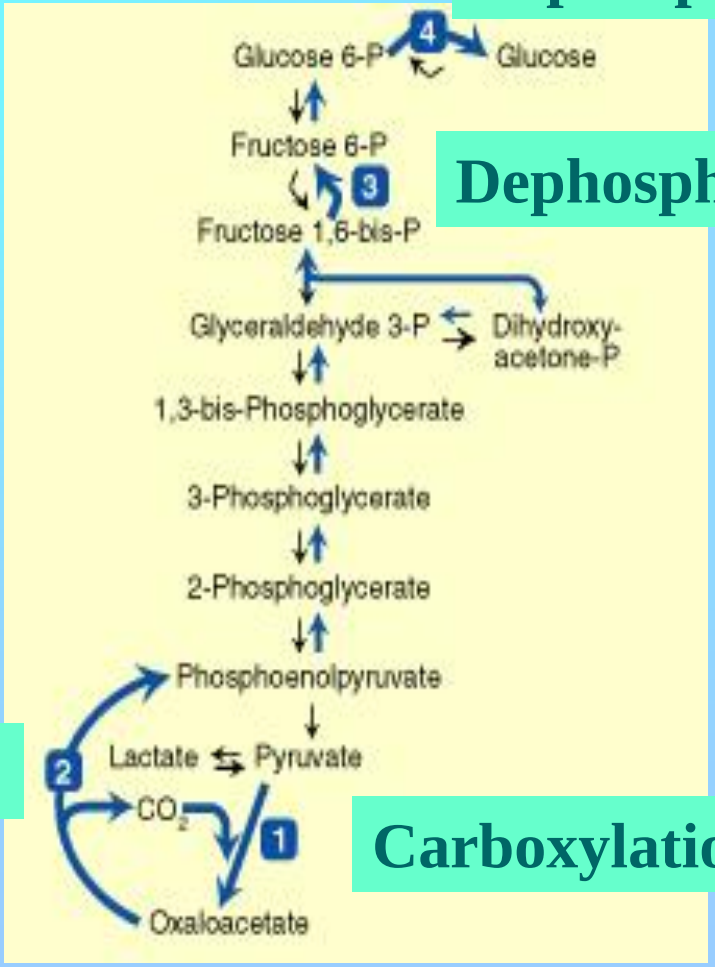
- Gluconeogenic substrates:

