بسم الله الرحمن الرحيم

Oxidative Decarboxylation and Krebs Cycle

By

Reem M. Sallam, M.D.; Ph.D.

Clinical Biochemistry Unit, Pathology Dept.
College of Medicine, King Saud University

Fates of Pyruvate

The enzyme requires Thyamine pyro phosphate as a coenzyme

Amino Group بنزع
Alanine من
Pyruvate يرجع الى

reversible reaction

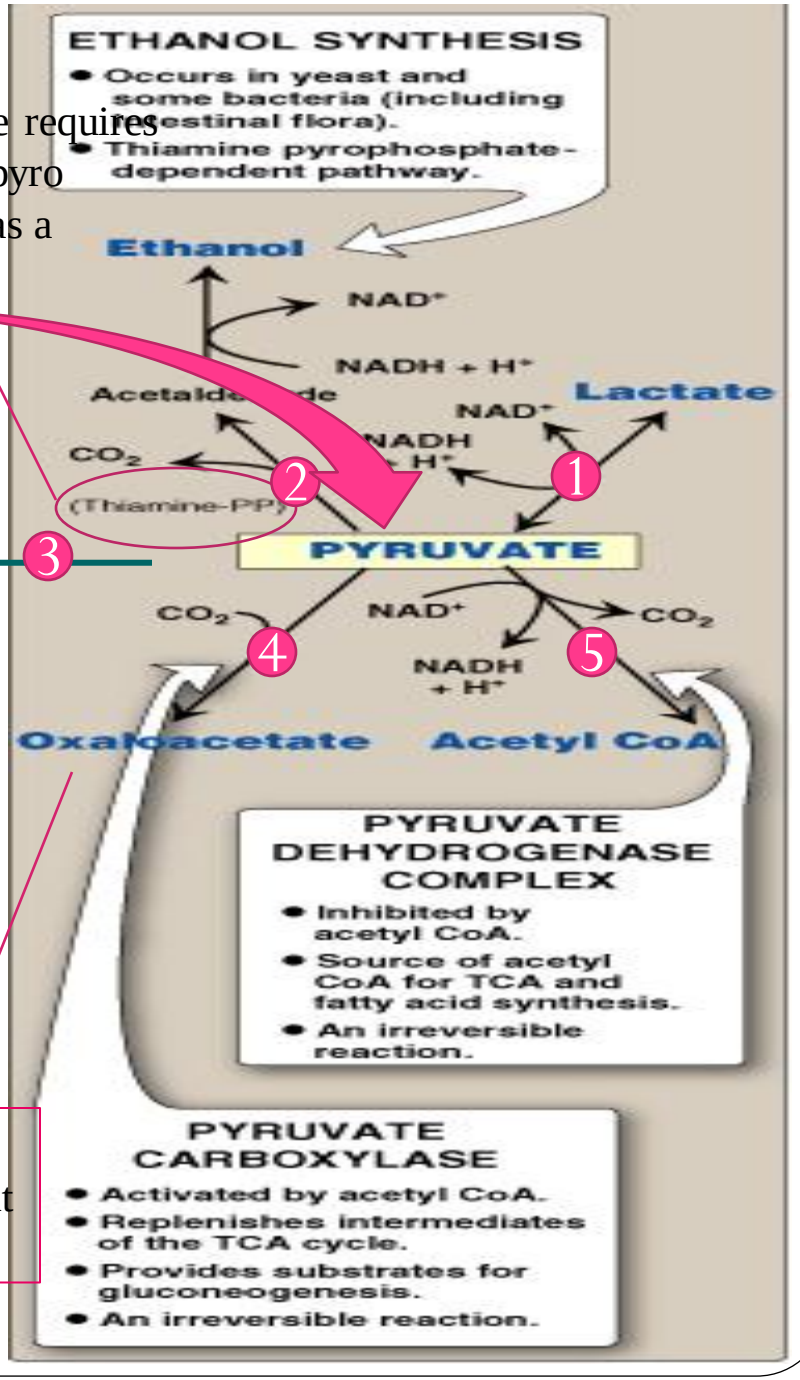
ALT (Alanine trimrase)

Alanine
(Glycogenic Amino acid)

