Krebs cycle

It is called Krebs according to Hans Adolf Krebs (person who discover it) ,**citric acid cycle** because the citrate is the first product in it,and **Tricarboxylic acid cycle** as it is first product (Acitate) has 3 carboxylic groups .

* **Acetyl CoA** is the substrate of it .

Why we need it??

We need it to produce energy, extract electrons by oxidant molecules …and it doesn't form electron carrier . (remember: oxidation is the losing of electrons which are carried by electron carrier molecules)

We have electron carriers without Krebs cycle but we need cycle to extract electrons which will be carried by electron carriers.

How the process of oxidation in our body , from time you ingest to get ATP , occur ??

1-INGESTION (of any type of food which all form acetyl CoA for "KREBS CYCLE")

2-DIGESTION

3-ABSORBTION

4-GO TO CELL (energy metabolism occur)

* Where it is occur?? In mitochondria (in matrix mainly)

*Products : electrons , CO2 (from carboxylic group)

CO2 which we exulted is the same which we produce by krebs cycle

⇨ **The cycle does not need O2**

Eectron carrier review

1)**NAD** : carry 2e from hydride (same source)

2)**FAD** : carry 2e from 2 different sources so it must remain tightly bound to enzymes or proteins in order not to form free radicals .

*Oxygen has most positive reduction potential

***NAD** has fixed negative reduction potential -3.20 mvolt **but FAD** has varying reduction potentials (not constant) we should know that reduction potential is product of both **structure** of coenzymes and **environment** surround them , so **FAD** has vary ΔE **according to enzyme or protein which bound to it** .

Proteins have different a.a some +vely charged , some –vely charged, some polar , some non polar all of these are electrostatic base of reduction potential of coenzyme , so electronegativity of FAD change according to enzyme or protein bound it

NADH can play regulatory role on pathway but FADH2 can not ….. why ??

Firstly, for any molecule to regulate process must be able to reach it (free)

And we know that NADH can move in solution can travel from one site to another **BUT** FADH2 is bound to enzyme and cannot travel , cannot affect on other protein in pathway .

FADH2 can only regulate the enzyme or protein which bound to it. Can regulate same protein , can't regulate pathway process.

Citric acid cycle

All different substance (carbohydrate, lipid, ketone bodies, proteins and some amino acids) finally will be converted to acetyl CoA which is the substance of Krebs cycle .

Remember that there is 3 metabolic pathways :

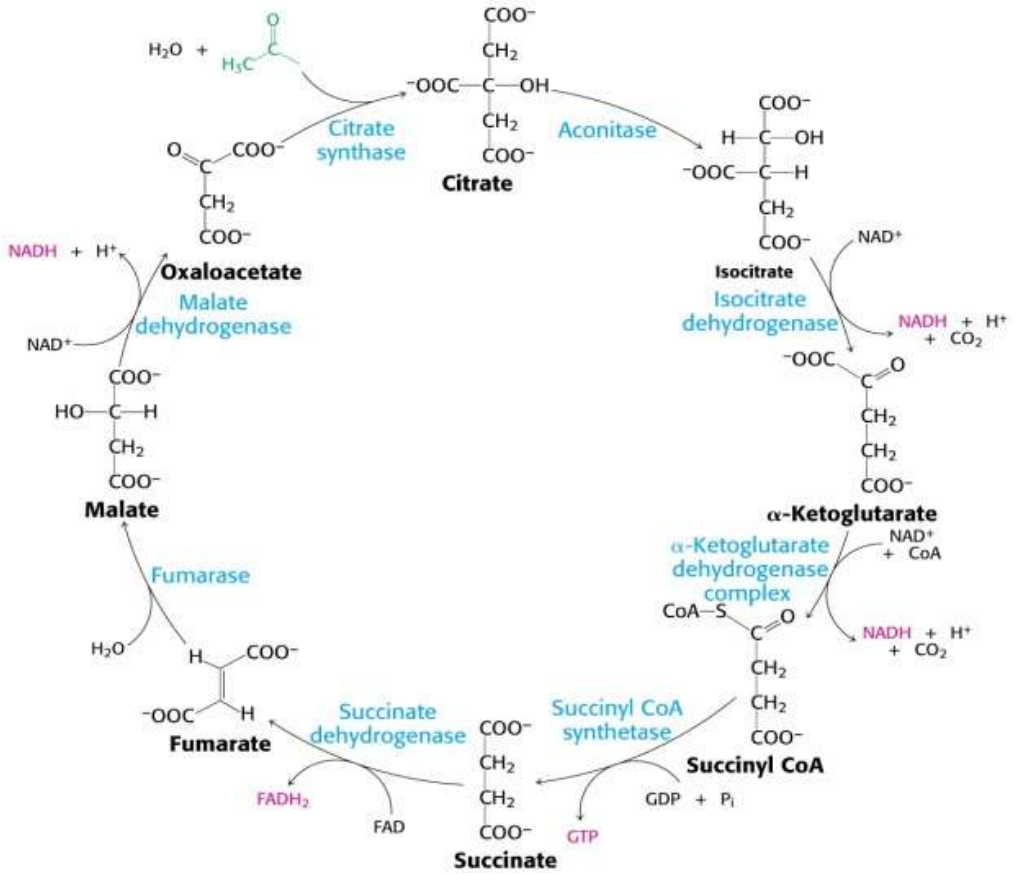
1. Linear
2. Spiral
3. **Cyclic** which regenerate the first material in cycle like Krebs cycle .