  Glycerol
  Lactate and Pyruvate
  Glucogenic amino acids

Gluconeogenic Pathway

Dephosphorylation of G-6-P

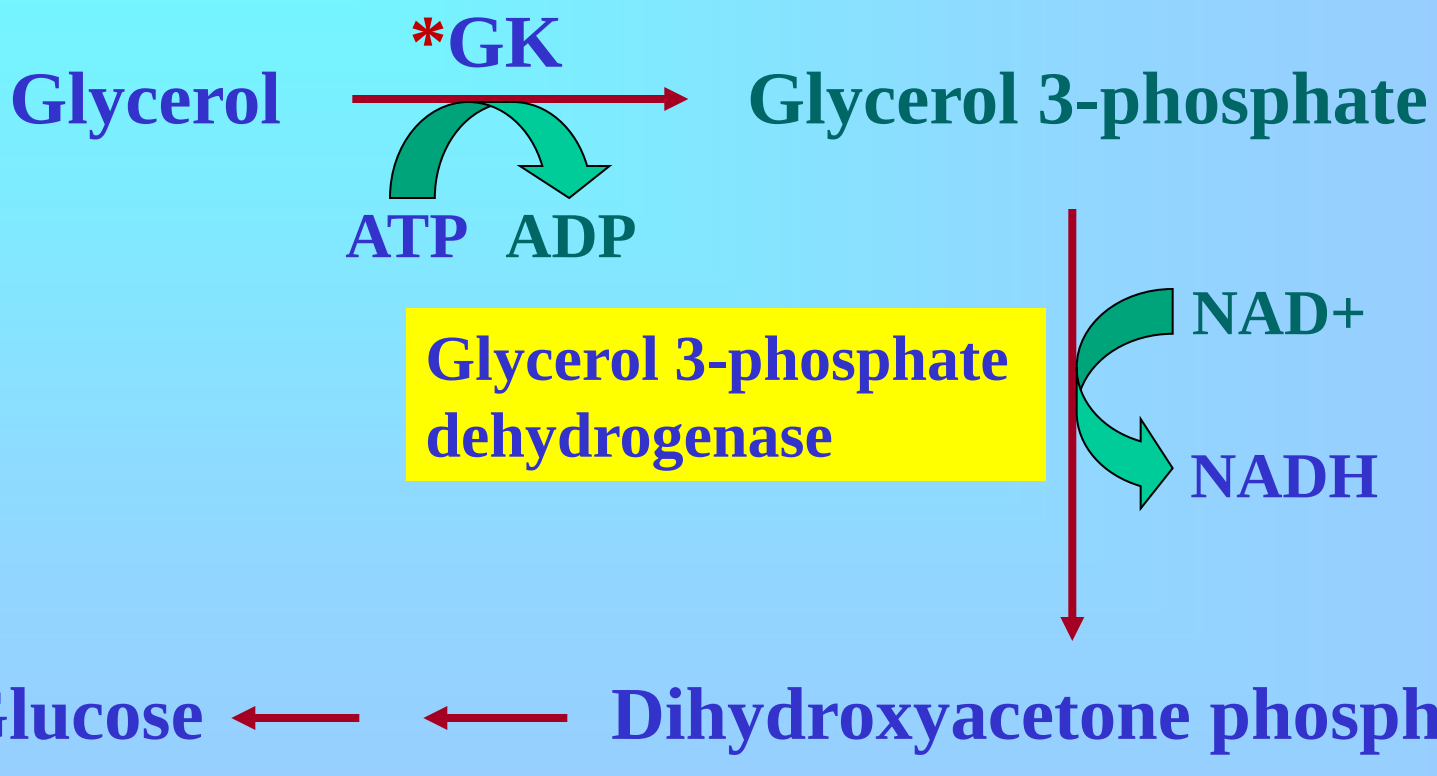
Dephosphorylation of F 1,6-P