PLP

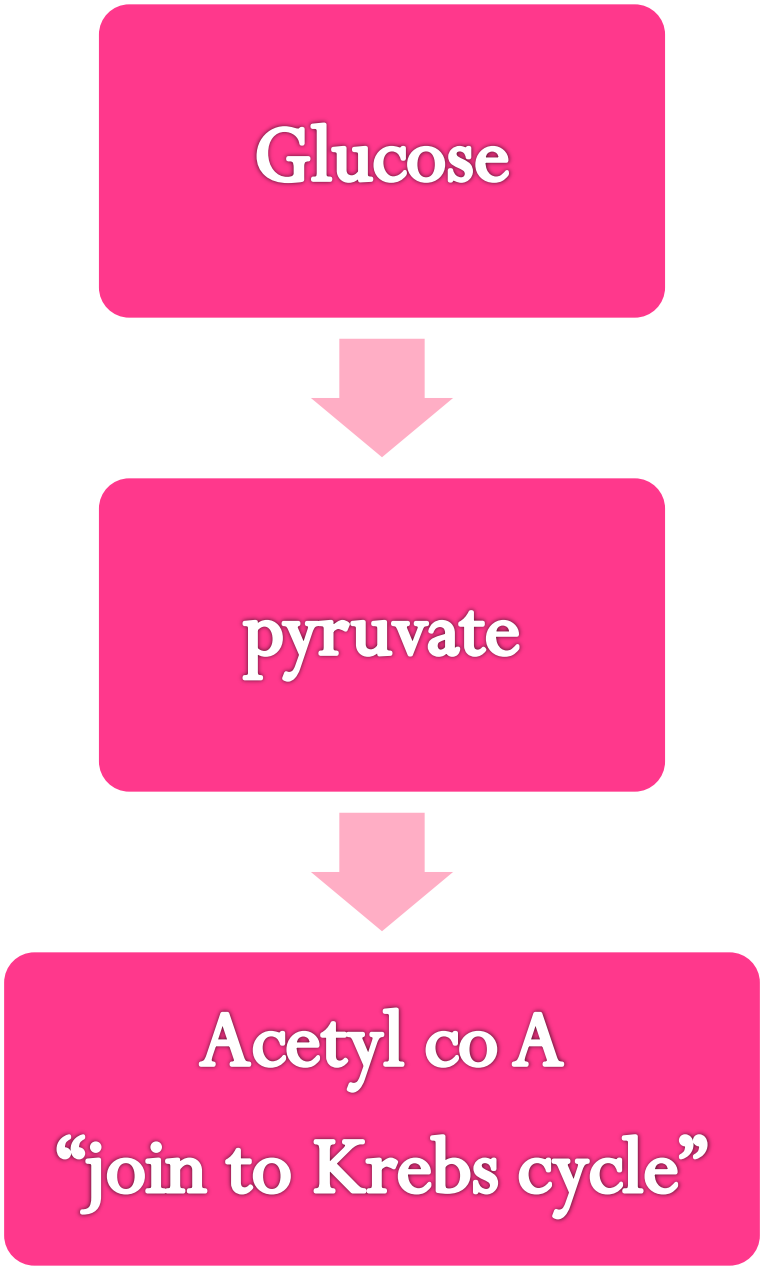
αKG
A keto glutarate (kreb cycle intermediate)

Glutamate
Glutamate was amino acid but it loosed its amino group

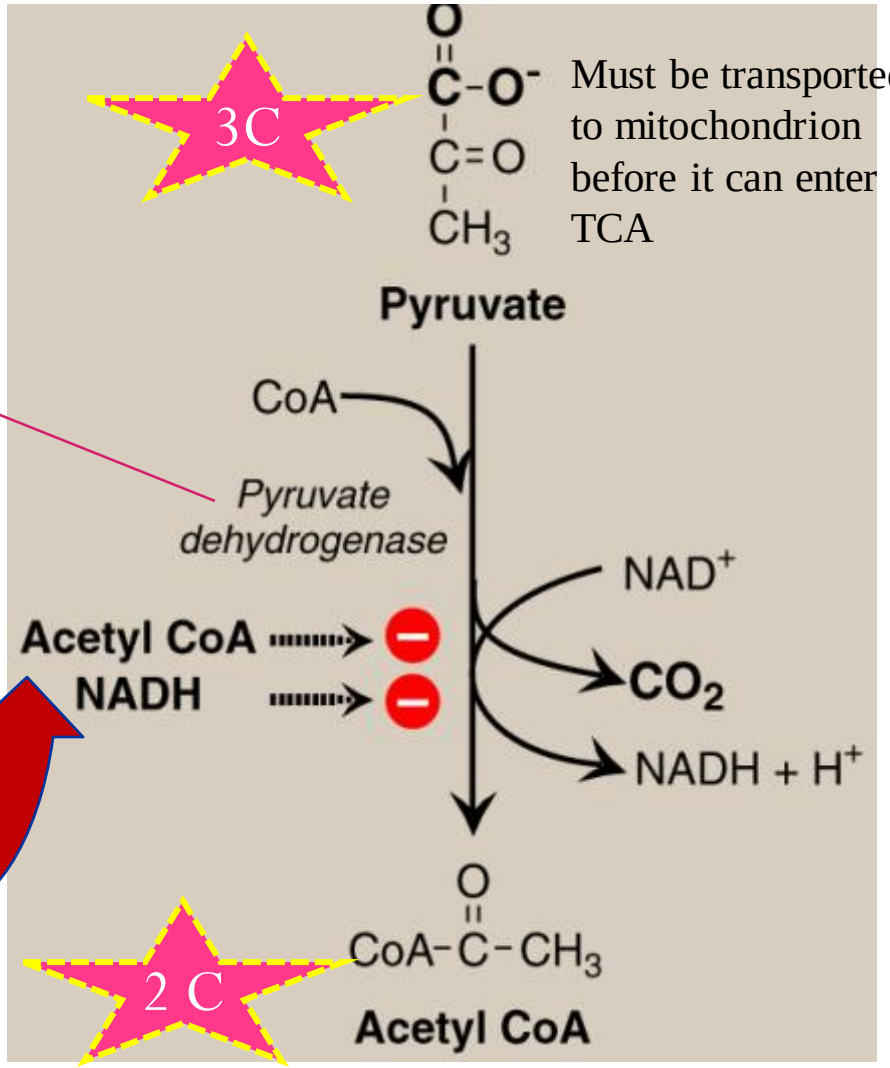


Biotin dependent reaction

Pyruvate goes in one of five reactions (no.5 before entering Krebs cycle)
All reactions are one way except forming lactate (no.1)


