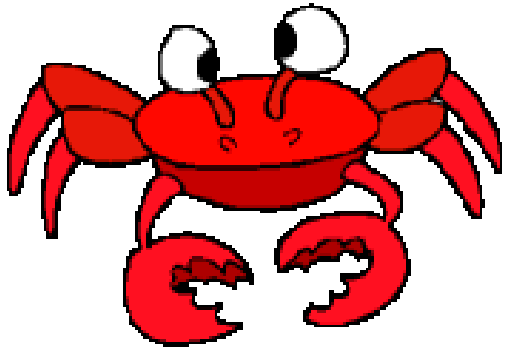
TCA CYCLE



POINTS TO REMEBER

- **Definition**
- **History**
- **Location**
- **Significance of TCA cycle**
- **Pathway**
- **Energetics of the TCA cycle**
- **Inhibitors of TCA cycle**
- **Regulation of the TCA cycle**
- **Anaplerosis / Anaplerotic reactions**

Acetyl CoA enters the Tricarboxylic Acid Cycle.

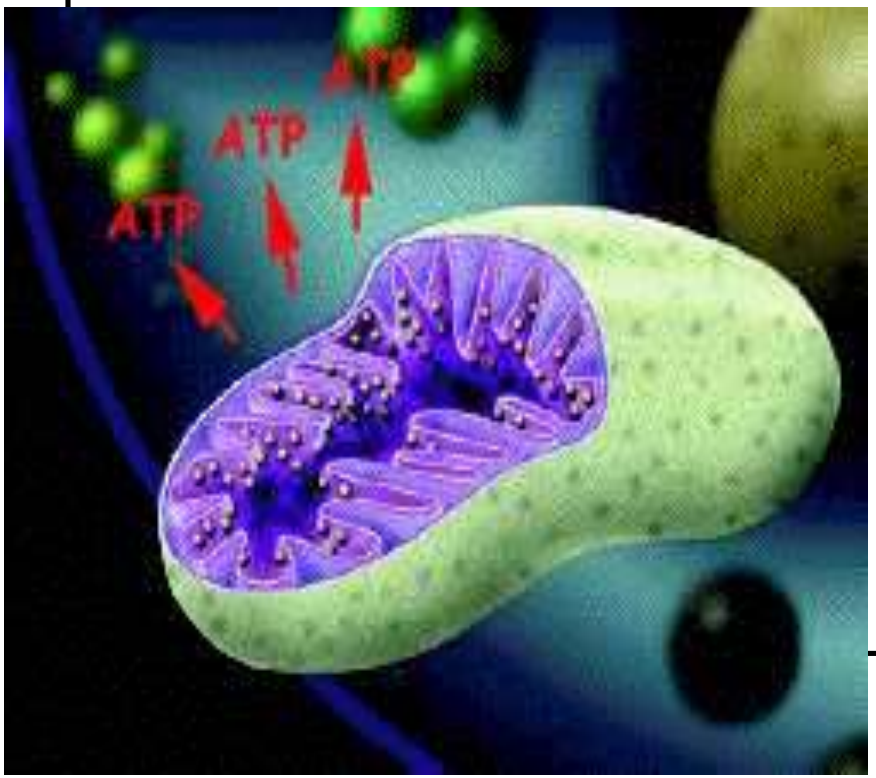
- TCA Cycle
- Kreb's Cycle
- Citric Acid Cycle
- Final Oxidation
- Amphibolic Pathway
- Common Metabolic Pathway for Carbohydrates, proteins, lipids