Transport of OAA

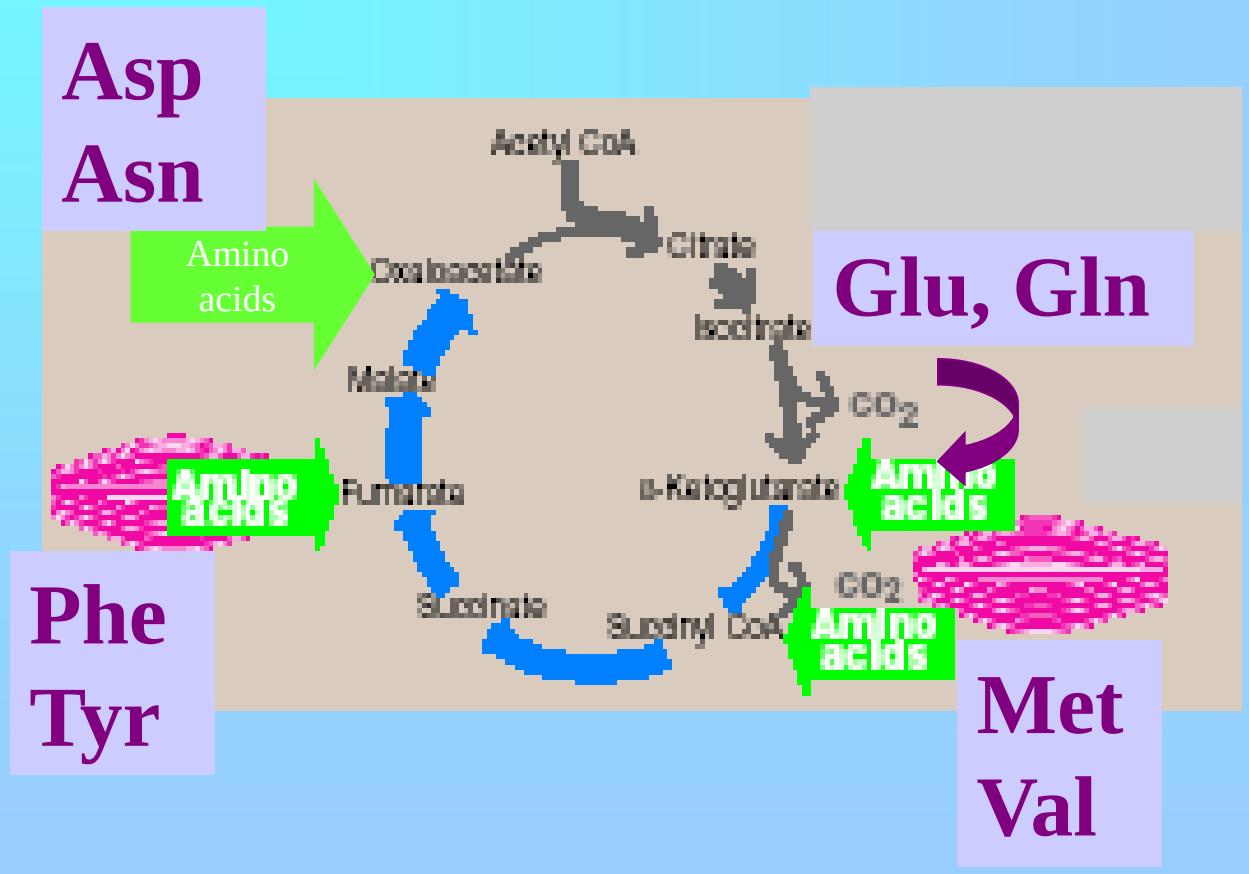
Carboxylation of pyruvate

Gluconeogenic Substrates: Glycerol



*GK: Glycerol kinase (present only in liver & kidneys)