Glucose
pyruvate
Acetyl co A
“join to Krebs cycle”

Oxidative Decarboxylation of Pyruvate



Not part of TCA cycle

Allosteric Regulation (means regulate by binding in another site)

irreversible reaction

- Reaction occurs in the matrix (reaction no.5)

1 Glucose gives 2 Pyruvate

PDH Complex: Covalent Regulation

induction

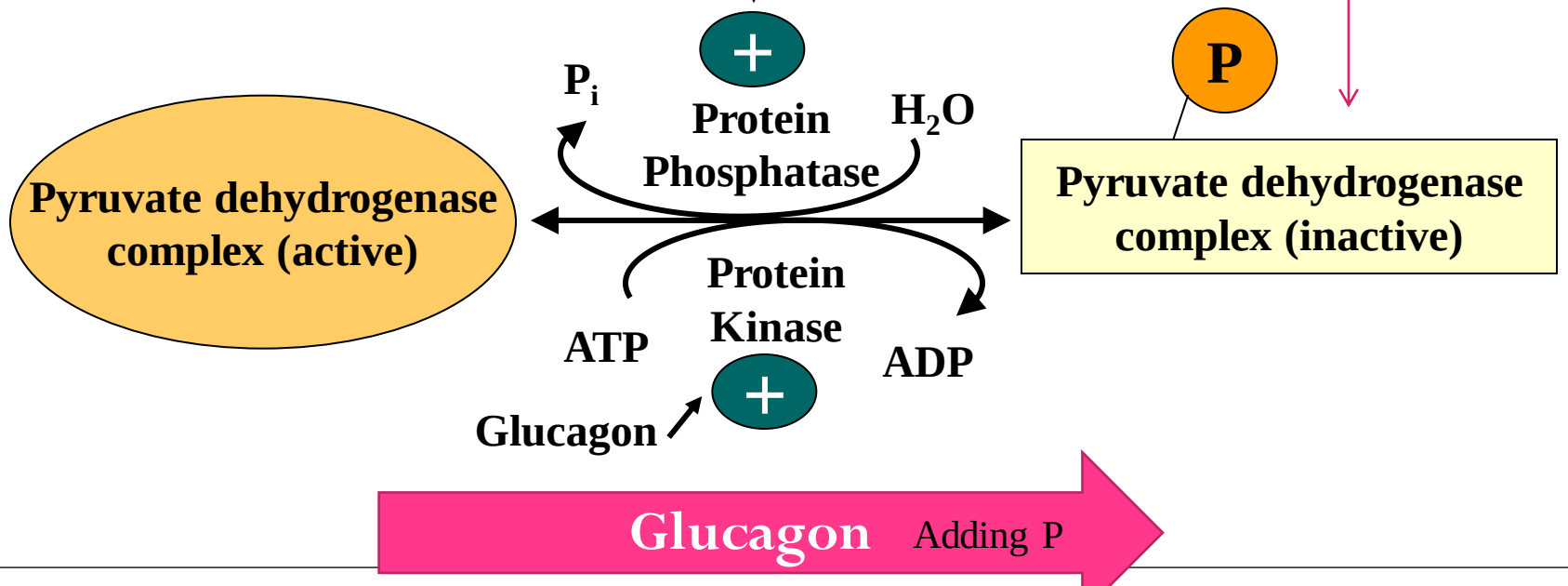
Insulin → (+) **PDH**

Glucagon → (-) **PDH**

Repression

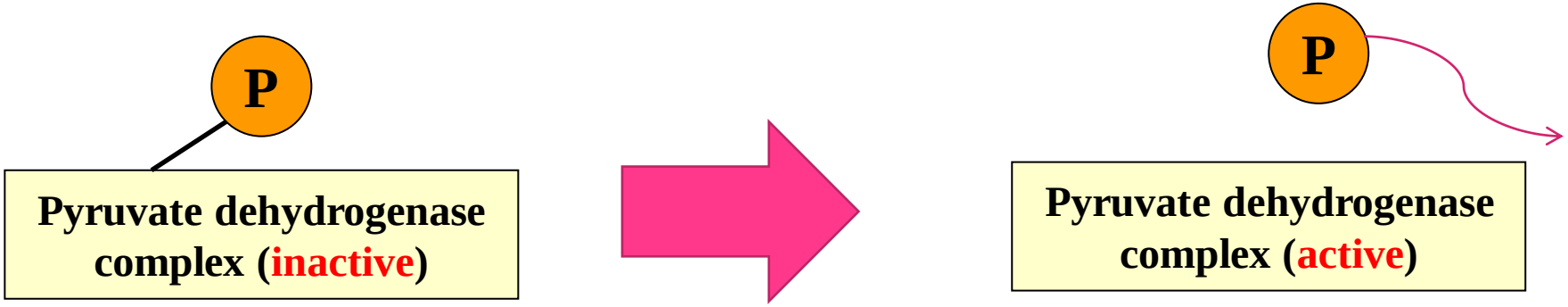
phosphate group binds, so it's turned into inactive form

