Kreb's Cycle
(Tri carboxylic acid (TCA)cycle, Citric acid cycle)

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biochemistry

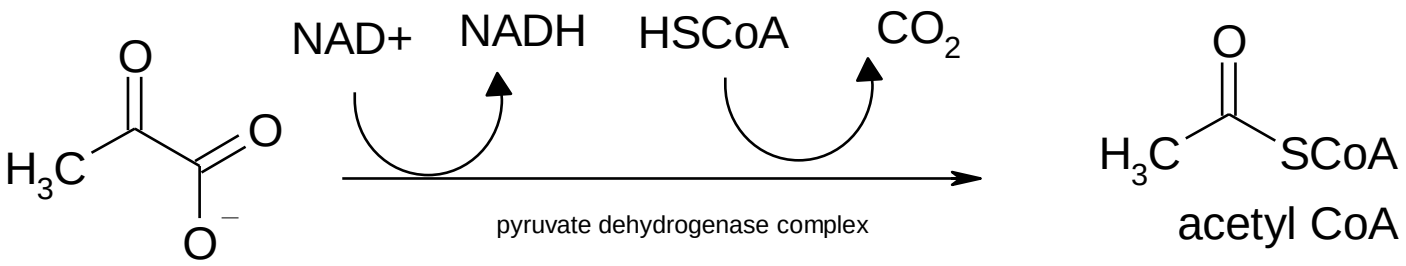
Overall goal

- Makes ATP
- Makes NADH
- Makes $FADH_2$
- Requires some carbohydrate to run .

Geography

- Glycolysis in the cytosol .
- Krebs in mitochondrial matrix .
- Mitochondrion
  - Outer membrane very permeable .
    - Space between membranes called inter membrane space .
  - Inner membrane
    - Permeable to pyruvate .
    - Impermeable to fatty acids, NAD, etc
  - Matrix is inside inner membrane .