Glucogenic Amino Acids



Gluconeogenic Substrates

Lactate

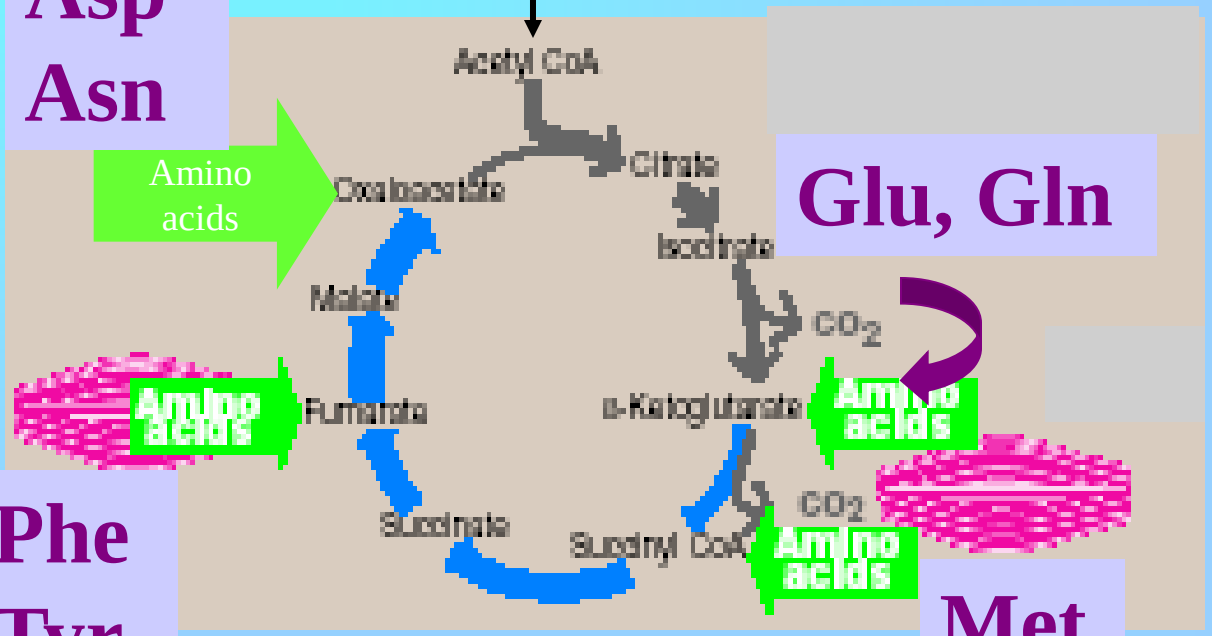
Gly, Ala

Amino acids

Pyruvate

Asp
Asn

Amino acids

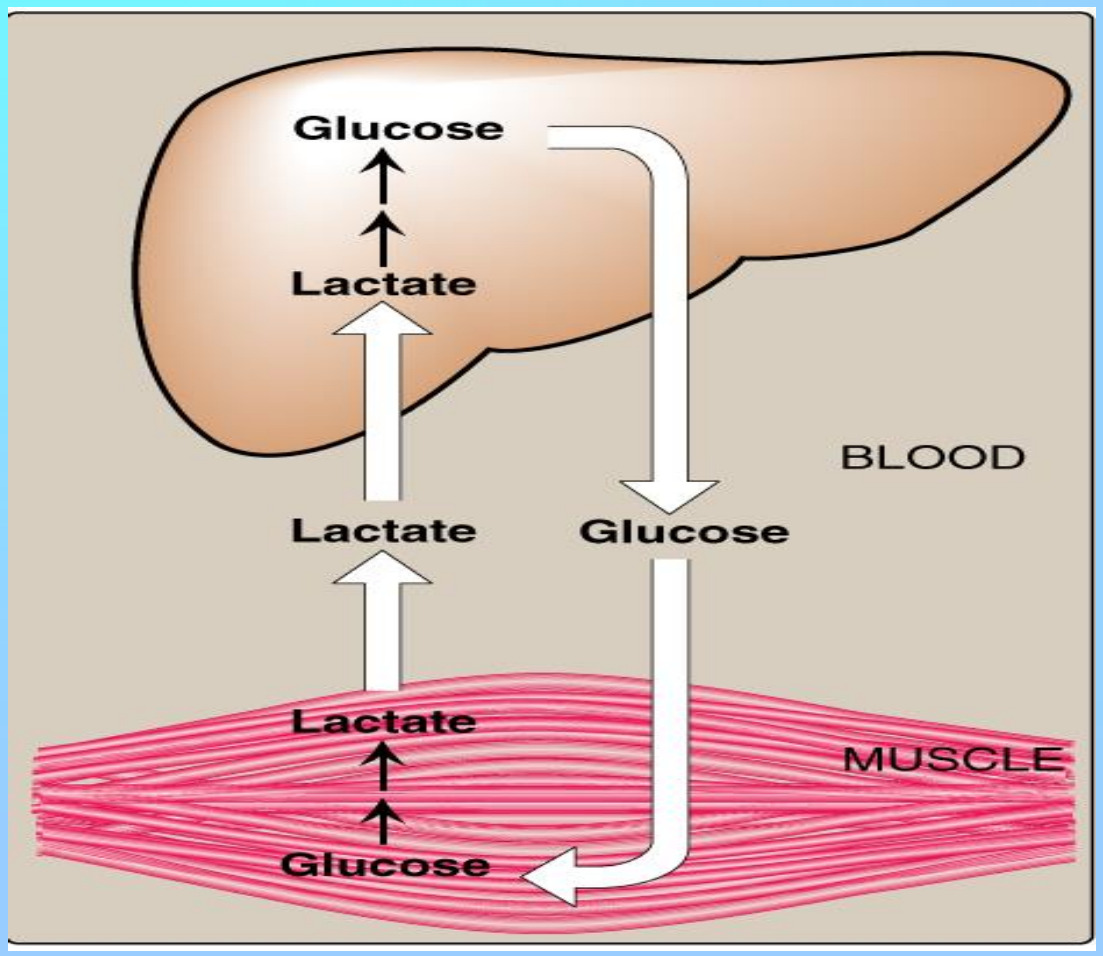


Glu, Gln

Phe
Tyr

Met
Val

Gluconeogenic Substrates: Lactate (Cori Cycle)