Insulin Removing P

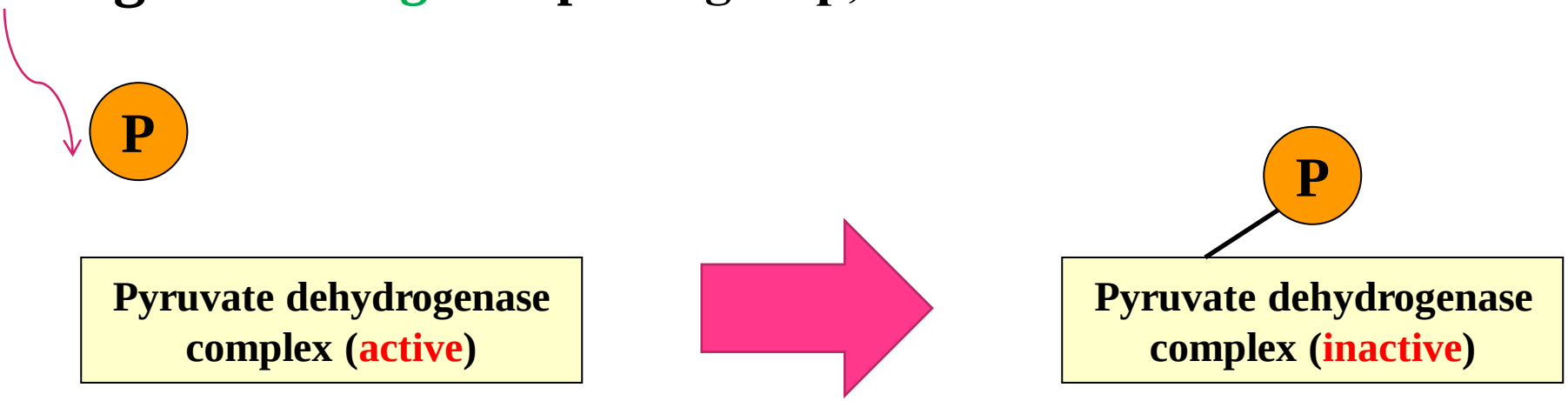


Glucagon Adding P

Insulin: Removing Phosphate group, so it's turned into active form



Glucagon: Adding Phosphate group, so it's turned into inactive form



Tricarboxylic Acid Cycle: Krebs Cycle

- Final common pathway for oxidation
- Exclusively in mitochondria
- Major source for ATP
- Mainly catabolic with some anabolic features
- Synthetic reactions (anabolic features):
  - Glucose from amino acids
  - Nonessential amino acids
  - Fatty acids
  - Heme

