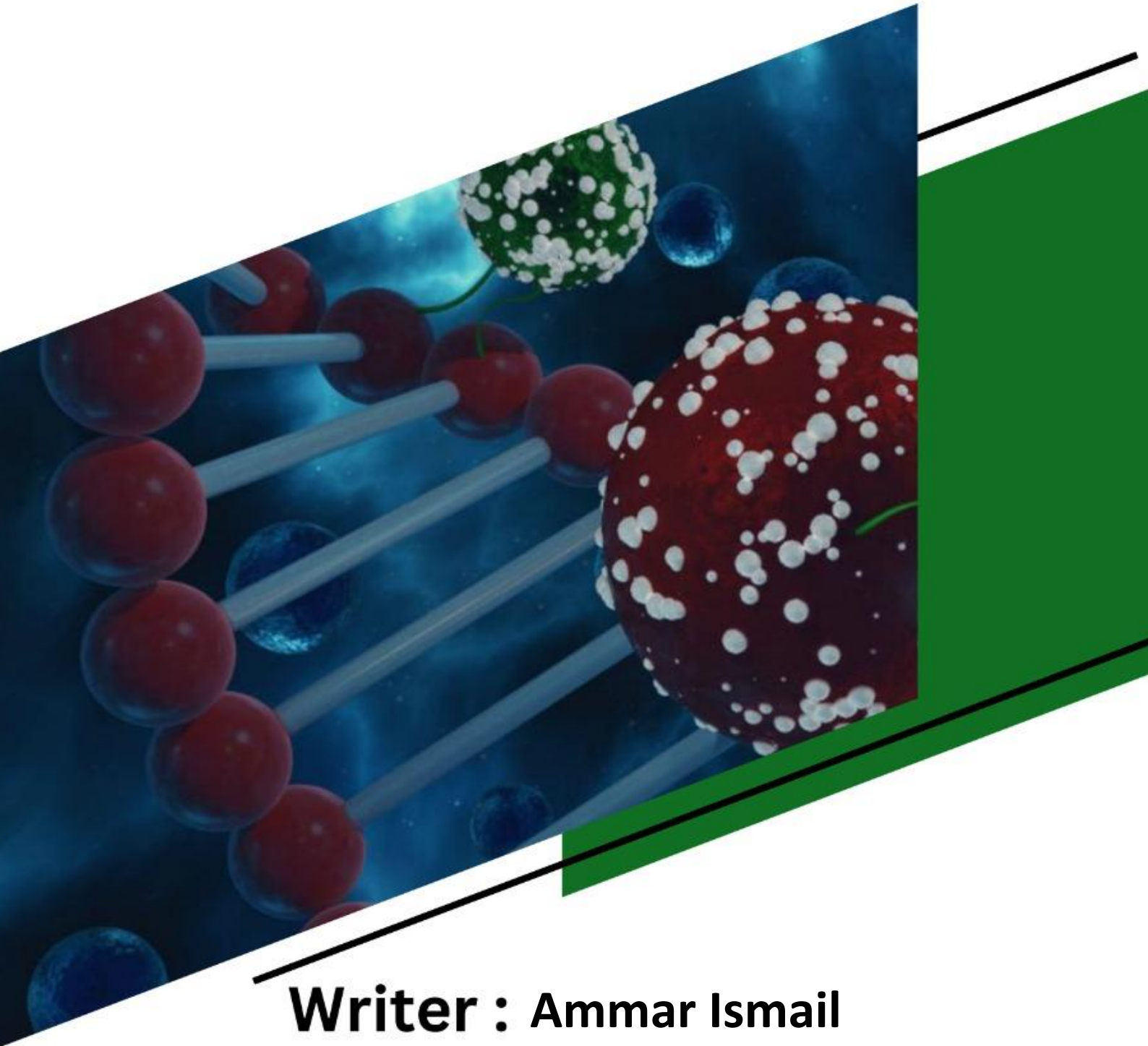




METABOLISM

Sheet no. 4



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CALCULATION OF ΔG° FROM ΔE°

➤ $\Delta G^\circ = -nf\Delta E^\circ$

➤ n is the number of transported electrons in the reaction, in case of NADH and FADH₂, it equals 2.