Gluconeogenic Pathway

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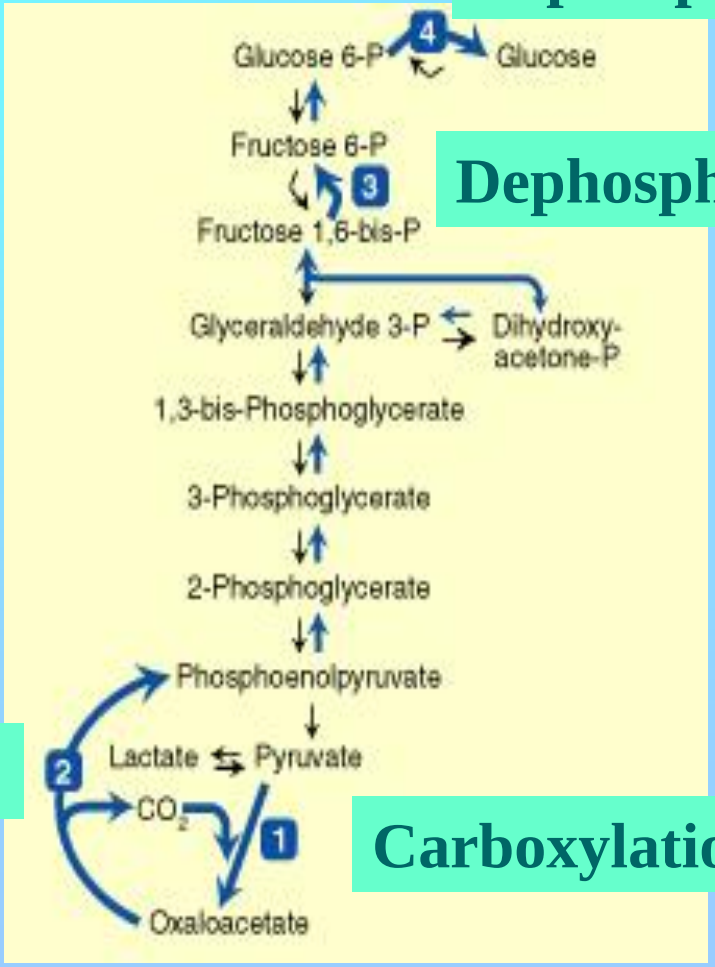


