بسم الله الرحمن الرحيم

Oxidative Decarboxylation and Krebs Cycle

By

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Objectives:

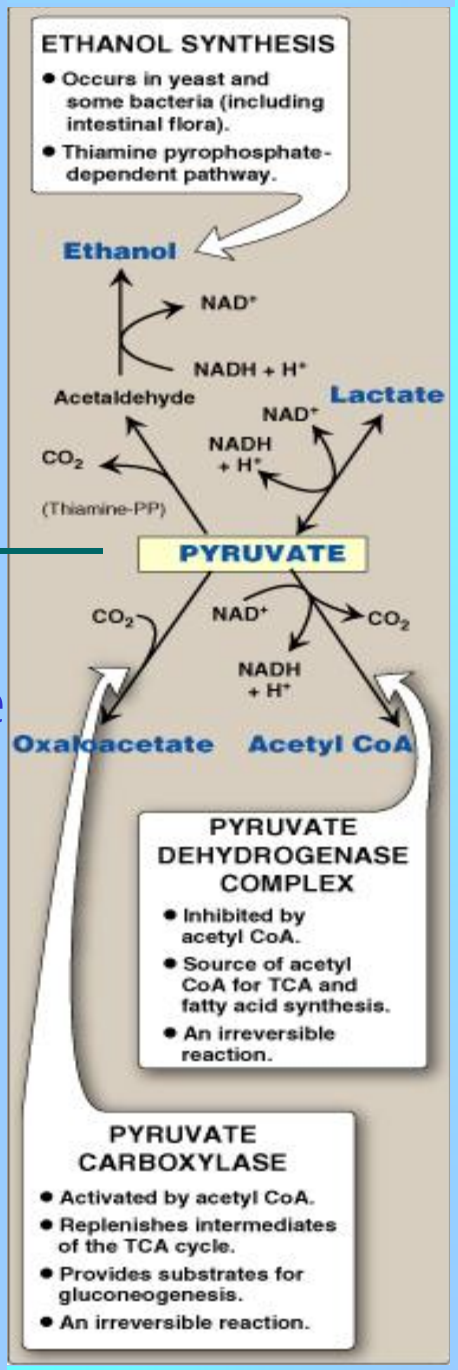
Oxidative decarboxylation of pyruvate:

- **ATP production**
- **Regulation**
- **Clinical correlation**

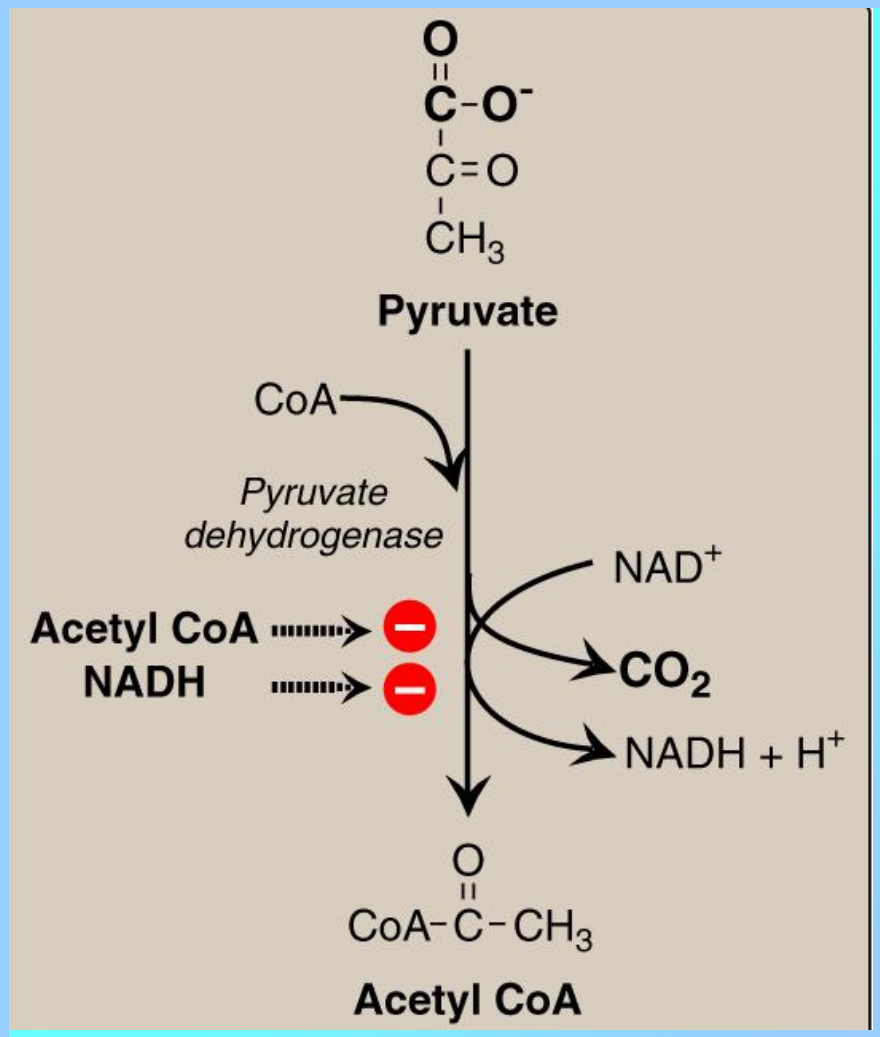
Krebs cycle:

- **Final common pathway for oxidation of all food stuff**
- **The main reactions**
- **ATP production**
- **Respiratory regulation**

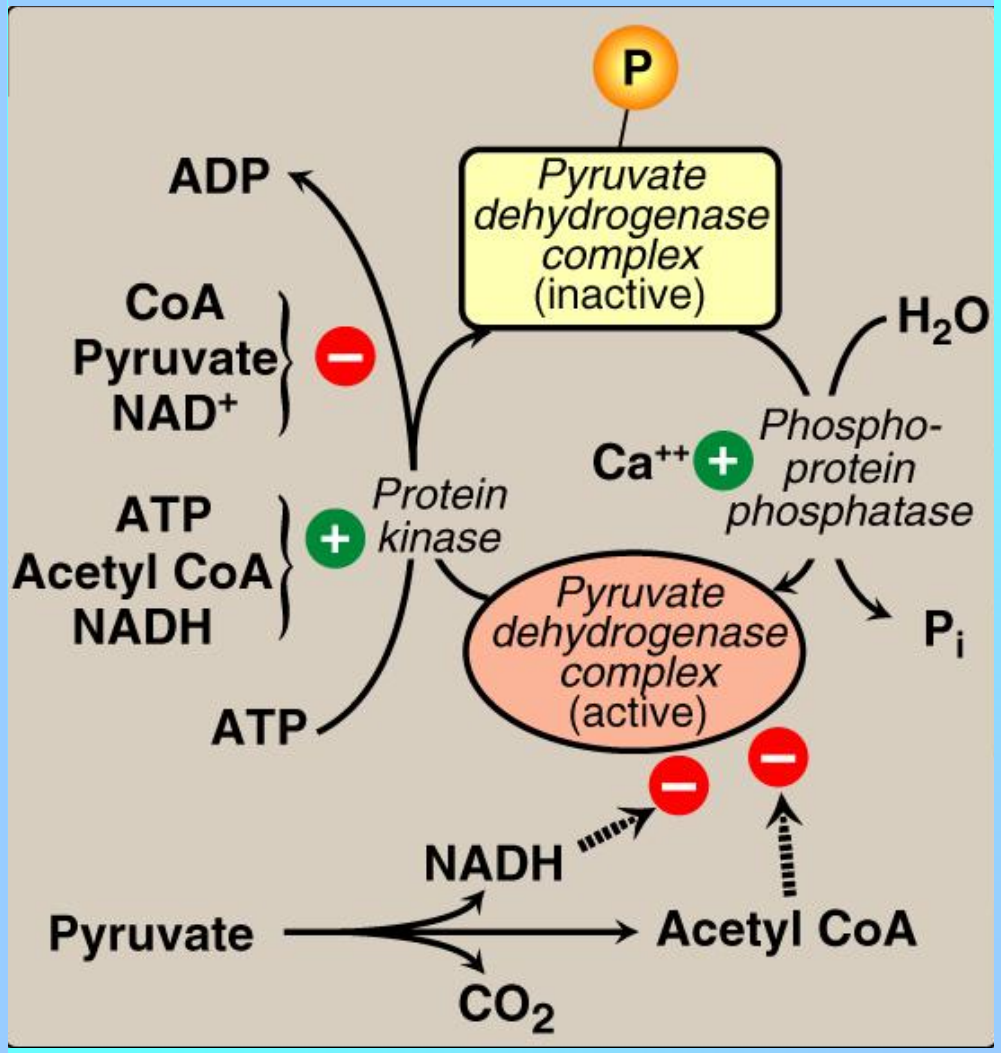
Fates of Pyruvate



Oxidative Decarboxylation of Pyruvate



Oxidative Decarboxylation of Pyruvate: Regulation



Pyruvate Dehydrogenase Deficiency: Congenital Lactic Acidosis

E1 deficiency of PDH complex

X-linked dominant

Affects mainly brain

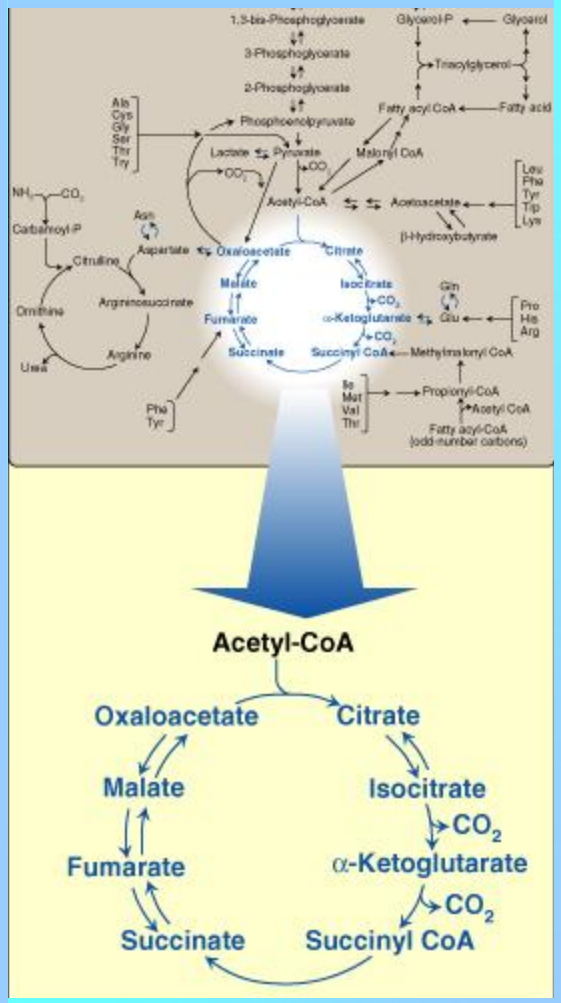
Clinically:

- **Lactic acidosis**
- **Developmental defects of nervous system**
- **Muscular spasticity**
- **Early death**