➤ $F = \text{Farady constant} = 23.06 \text{ kcal/Volt}$

➤ $\Delta E^\circ = E^\circ_{\text{reduction of cathode}} - E^\circ_{\text{reduction of anode}}$

➤ Cathode: the **highest** $E^\circ_{\text{reduction}}$ value.

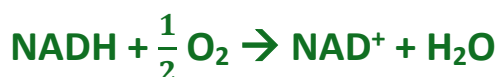
➤ Anode: the **lowest** $E^\circ_{\text{reduction}}$ value.

➤ For example, if a reaction has $E^\circ_{\text{reduction}}$ values of -2 and -1, the -2 is the anode and -1 is the cathode.

➤ Side note: the doctor didn't mention the cathode and anode, but I added them to make things easier.

$$\Delta E^\circ = E^\circ_{\text{reduction of cathode}} + E^\circ_{\text{oxidation of anode}}$$

➤ Calculate ΔG° of the following reaction:



Extra explanation: notice that the first reaction is for oxidation of NADH, so the given ΔE° value is for **oxidation potential**. Meanwhile, the second reaction is for reduction of O₂, so the given ΔE° value is for **reduction potential**, our ΔE° equation needs to have both ΔE° values for reduction. Therefore, we multiply ΔE° for the first reaction by -1, becoming -0.32.

$$\Delta E^\circ_{\text{reduction for NADH}} = -0.32$$

$$\Delta E^\circ_{\text{reduction for O}_2} = +0.82. \text{ Now, we can use the equation:}$$

$$\Delta E^\circ = E^\circ_{\text{reduction of cathode}} - E^\circ_{\text{reduction of anode}}$$

$$\Delta E^\circ = 0.82 - (-0.32) = 1.14 \text{ V}$$

$$\Delta G^\circ = -2 * 23.06 * 1.14$$

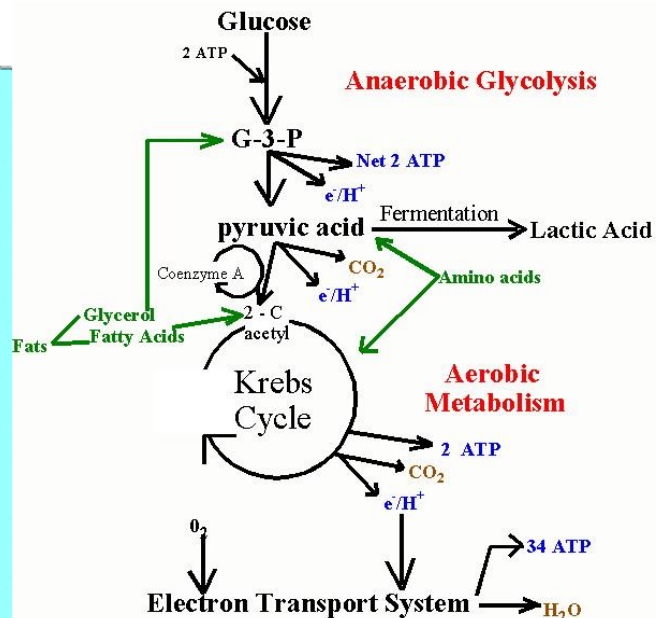
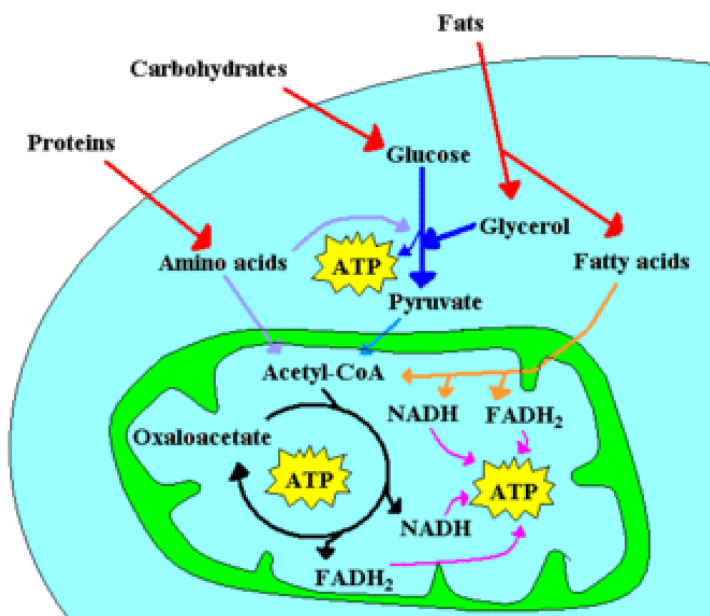
$$\Delta G^\circ = -52.6 \text{ kcal/mol}$$