It's Aerobic because O2 is required as the final electron receptor

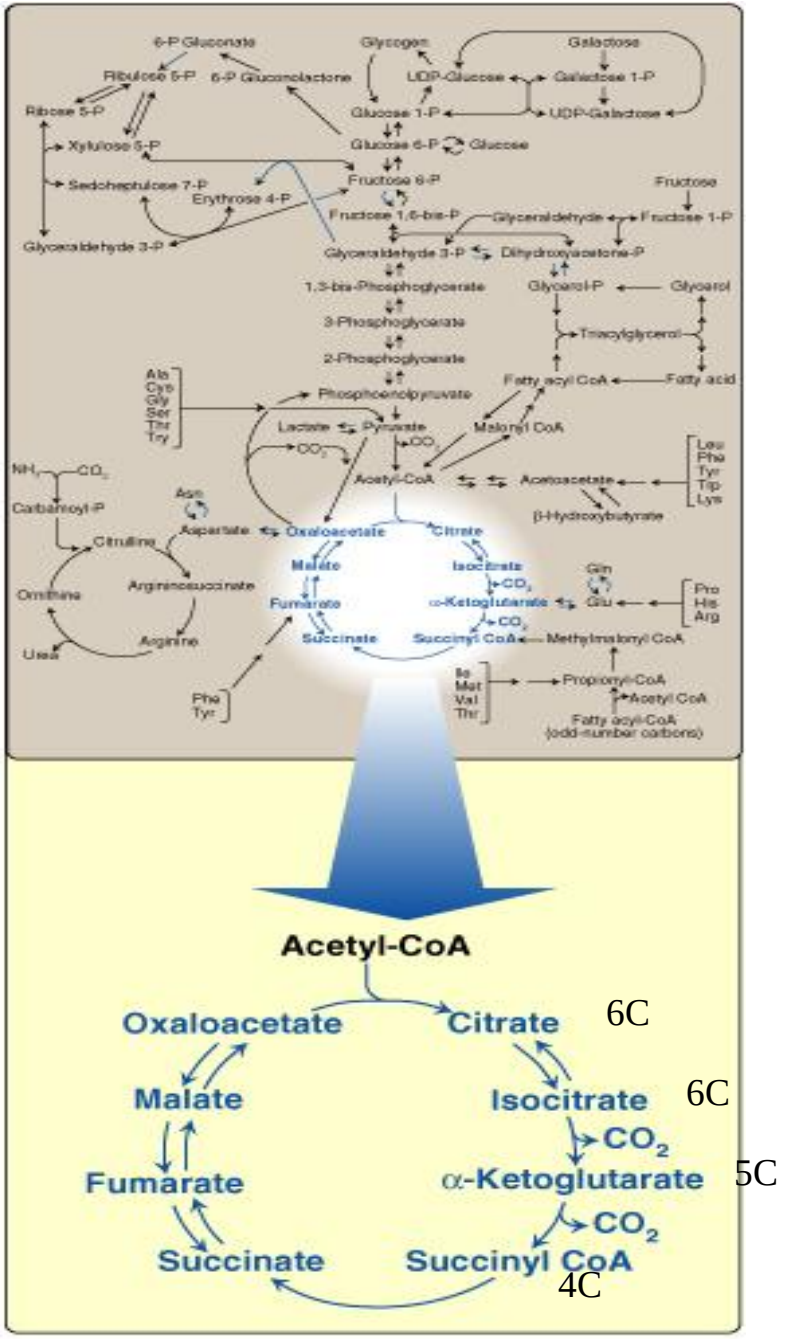
Krebs Cycle

considers metabolic pathway for (carbohydrates,lipid, protein)

intermediate: products become substrate

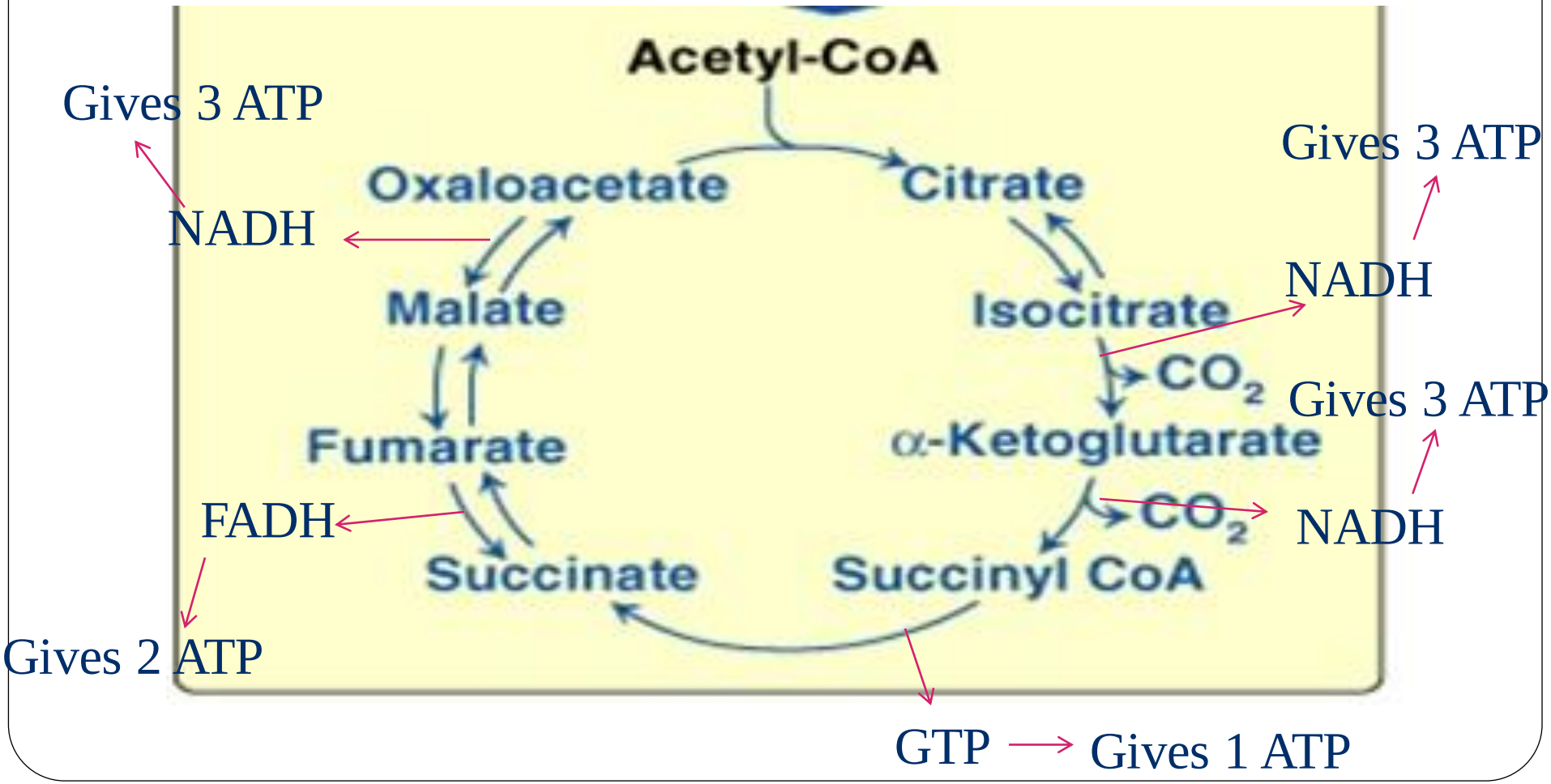
Replenish:starts and end with the same product