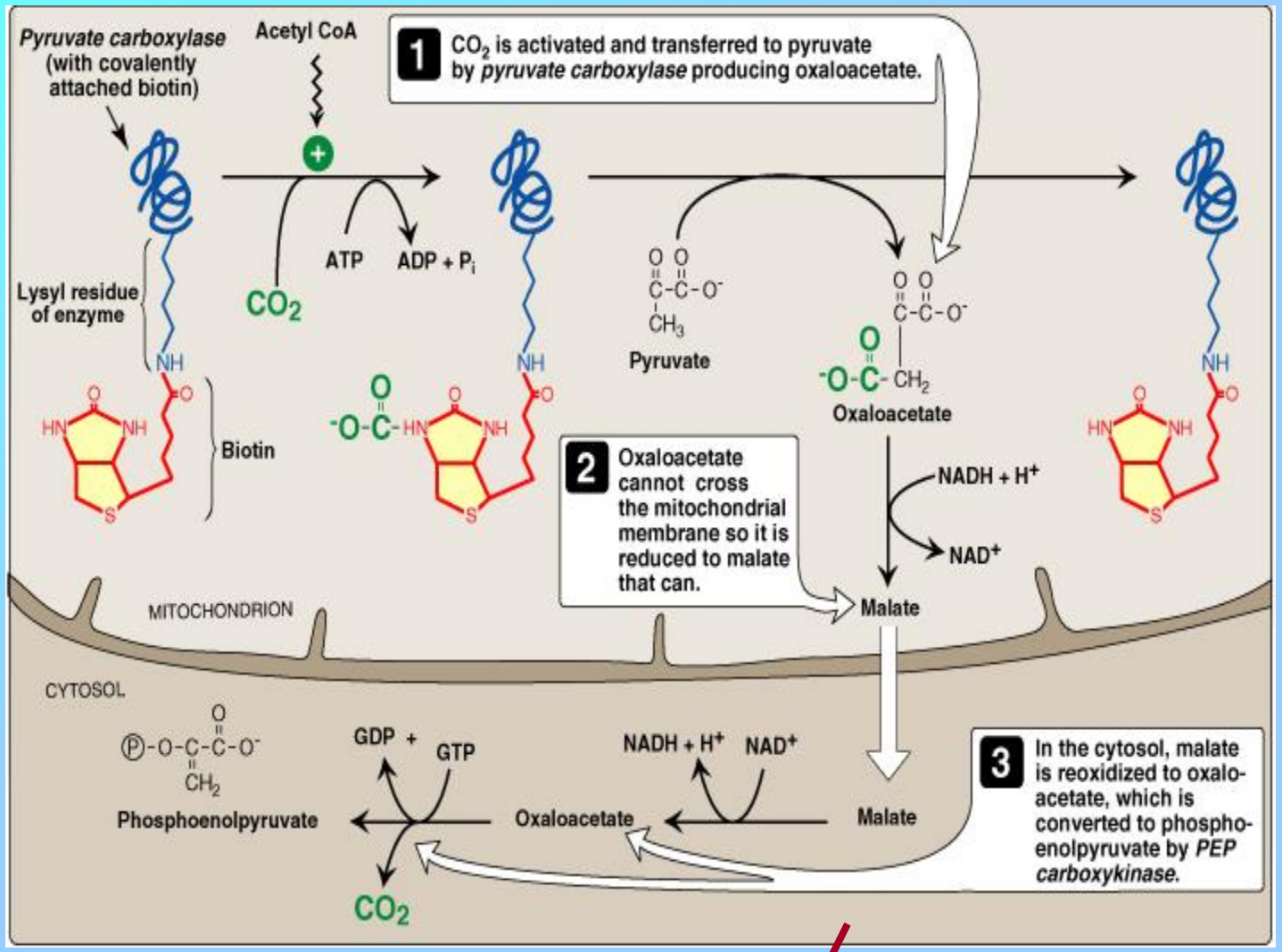
Transport of OAA

Carboxylation of pyruvate

Pruvate Carboxylase and PEP-CK

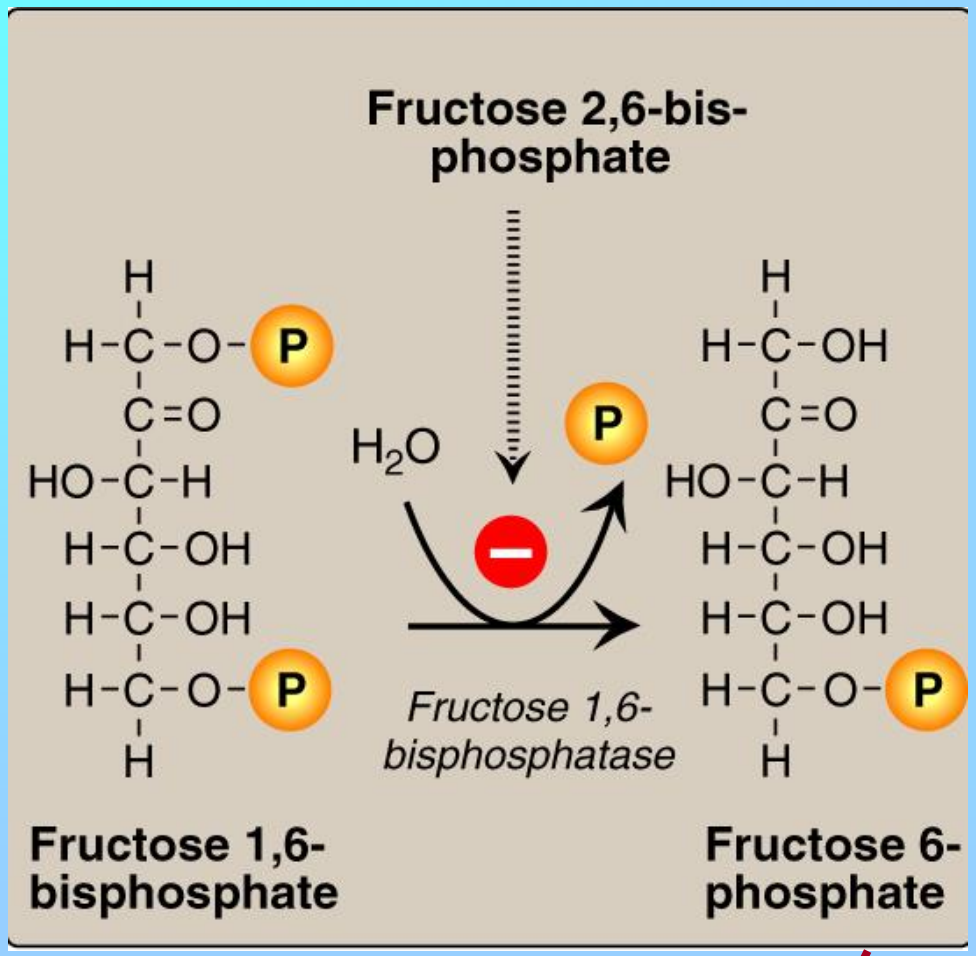