OXIDATION REDUCTION REACTIONS (REDOX)

- $\Delta E = E_A - E_D$ (the same as the equation I mentioned above).
A: acceptor of electrons, D: donator of electrons. You can use it too.
- ΔE = Redox difference of a system in any condition.
- ΔE° = Redox difference of a system in standard condition (25 C° and 1 atmosphere pressure, pH = 7).
- Does ΔE determine the feasibility of a reaction?
Yes, From the formula above, if ΔG has a negative value, ΔE° must have a positive value. So, for a spontaneous reaction, ΔE° is always positive.
- $\Delta G^\circ = -nf\Delta E^\circ$
- In other words, energy (work) can be derived from the transfer of electrons, or oxidation of food can be used to synthesize ATP.

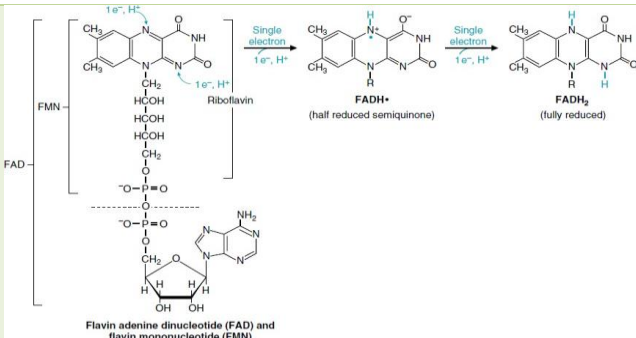
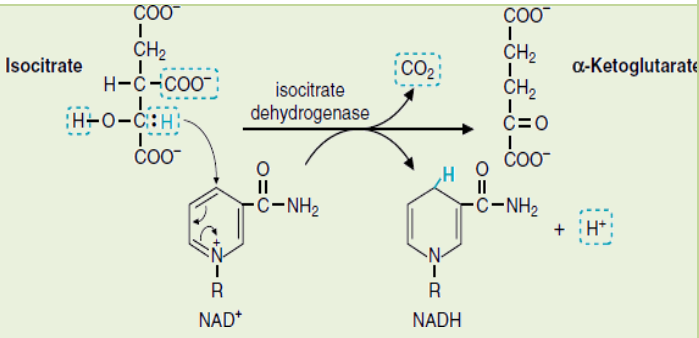
(KREBS, CITRIC ACID OR TCA) CYCLE

HOW DOES IT FIT?



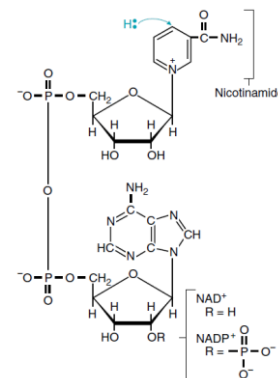
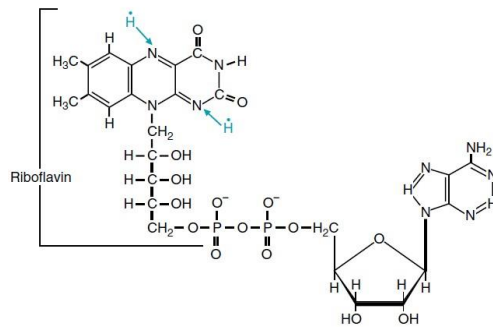
- It's named Krebs for the scientist's name, citric acid cycle because of the intermediate, and TCA (tricarboxylic acid) because citric acid has three carboxyl groups.
- All metabolic processes have in their pathways acetyl CoA, it is a product of fats, carbohydrates, and proteins degradation.
- Acetyl CoA can be used, in addition to Krebs cycle, in making many structures (for e.g. fatty acids, etc..).