- **Mainly** catabolic, but could be anabolic in some situations

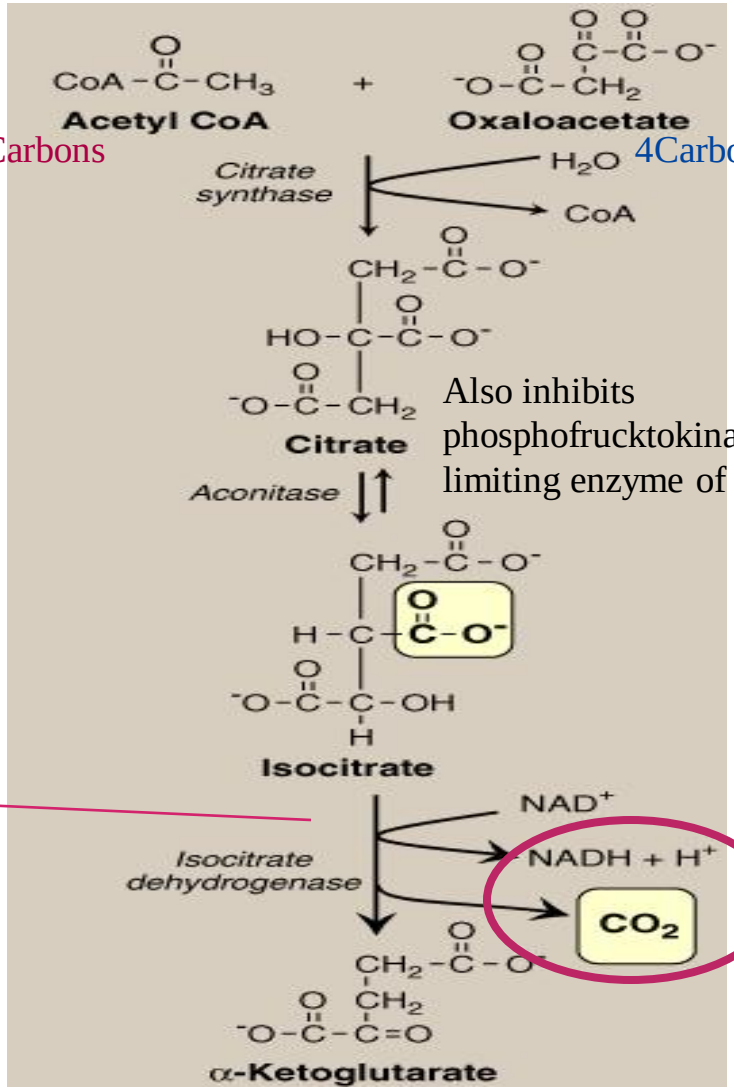


1 Acetyl co A gives 12 ATP

Acetyl co A synthesis P fatty acid



Krebs Cycle Reactions (1)



2Carbons

4Carbons

Also inhibits phosphofrucktokinase the rate limiting enzyme of glycolysis.