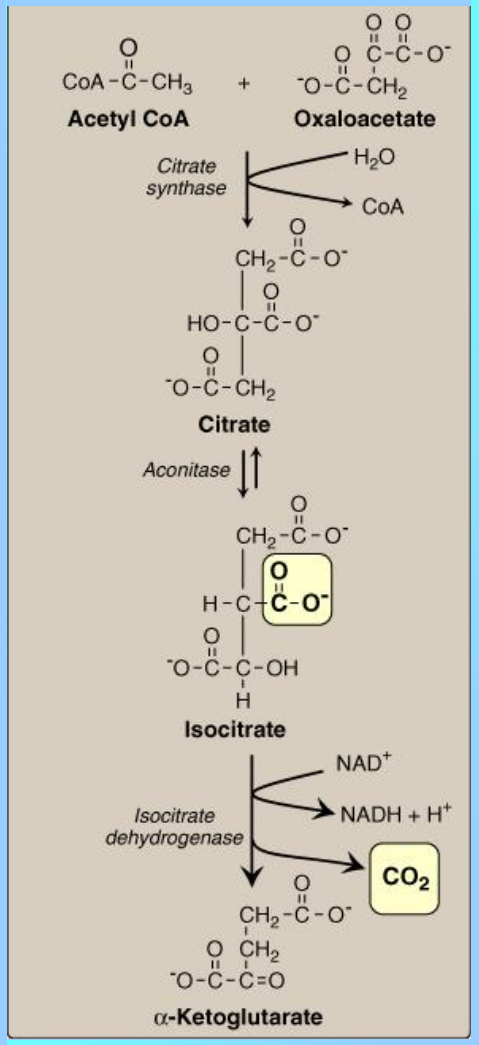
Tricarboxylic Acid Cycle: Krebs Cycle

- Final common pathway for oxidation
- Exclusively in mitochondria
- Major source for ATP
- Both catabolic and anabolic
- Synthetic reactions:
  - Glucose from amino acids
  - Nonessential amino acids
  - Fatty acids
  - Heme

Krebs Cycle

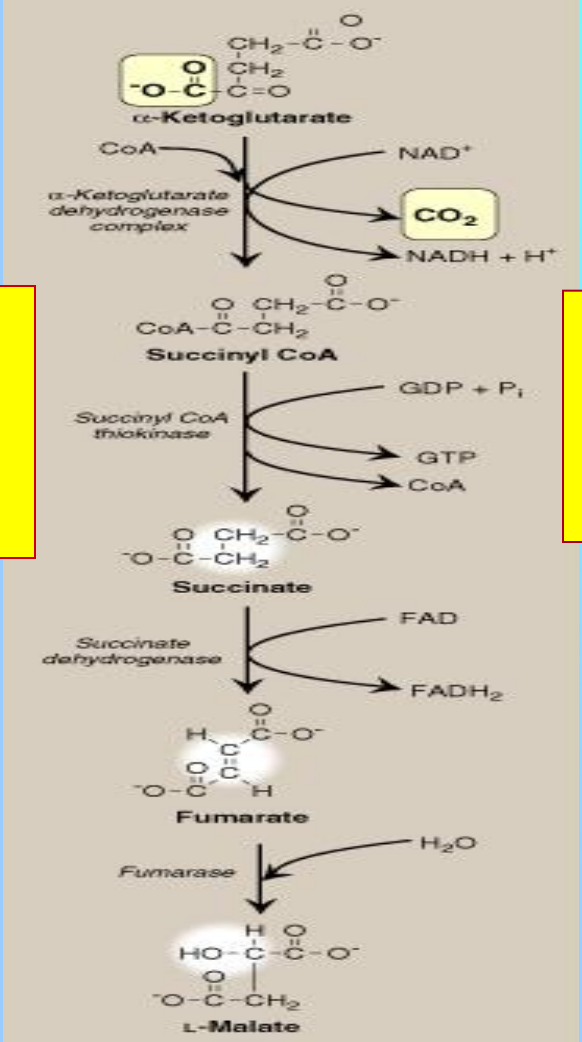

1,3-bis-Phosphoglycerate
3-Phosphoglycerate
2-Phosphoglycerate
Phosphoenolpyruvate
Lactate
Pyruvate
Acetyl-CoA
Malonyl CoA
Fatty acyl CoA
Fatty acid
Glycerol-P
Glycerol
Triacylglycerol
Ala
Cys
Gly
Ser
Thr
Try
Leu
Phe
Tyr
Trp
Lys
Acetoacetate
β-Hydroxybutyrate
Carbamoyl-P
Asp
Aspartate
Oxaloacetate
Citrate
Citrulline
Malate
Isocitrate
Ornithine
Argininosuccinate
Fumarate
α-Ketoglutarate
Gln
Glu
Pro
His
Arg
Arginine
Urea
Succinate
Succinyl CoA
Methylmalonyl CoA
Phe
Tyr
Ile
Met
Val
Thr
Propionyl-CoA
Acetyl CoA
Fatty acyl-CoA
(odd-number carbons)
Acetyl-CoA
Oxaloacetate
Citrate
Malate
Isocitrate
CO2
Fumarate
α-Ketoglutarate
CO2
Succinate
Succinyl CoA