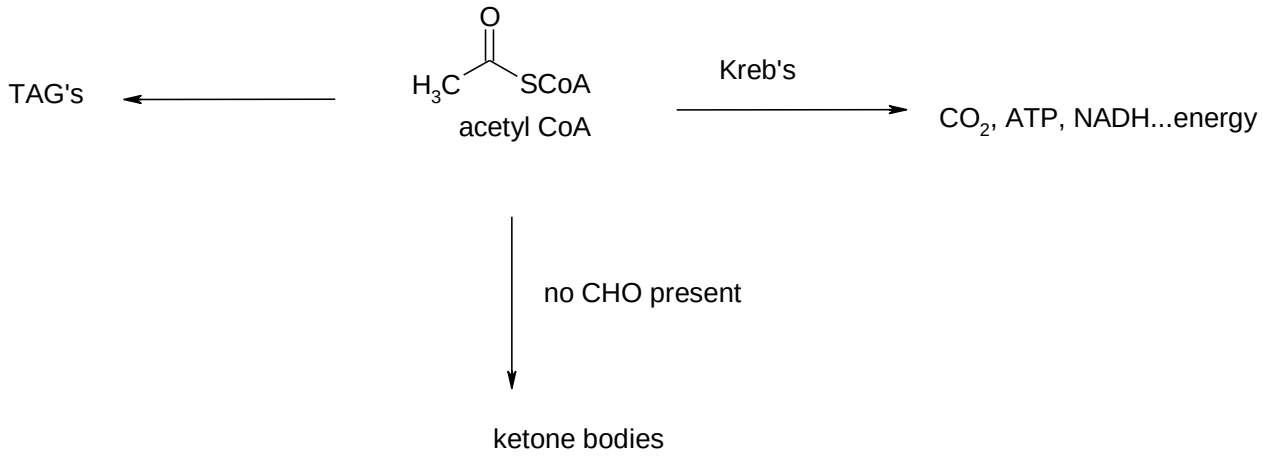
Conversion of pyruvate to acetyl CoA



pyruvate

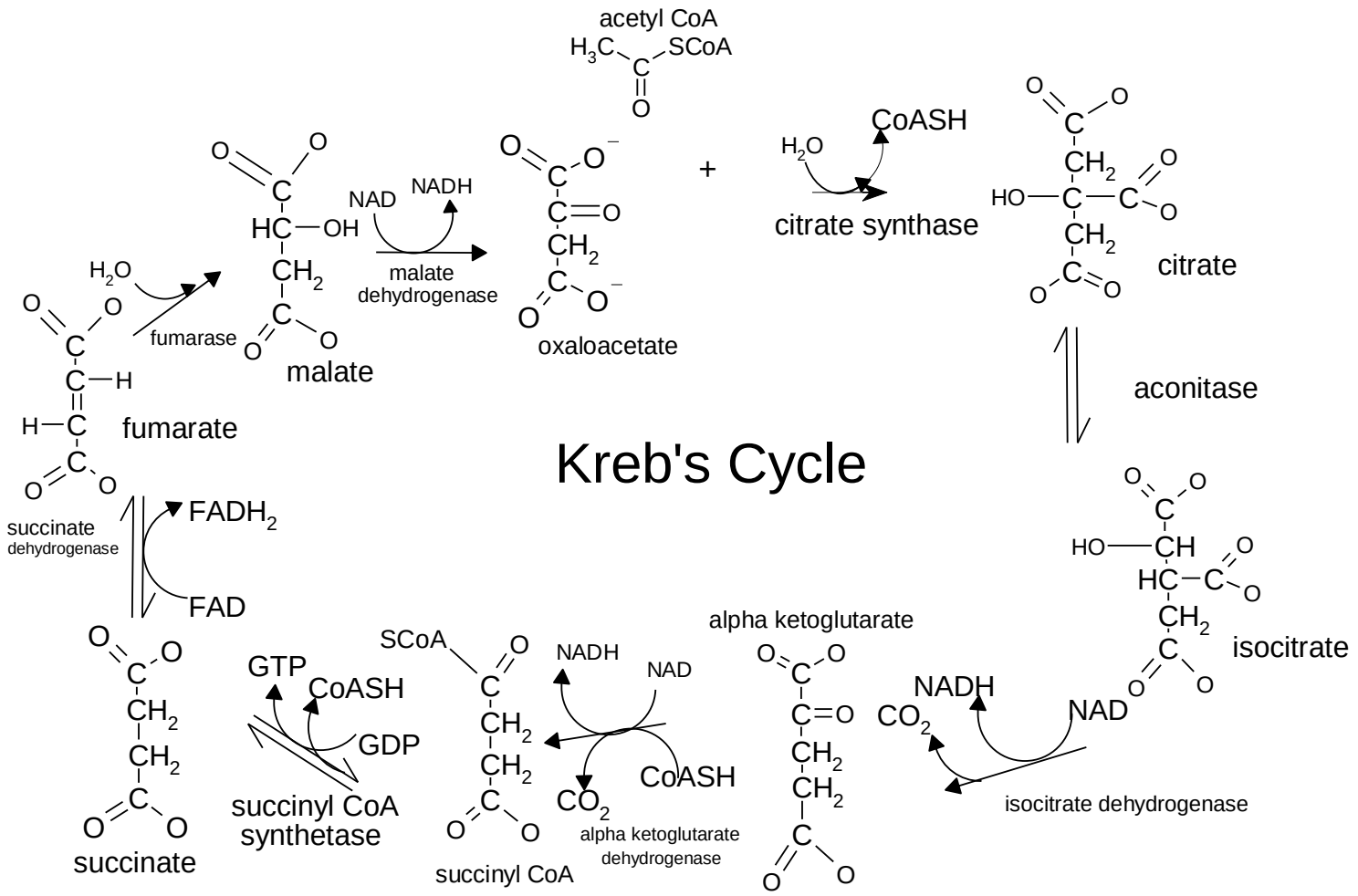
- PDH inhibited by dietary deficiency of thiamine (vitamin B1) , arsenite and mercuric ions .
- The reaction is irreversible .

Fates of Acetyl CoA



- In the presence of CHO an using energy
  - Metabolized to CO_2, NADH, $FADH_2$,GTP and, ultimately, ATP
- If energy not being used (Lots of ATP present)
  - Made into fat
- If energy being used, but no CHO present
  - Starvation
  - Forms ketone bodies
  - Danger!