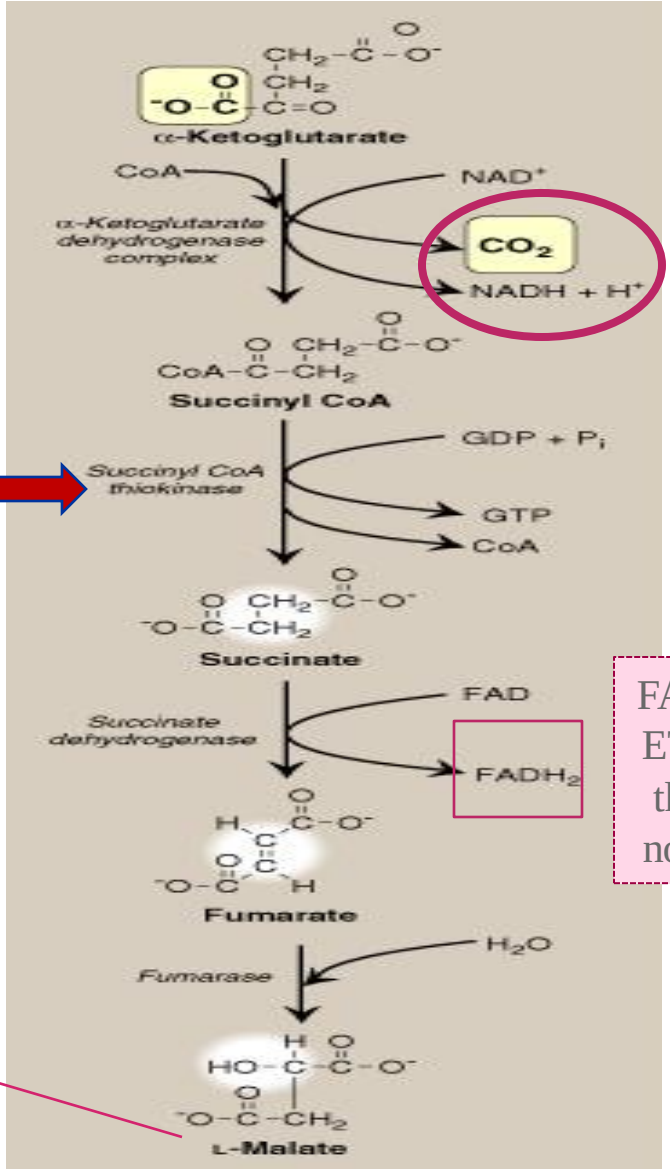
Rate limiting step

Most important results

Krebs Cycle Reactions (2)

Succinate Thiokinase

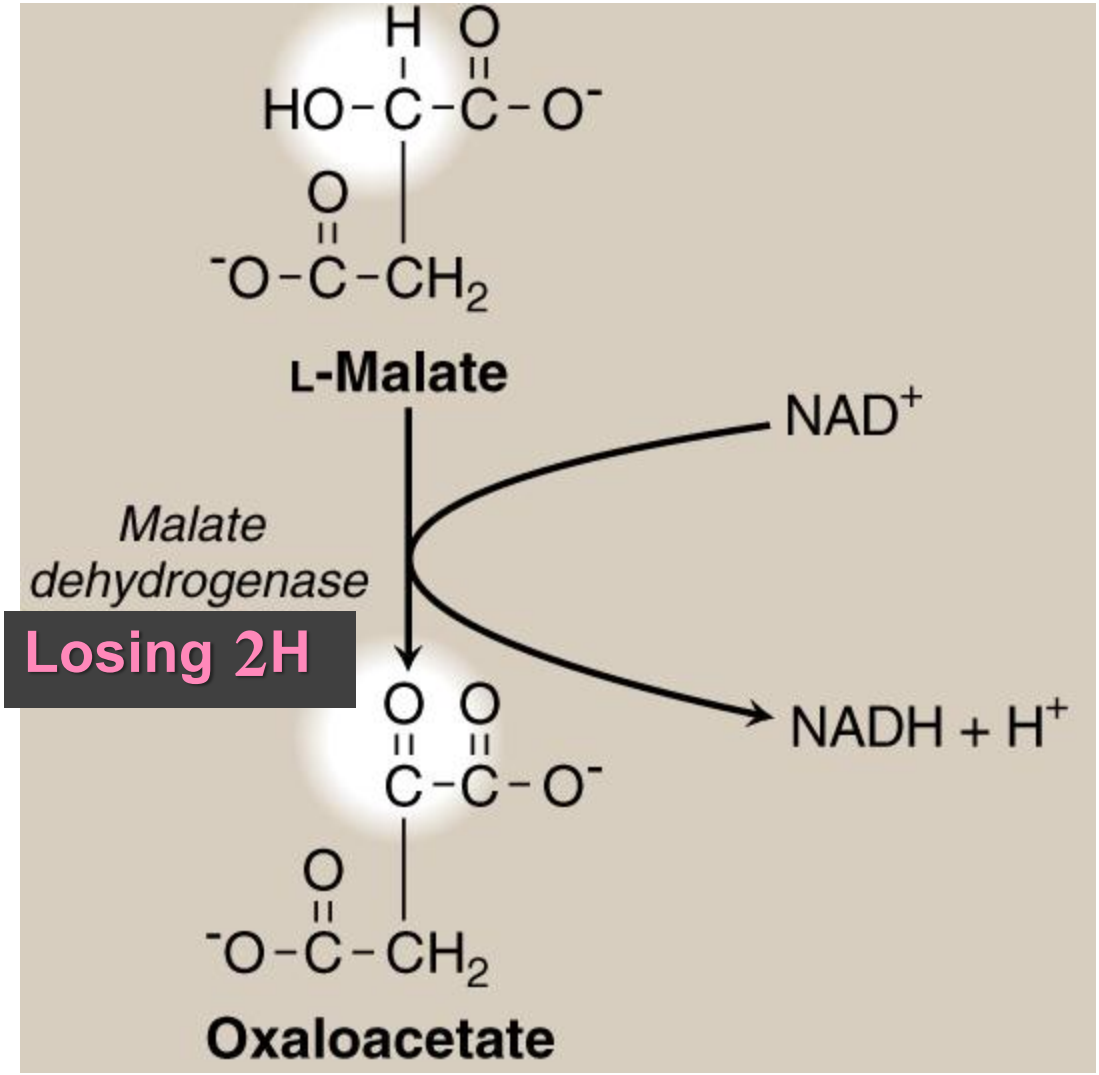
Substrate-Level Phosphorylation (energy is taken from CoA bond)