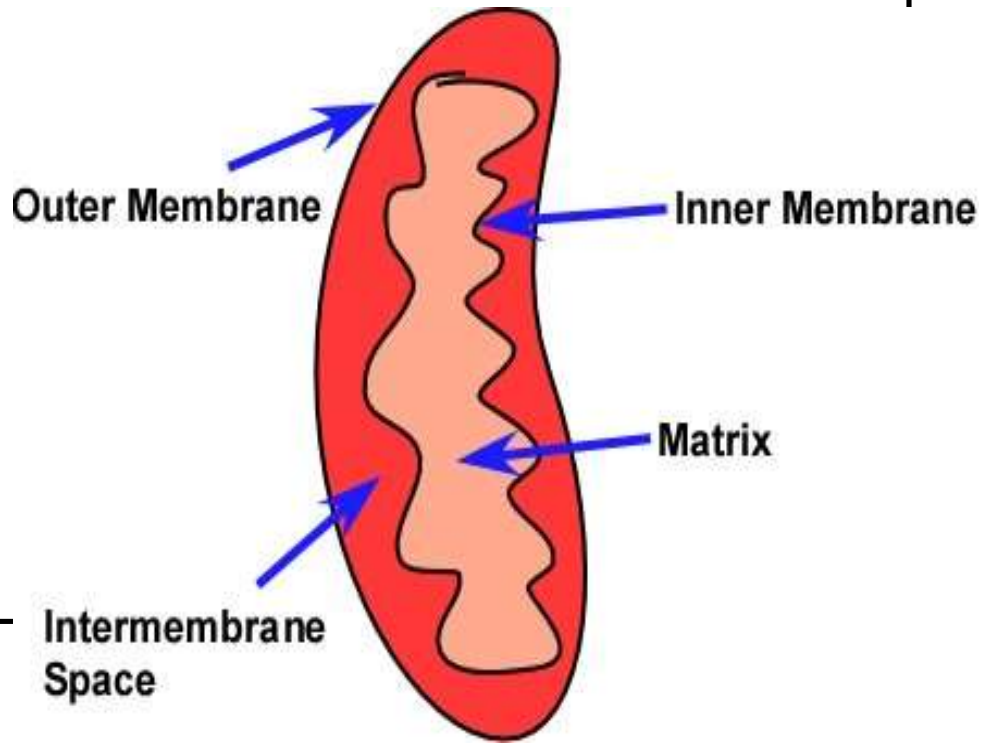
Def: **Complete oxidation of Acetyl-co-A to CO_2 .**

- **It is a final common oxidative pathway of glucose.**

History **:- Proposed by Hans Adolf Krebs in 1937.(Nobel Prize- 1953).**

- **Location :- Enzymes of the TCA cycle are located in the mitochondria in close proximity to the ETC.**





Significance of TCA cycle :-

1. **Contributes 60-70% of total ATP synthesized in the body. Total 12 ATP**
2. **Utilizes 2/3rd of the total oxygen consumed by the body.**
3. **Final common oxidative pathway for carbohydrates, fats & amino acids.**
4. **Intermediates act as precursors for synthesis of amino acids, glucose, heme & nucleotides. (Anaplerotic reactions)**
5. **Reduced coenzymes act as substrates for the respiratory chain.**
6. **Acts as link between catabolic & anabolic pathways (amphibolic).**
7. **Has controlling effect on key enzymes of other pathways.**

- Significance should be in detail from the DM Vasudevan Book or other reference book.

- First Reaction also in detail from the book i.e By PDH enzyme which is multi enzyme complex.