Fasting:
↑ Acetyl CoA
(From FAO)*

***Fatty Acid Oxidation**



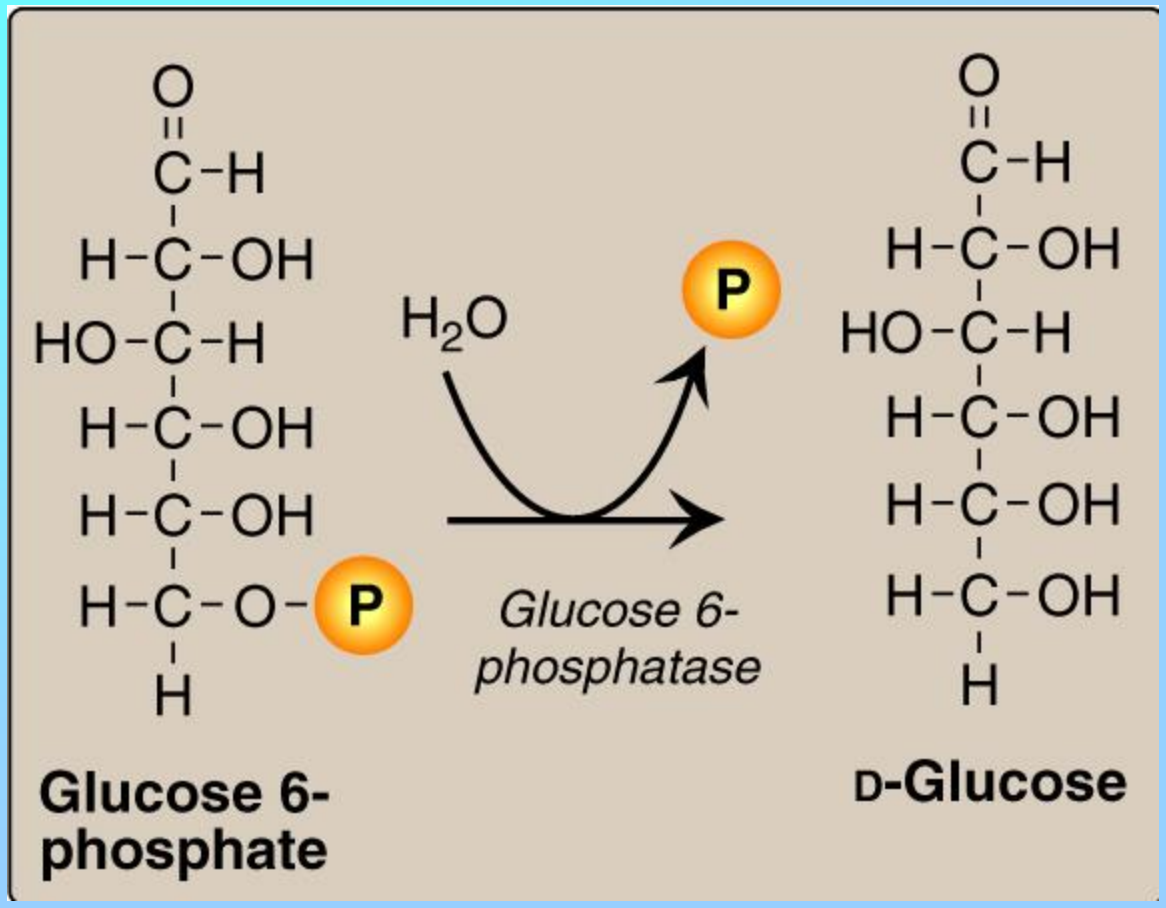
Pyruvate carboxylase + PEP-CK ≠ Pyruvate kinase