FADH2 enters the ETC in a position that takes 2 ATP not 3 like NADH

L not D

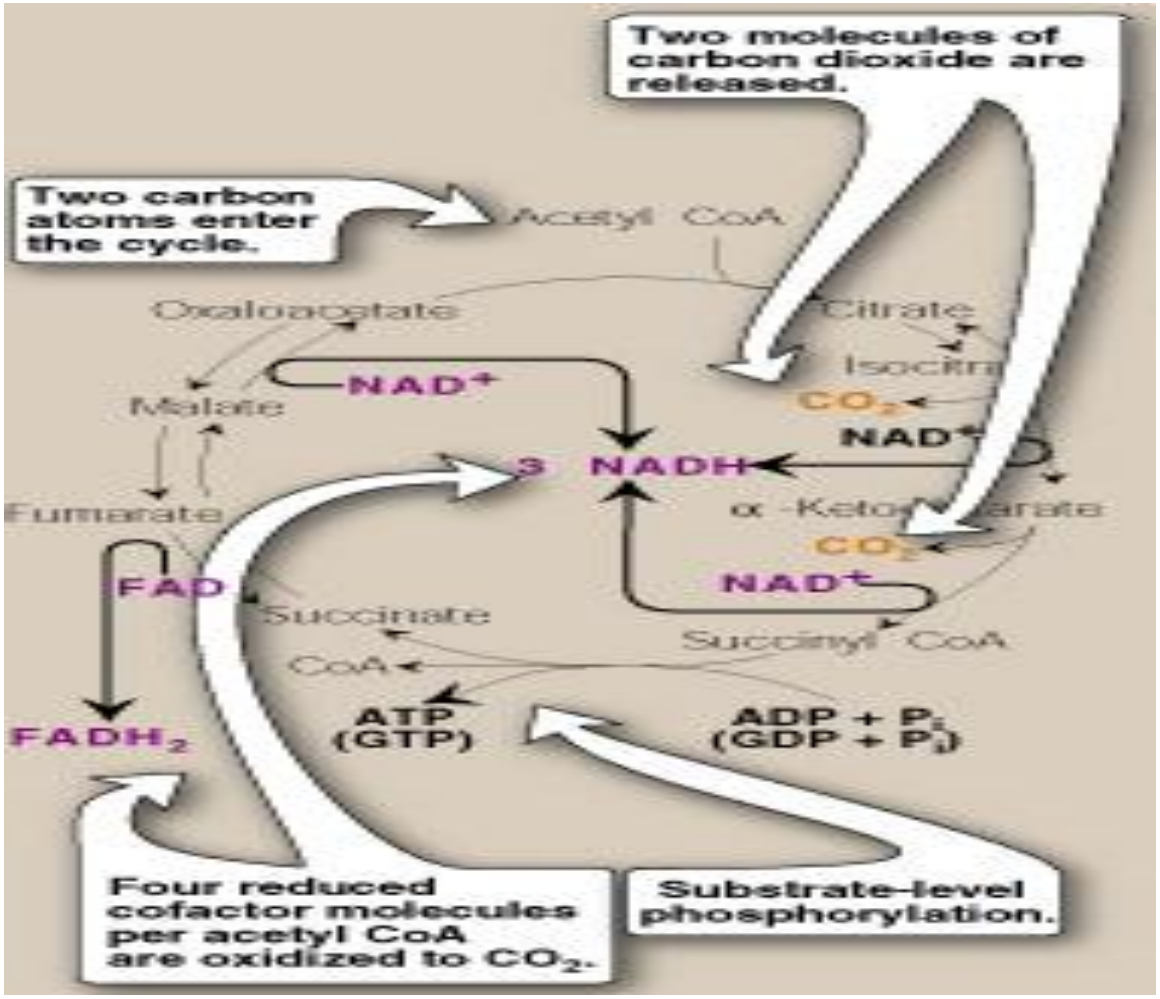
Krebs Cycle Reactions (3)



Krebs Cycle: Energy Yield

For every single Pyruvate :

- 3 NADH
- 1 FADH
- 1 ATP
- 2 CO_2



Krebs Cycle: Energy Yield

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

Net ATP Production by Complete Glucose Oxidation

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

Take Home Message

- **Pyruvate is oxidatively decarboxylated by PDH to acetyl CoA inside the mitochondria**
- **Krebs cycle:**
  - **Final common pathway for the oxidation of carbohydrates, fatty acids and amino acids**
  - **occurs in the mitochondria**
  - **Aerobic**
  - **Mainly catabolic, with some anabolic reactions**
- **The complete oxidation of one glucose molecule results in a net production of 38 ATP molecules**

Thank you