Kreb's Cycle


acetyl CoA
SCoA
citrate synthase
CoASH
citrate
aconitase
isocitrate
isocitrate dehydrogenase
NADH
NAD
alpha ketoglutarate
alpha ketoglutarate dehydrogenase
succinyl CoA
succinyl CoA synthetase
GTP
GDP
succinate
succinate dehydrogenase
FADH2
FAD
fumarate
fumarase
malate
malate dehydrogenase
oxaloacetate
Kreb's Cycle

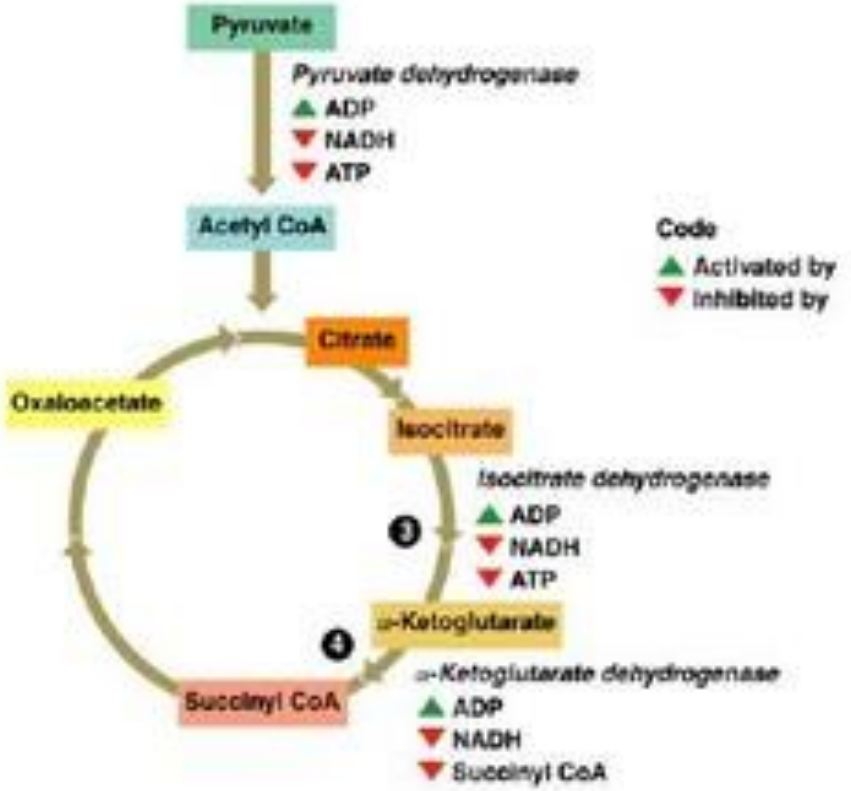
* Intermediates of the TCA cycle are utilized in the fasting state in the liver for the production of glucose (this by the pathway of gluconeogenesis which involves intermediates of the TCA cycle , for example oxaloacetate) and in the fed state for the synthesis of fatty acids (from glucose , pyruvate is produced and converted to OAA by pyruvate carboxylase and to acetyl CoA by pyruvate dehydrogenase).

OAA and acetyl CoA condense to form citrate which is used for fatty acid synthesis .

* Intermediates of the TCA cycle are also used to synthesis amino acids by transamination or by convert one amino acid to another (for example , α - keto glutarate produce glutamate , glutamine , proline and arginine) .

Regulation of Citric Acid Cycle

- Low levels of ATP stimulate the formation of acetyl CoA for the citric acid cycle.
- High ATP and NADH levels decrease the formation of acetyl CoA and slow down the citric acid cycle.



ATP from Citric Acid Cycle

Reaction Pathway	ATP for One Glucose
ATP from Citric Acid Cycle	
Oxidation of 2 isocitrate (2NADH)	6 ATP
Oxidation of 2 α-ketoglutarate (2NADH)	6 ATP
2 Direct substrate phosphorylations (2GTP)	2 ATP
Oxidation of 2 succinate ($2FADH_2$)	4 ATP
Oxidation of 2 malate (2NADH)	6 ATP