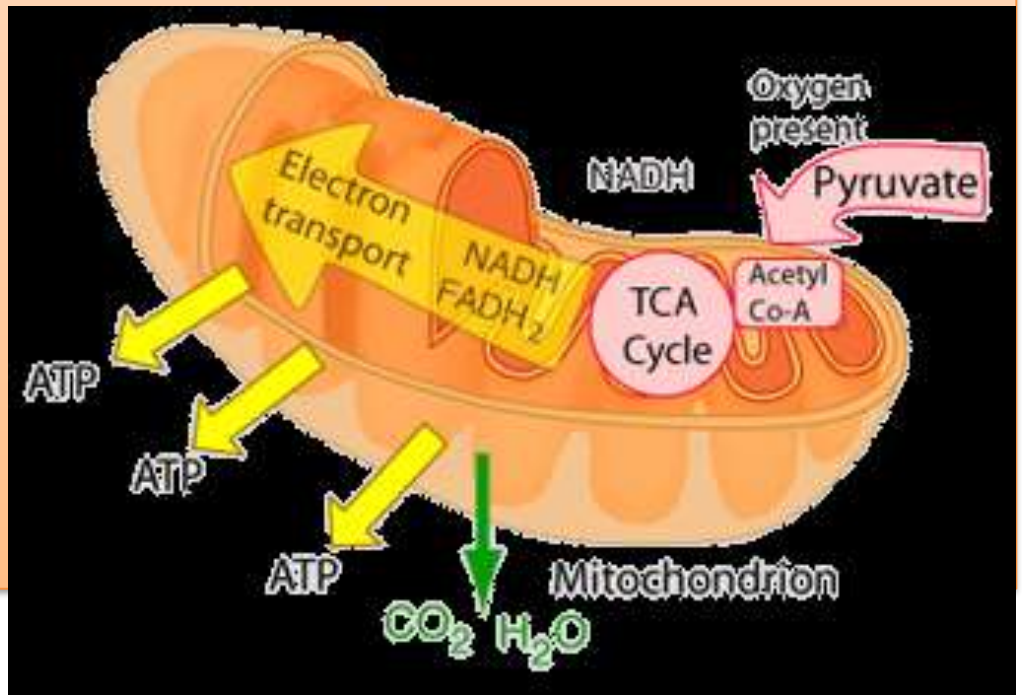
- You can also mentioned about which reactions are substrate level phosphorylation in the pathway.

Overview of the TCA cycle :-

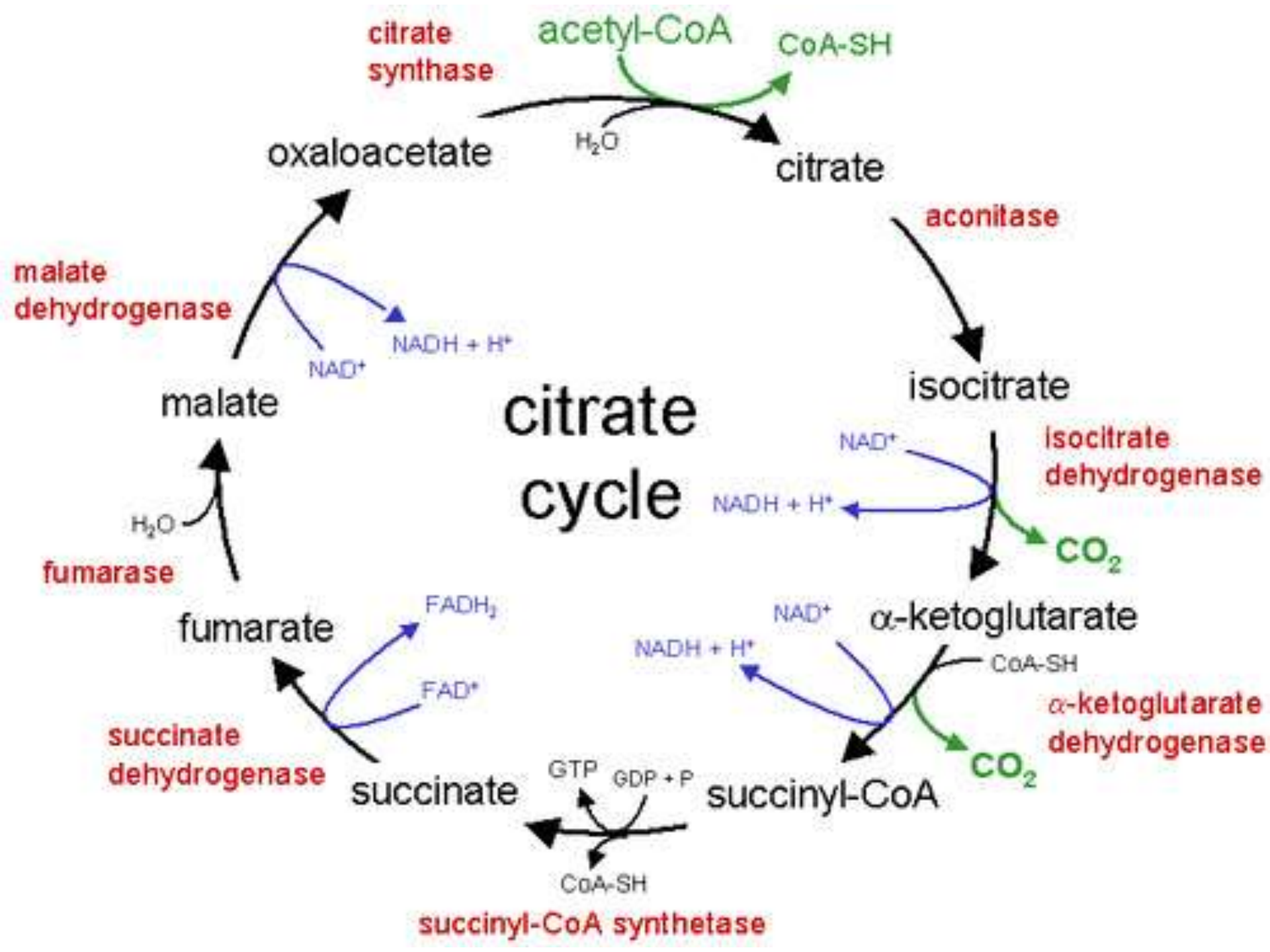
- 2-C Acetyl CoA combines with 4-C Oxaloacetate to produce 6-C tricarboxylic acid, Citrate.