ELECTRON (ENERGY) CARRYING MOLECULES (NAD⁺ AND FAD)

FAD	NAD ⁺
Single electrons (H [•]), different sources	Pair of electrons (H ⁻), same source
Succinate to fumarate, lipoate to lipoate disulfide in α -KG (will be clarified soon).	Alcohols to ketones by malate dehydrogenase & isocitrate dehydrogenase (will be clarified soon).
FAD must remain tightly, sometimes covalently, attached to its enzyme.	NADH plays a regulatory role in balancing
E° for enzyme-bound FAD varies	Energy metabolism
 <p>Flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN)</p>	 <p>Isocitrate dehydrogenase</p>

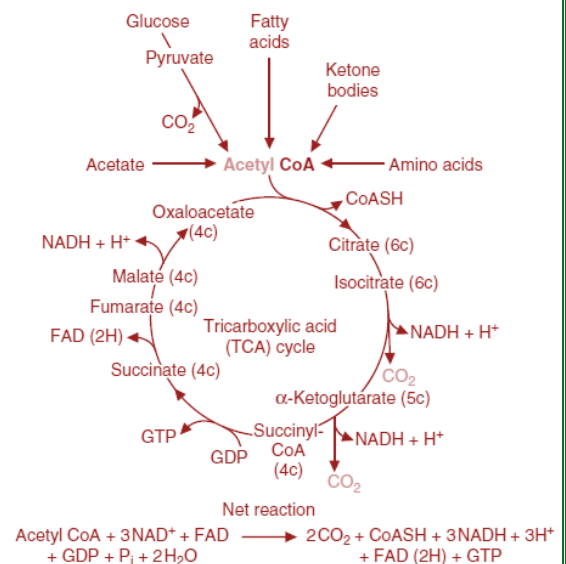
- Always involve a pair of chemicals: an electron donor and an electron acceptor (food vs. NAD⁺).
- NAD⁺ vs. FAD
- NAD⁺ vs. NADP⁺ (fatty acid synthesis and detoxification reactions).
- Look at the pictures on the next page, the picture on the right is for NAD⁺ and the other one is for FAD.
- NAD⁺ loses its two electrons at the same time, but FAD can lose them in a sequential manner (one by one), so it passes through free radical state. So, FAD[•] can't exist in solutions by itself, it needs to be covered, and this makes perfect sense, because it can form a free radical which is dangerous. Heme also normally exists inside a protein.
- Both FAD[•] and heme don't have constant reduction potential.
- NADP⁺ differs from NAD⁺ in having an extra phosphate group and regulation (where to use), they can do the same job anyways.

- ΔE° for NADH and O_2 is more than ΔE° for $FADH_2$ and O_2 . Therefore, ΔG° and energy from NADH when it loses its two electrons is more than that of $FADH_2$.
- FMN (flavin mononucleotide) differs from FAD only in not having adenine.



COMPONENTS & STEPWISE REACTIONS

- **No introduced O_2 , two CO_2 exit.**
- It has 8 reactions, 8 intermediates and 8 enzymes. All of them are for memorizing.
- Citric acid (the first molecule in the cycle) has 6 carbons, the last molecule in the cycle is oxaloacetate which has 4 carbons. So, obviously, there are two carbons lost in the cycle as two CO_2 molecules.



- The cycle has two parts:
 - The first part (from citrate to succinyl CoA): responsible for getting rid of the two carbons as CO_2 .
 - The second part (from succinyl CoA to oxaloacetate): responsible for regeneration of oxaloacetate.
- **CIA Sent Soldiers For My Office (Citrate, isocitrate, α -KG, succinyl CoA, succinate, fumarate, malate, and oxaloacetate). You can use this mnemonic to memorize the structures in it.**
- Side note: don't forget to look at the picture in the previous page when reading each step.

STEPS OF KREBS CYCLE

1. Acetyl CoA (2C) + oxaloacetate (4C) → citrate (6C)

- There is bond formation here, so the reaction needs energy that comes from breaking acetyl CoA down.
- Enzyme: citrate synthase.
- Remember, citrate has three carboxyl groups.

2. Citrate (6C) → isocitrate (6C)

➤ Why to make Isocitrate from citrate?

The goal of this cycle is to produce energy, and as we said before, oxidation of food produces energy. Now, because citrate has a tertiary alcohol group, it can't be oxidized unless it's converted to its secondary form (isocitrate).