Fructose 1,6-Bisphosphatase



Fructose 1,6-bisphosphatase ≠ PFK-1

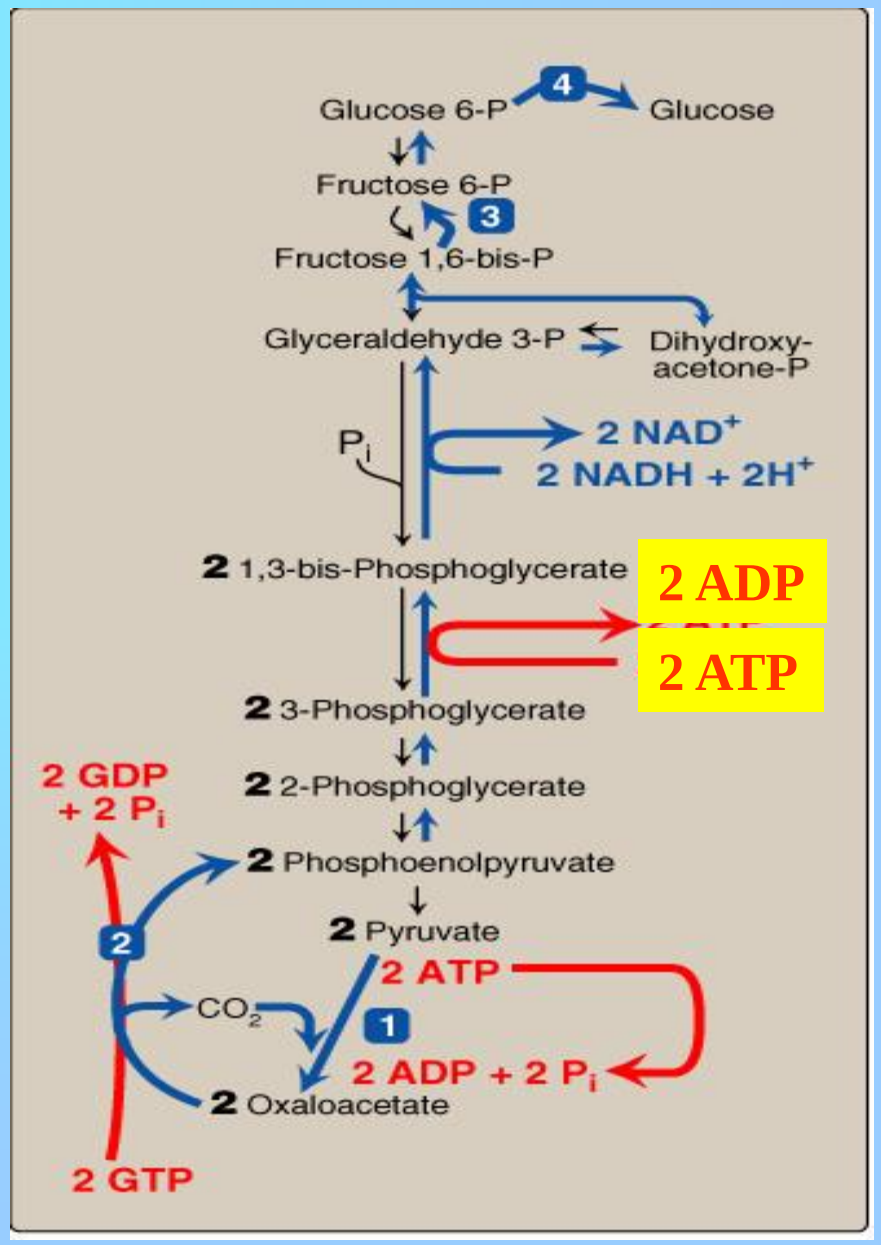
Glucose 6-Phosphatase



Glucose 6-phosphatase ≠ Glucokinase

Gluconeogensis:
Energy- Consumed

Six High-Energy Phosphate Bonds From Pyruvate to Glucose



Gluconeogenesis: Regulation

- **Reciprocal control**

  Gluconeogenesis & Glycolysis

- **Allosteric:**

  Acetyl CoA (+) Pyruvate carboxylase

  AMP (-) or ATP (+)
  F 2,6-Bisphosphate (-) } **F 1,6-bisphosphatase**

- **↑ Glucagon (↓ I/G ratio) stimulates gluconeogenesis**

  -Allosteric (↓ F 2,6-Bisphosphate)

  - Induction (PEP-CK)

Take Home Message

- **Gluconeogenesis:**
  Synthesis of glucose from noncarbohydrates
  Anabolic
  Energy-consuming
- **4 Unique enzymes are required for reversal of the 3 irreversible reactions of glycolysis**
- **Both gluconeogenesis & glycolysis are reciprocally-regulated**