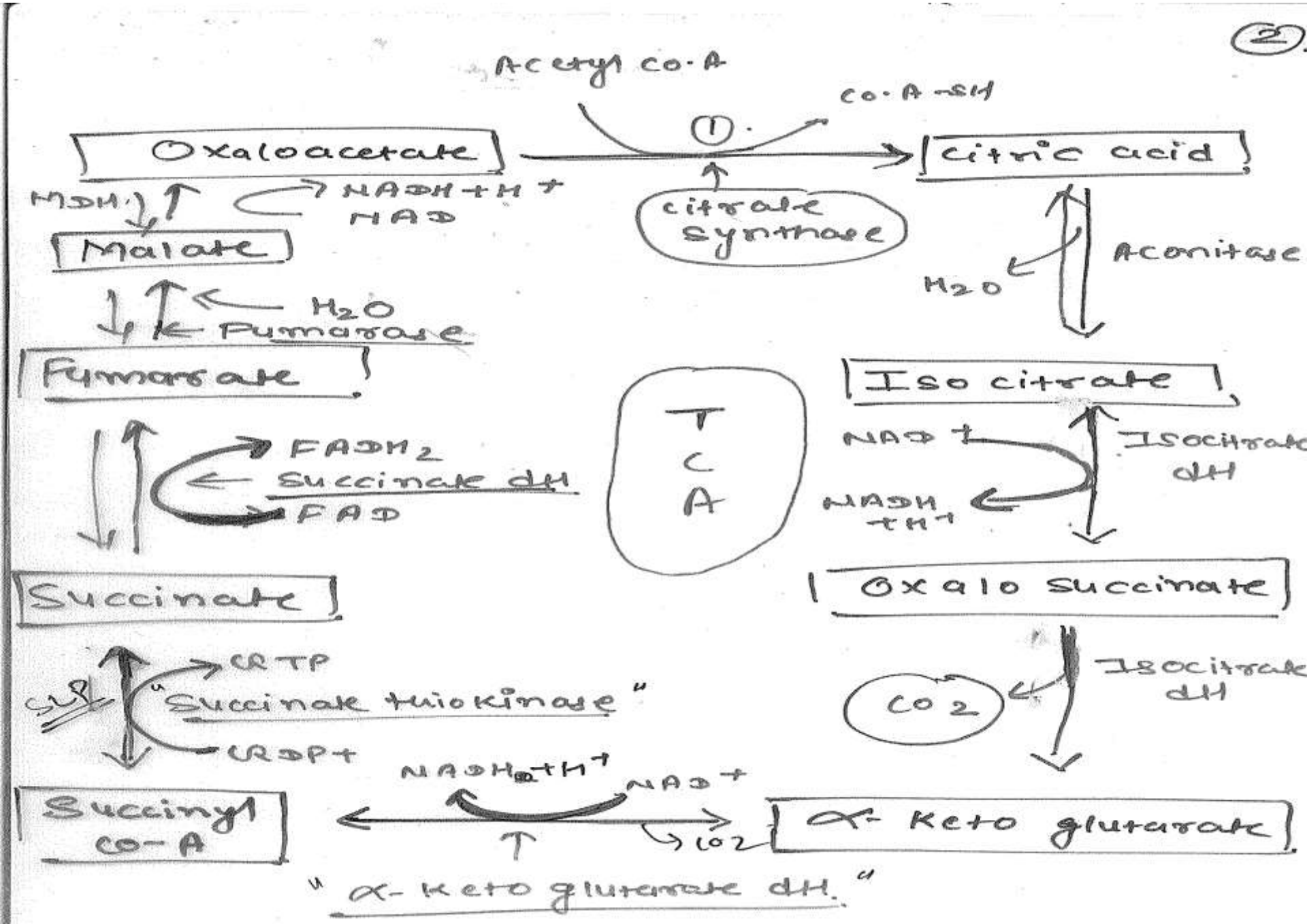
- 2 Carbons released as CO_2 , Oxaloacetate regenerated and recycled.(oxaloacetate acts as a catalyst)