Krebs Cycle Reactions -1



Krebs Cycle Reactions -2

Succinate Thiokinase

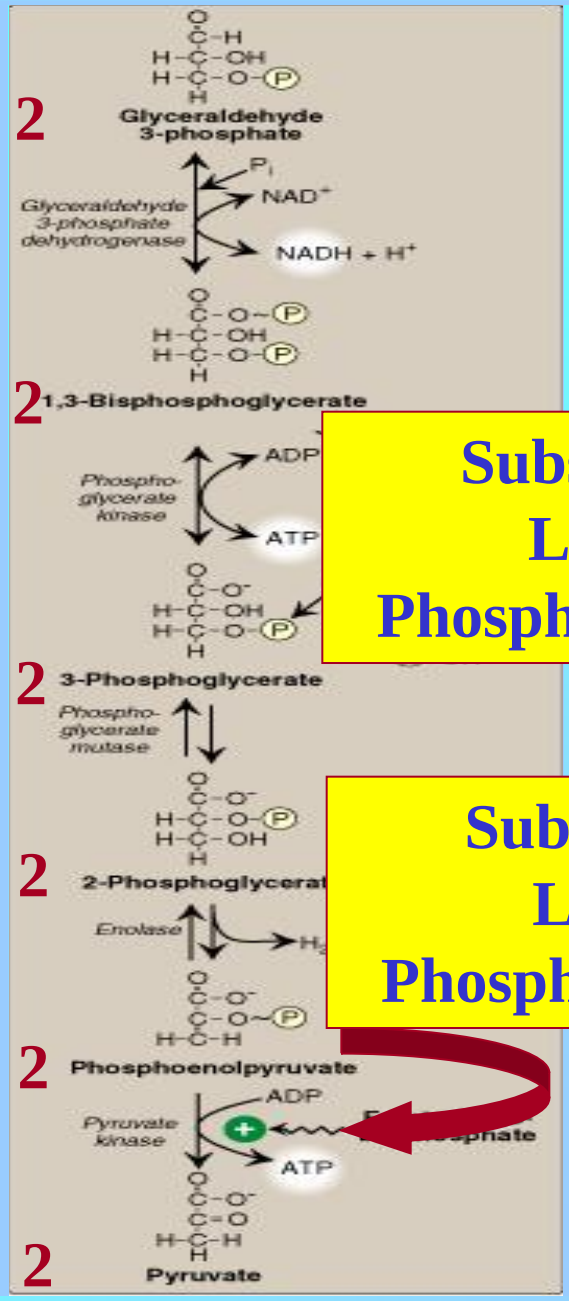


Substrate-Level Phosphorylation

Glycolysis (Cytosol)