Summary: $2\text{Acetyl CoA} \longrightarrow 4CO_2 + 2H_2O + 24\ \text{ATP}$

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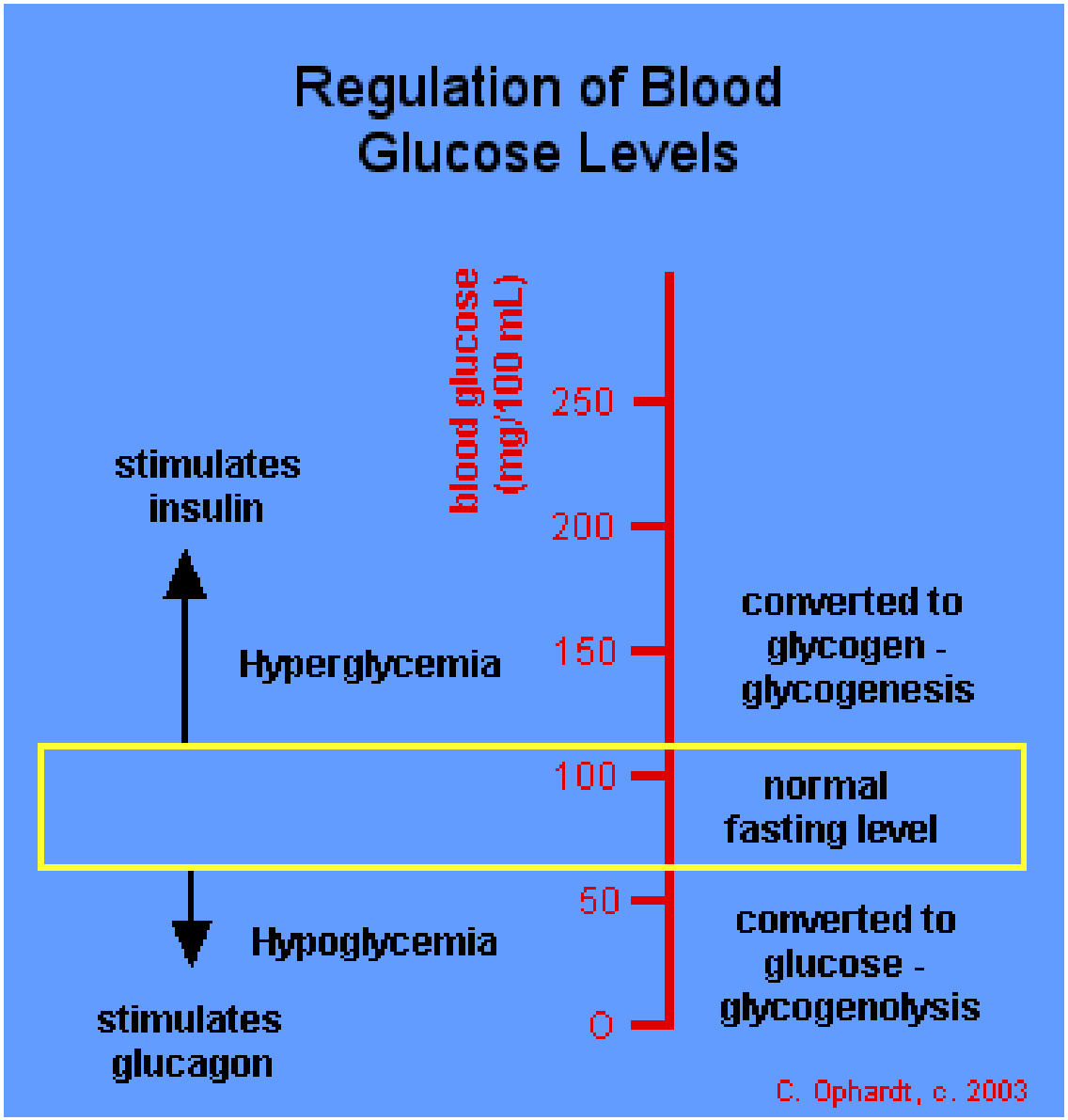
Hormone Regulation of Carbo-Metabolism



(Role of vitamins in the citric acid cycle)

Four water soluble vitamins are essential for the functioning of the citric acid cycle as a coenzyme :

1 . Riboflavin in the form of (FAD) flavin adenine dinucleotide .

2 . Niacin in the form of (NAD) nicotinamide adenine dinucleotide.

3 . Thiamin (B1) in the form of thiamine pyrophosphate .

4 . Pantothenic acid as part of coenzyme- A .