- **Pyruvate with help of enzyme pyruvate dehydrogenase forms acetyl.co A.**
- **Acetyl co a enters in to the TCA CYCLE**



- Diagram or Pathway should be neat and clean.
- It should be perfectly **round or in square** along with Energetic and Enzymes which is to be highlighted.
- All the Point should be cover when you write pathways.


citrate synthase
acetyl-CoA
CoA-SH
H_2O
oxaloacetate
citrate
aconitase
malate dehydrogenase
NADH + H+
NAD+
malate
citrate cycle
isocitrate
NAD+
isocitrate dehydrogenase
NADH + H+
CO_2
H_2O
fumarase
fumarate
$FADH_2$
FAD+
NAD+
α-ketoglutarate
NADH + H+
CoA-SH
α-ketoglutarate dehydrogenase
CO_2
succinate dehydrogenase
succinate
GTP
GDP + P
succinyl-CoA
CoA-SH
succinyl-CoA synthetase


Acetyl co-A
co-A-SH
Oxaloacetate
①
citric acid
MDH
NADH+H+
NAD
citrate synthase
Malate
Aconitase
H2O
H2O
Fumarase
Fumarate
Iso citrate
FADH2
Succinate dH
FAD
NAD+
NADH+H+
Isocitrate dH
T
C
A
Succinate
Oxalo Succinate
GTP
"Succinate thiokinase"
GDP+
Isocitrate dH
CO2
NADH+H+
NAD+
Succinyl co-A
α-Keto glutarate
CO2
"α-Keto glutarate dH."

The reaction catalysed by PDH multienzyme complex is the connecting link between Glycolysis & TCA cycle.

Steps:-

1. **Formation of Citrate.**
2. **&3. Isomerisation of Citrate to Isocitrate.**
4. **& 5. Formation of α-ketoglutarate.**
6. **Conversion of α-kg to Succinyl CoA.**
7. **Formation of Succinate.**
8. **Conversion of Succinate to Fumarate.**
9. **Formation of Malate.**
10. **Conversion of Malate to Oxaloacetate.**

Energetics of the TCA cycle (Old Energetics)

1. **Iso citrate to alpha ketoglutarte -NADH= 3ATP**
2. **alpha ketoglutarte to Succinyl Co-A – NADH= 3 ATP**
3. **Succinyl Co-A to Succinate – GTP = 1 ATP**
4. **Succinate to Fumarate -- FADH = 2 ATP**
5. **Malate to Oxaloacetate – NADH = 3 ATP**