➤ 3° to 2° alcohol.

- Enzyme: aconitase.

3. isocitrate (6C) → α-ketoglutarate (5C)

➤ Oxidative decarboxylation, CO₂.

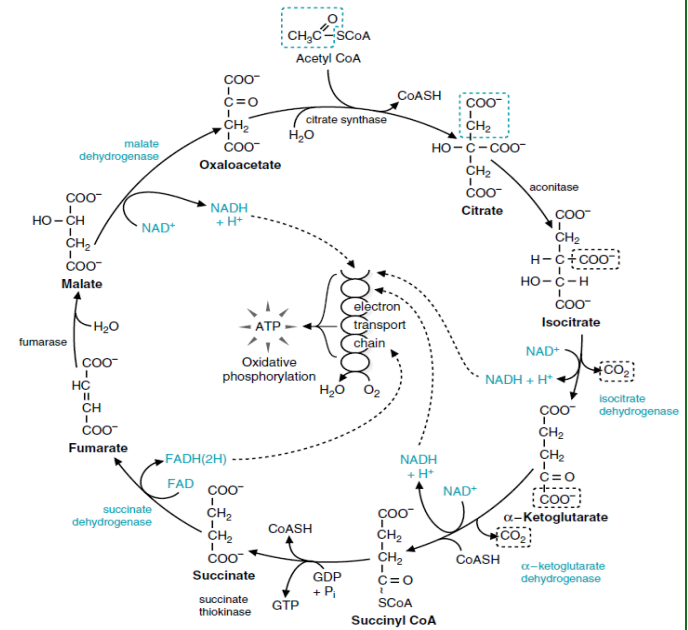
➤ Where does the CO₂ exit?

The doctor didn't answer this question but google says "waste gas".

- Gluta means five.
- Enzyme: isocitrate dehydrogenase.
- Side note from me: wherever there is a dehydrogenase enzyme in this cycle, there will be NADH or FADH₂ produced, because there is a hydrogen that is removed from the structure.
- Side note from me: isocitrate dehydrogenase is a complex enzyme that has two functions; decarboxylation and dehydrogenation.
- CO₂ and NADH are produced

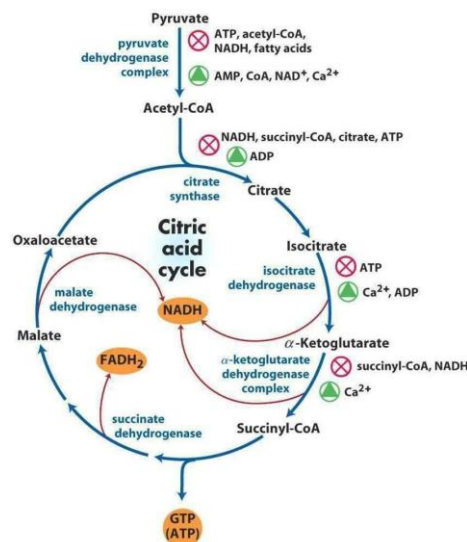
4. α -ketoglutarate (5C) \rightarrow succinyl CoA (4C)

- **Oxidative decarboxylation.**
- **Thiamine pyrophosphate, lipoic acid, and FAD.**
- **Keto group oxidized to acid, CoA-SH, succinyl CoA.**
- **Energy conserved as NADH, thioester bond.**
- **The only irreversible step in the whole reaction cycle.**



- The mechanism of this reaction will be totally clarified in the next lecture.
- Enzyme: α -ketoglutarate dehydrogenase (a complex enzyme too).
- The lost carboxyl group here is terminal, the compound will have a free terminal carbonyl group, so the molecule is unstable. That's why it binds to CoA.

- This picture is in the slides, the doctor didn't talk about it, it is about regulation of the cycle's enzymes.



أَنْ تَحْسَبَ الشَّحْمَ فَيَمَنْ شَحْمُهُ وَرَمَ
بِأَنْتِي خَيْرُ مَنْ تَسْعَى بِهِ قَدَمُ

أَعْيَضُهَا نَظَرَاتٍ مِنْكَ صَادِقَةٌ
سَيَعْلَمُ الْجَمْعُ مَن ضَمَّ مَجْلِسُنَا