Phospho-glycerate Kinase

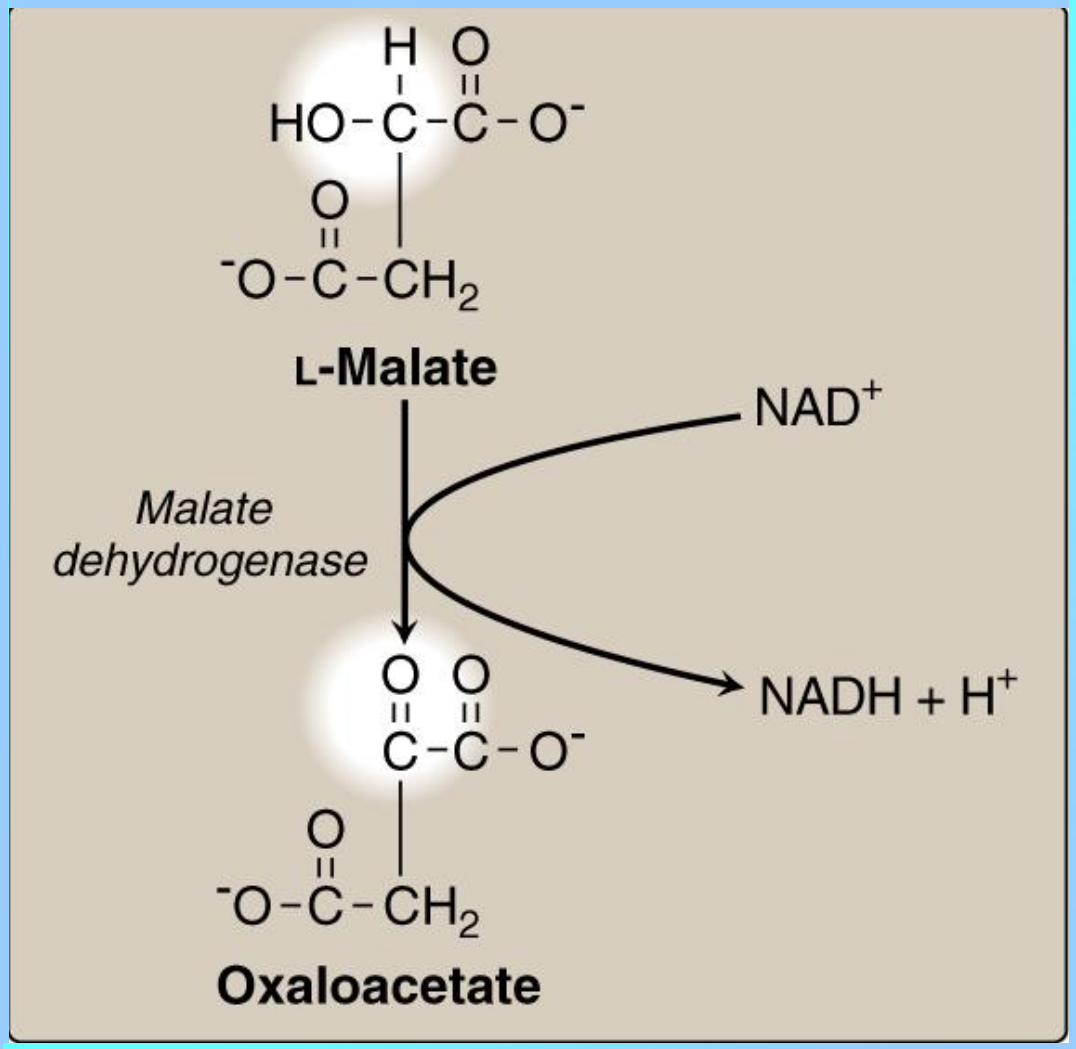
Pyruvate Kinase



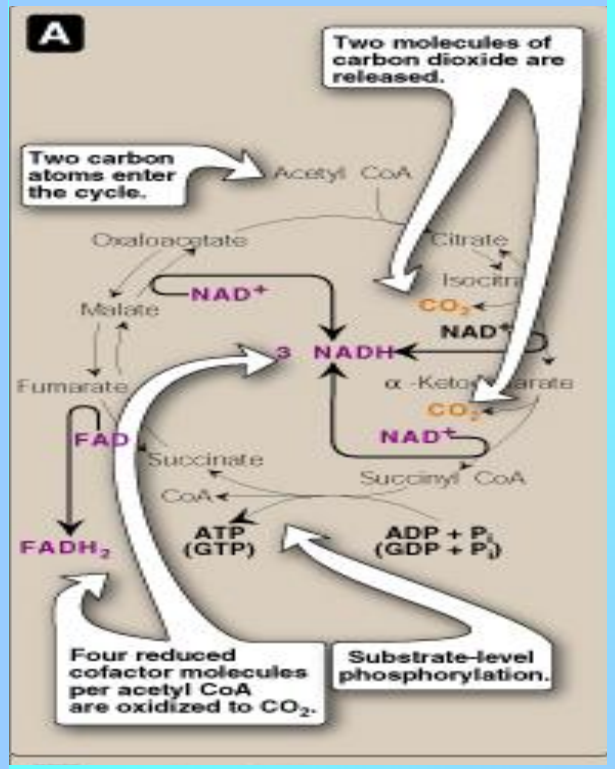
Substrate-Level Phosphorylation

Substrate-Level Phosphorylation

Krebs Cycle Reactions -3



Krebs Cycle: Energy Yield -1



Krebs Cycle: Energy Yield -2

Energy-producing reaction	Number of ATP produced
3 NADH $\longrightarrow$ 3 NAD^+	9
$FADH_2 \longrightarrow FAD$	2
$GDP + P_i \longrightarrow GTP$	1
	12 ATP/acetyl CoA oxidized

Complete Glucose Oxidation: Net ATP Production

Aerobic glycolysis:		**8 ATP**
Oxidative decarboxylation:	**2 X 3 =**	**6 ATP**
Krebs cycle:	**2 X 12 =**	**24 ATP**
Net:		**38 ATP**

Krebs Cycle: Regulation