12 ATP

Inhibitors of TCA cycle:-

- **Fluoroacetate is a non-competitive inhibitor of enzyme Aconitase.**
- **Arsenite is a non-competitive inhibitor of α-ketoglutarate Dehydrogenase.**
- **Malonate is the competitive inhibitor of Succinate Dehydrogenase.**

Regulation of the TCA cycle :-

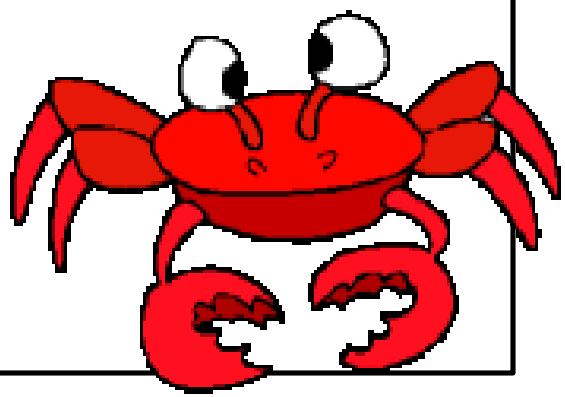
- **Regulatory enzymes –**

  1. Citrate Synthase - inhibited by ATP, NADH, acetyl CoA & succinyl CoA.

  2. Isocitrate dehydrogenase – activated by ADP & inhibited ATP & NADH.

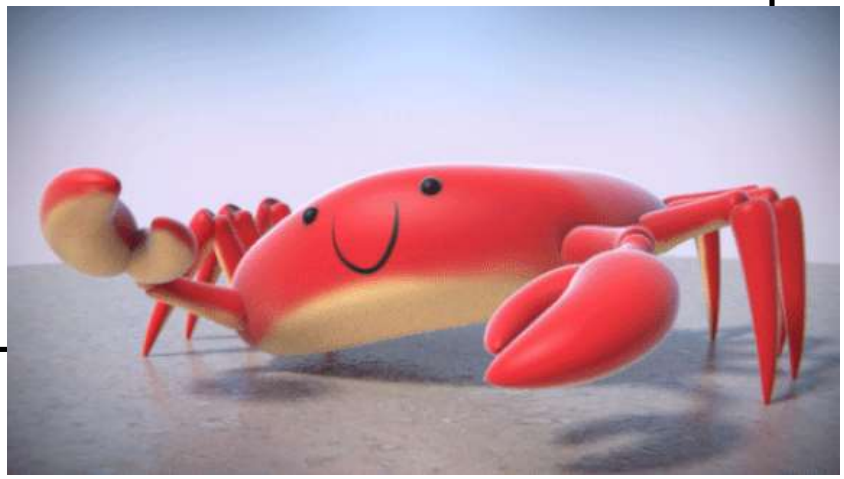
  3. α-Ketoglutarate dehydrogenase – inhibited by succinyl CoA .

- **Availability of ADP.**
- **It should be in detail from the book.**



Anaplerosis / Anaplerotic reactions :-

- **Intermediates act as precursors for synthesis of amino acids, glucose, heme & nucleotides. (Anaplerotic reactions)**



END OF THIS DID U???

MCQ

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1.All the enzyme of TCA cycle located in

a) Mitochondria

b) Endoplasmic reticuam

c) Lysosome

d) Golgi body

2. Number of ATP formed per cycle in TCA cycle

a) 50

b) 12

c) 6

d) 2

3. Inhibitors in TCA cycle

a) Malonate

b) Fluoroacetate

c) Arsenite

d) All of above

4. Malonate is the competitive inhibitor of

a) Lactate

b) Succinate Dehydrogenase

c) Hexokinase

d) Pyruvate kinase

5. The number of NADH formed in TCA Cycle

a) 1

b) 2

c) 4

d) 3


Thank you


thank you
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