*Krebs cycle is divided into two parts , **the 1st one** will be involved in converting the 6c atoms molecule to 4 carbon molecule .(Bcz it's a cycle it will end up with 4 carbon atom (start point) .

*1st part involve in removing 2 carbon atoms from cycle to get molecule back to 4 carbons (Regardless the nature of that molecule)

***In second half** of cycle the RXN will reform these 4 carbons molecule (which result from 1st part , succinate). At end, give you the first molecule (**oxaloacetate**).

#We must know the molecules in this cycle , its structures ,and enzymes in each step .

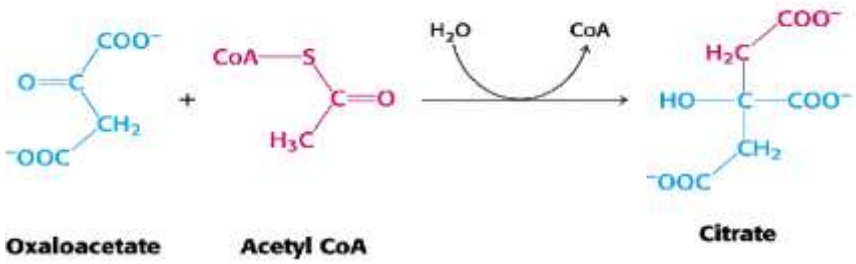


*Steps of First part of krebs cycle :

❶ Acetyl CoA(2c) + Oxaloacetate(4c) ⟶ citrate (6c , 3 carboxylic groups)

*Citrate syntheses enzyme (activate this step)

Note : name of enzyme depend on Rxn which catalyes by it .



Remember :Alcohol is molecules has hydroxyl groups oH .

***1ry alcohol can be oxidized to Aldehyde and 2ry to Ketone but 3ry can't be oxizide .**

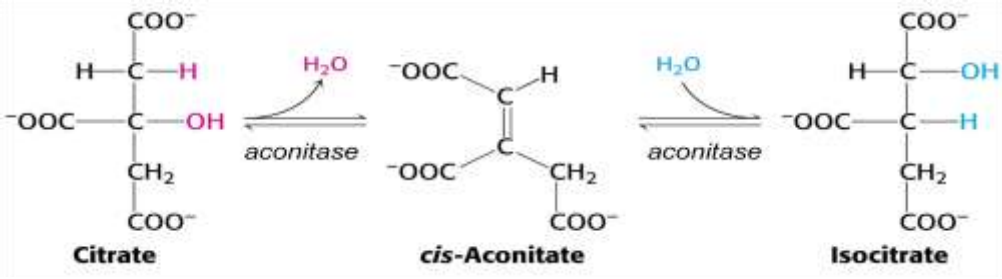
* **Citrate is 3ry alcohol and has 3 carboxylic groups so it can't be oxidize .**

***As we know all processes of citric acid cycle is oxidation process (Break bonds down), but the citrate is 3ry alcohol (can't be oxidize), thus how the cycle continue ?

⇨ Citrate will convert to isocitrate which is 2ry alcohol (can be oxidized to ketone)

❷ Citrate (3ry alcohol) ⟶ isocitrate (2ry alcohol)

Enzyme : aconitase , **Called : Aconitase bcz this step form intermediate called aconitate .**



❸Then isocitrate (2ry alcohol)oxidized to ketoglutarate (keton , as doctor said ,) by isocitrate dehydrogenase.

*During this step the 1st carbon atom leave cycle , carboxyllic group release as co2 **Decarboxylation** process .(This step is the 1rst oxidation process,co2 leaves, electrons will be harvested by 1rst NAD molecule).

*So 6 carbon atoms molecules (isocitrate) will convert to 5 carbon atoms molecules (α-ketoglutarate).

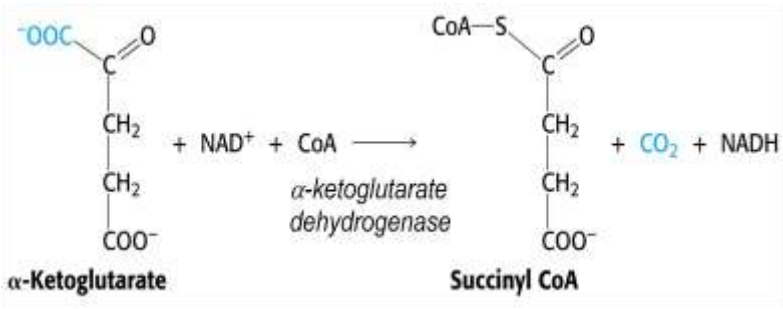
* Dehydrogenase enzyme remove hydroden .

Important : the 2 carbon atoms which were introduced by Acetyl coA are not the same which leave cycle as carbon dioxide .

> In Krebs cycle there is 4 dehydrogenases for oxidation process , 1rst one is used to form α-ketoglutarate .

❹ The last Rxn in 1rst half of of Krebs cycle,which will use another dehydrogenase.

α-ketoglutarate ⟶ succinyl coA ⟶ succinate (4 c atomes)



GTP + ADP ⟷ GDP + ATP

*as we see one co2 release and electrons carry by 1 NAD molecule.

till this step 2co2 and 2NADH release.

* α-ketoglutarate dehydrogenase enzyme use to oxidize α-ketoglutarate .

*end product of this step is Succinate (4 c) >>>>>> aim of 1rst half of cycle

Believe in yourself ☺