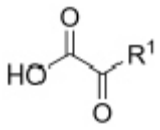
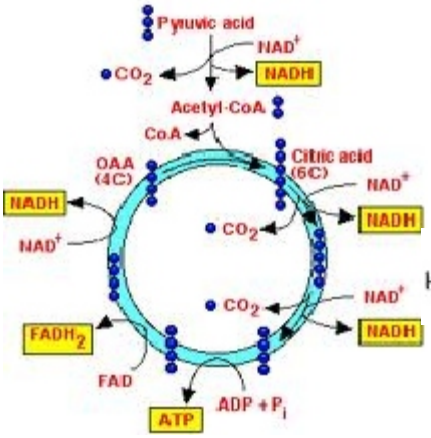
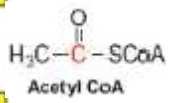
TRICARBOXYLIC ACID CYCLE:

Alpha keto acid



rvsd 11/5/93, 11/7/94, 11/6/95, 11/13/96, 9 Nov 01, 18 Nov 02, 10 Nov 03, 24 Oct 07, 29Oct08, 3Nov10, 28Oct11; p. 344- , BHK 5th: 405-415, 6th: 255-265, 7th: 258-





ELUCIDATED BY KREBS, got Nobel prize in 1953.
Pyruvate enters mitochondrial matrix where:

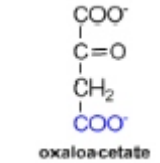
Oxidation to Acetyl CoA: pyruvate dehydrogenase: pyruvate is **alpha keto acid** (keto draws e^- away)

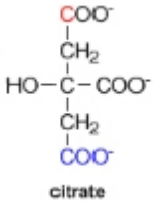
a: **decarboxylation** (requires TPP) *yields energy which drives the reaction*
b: **oxidizes substrate**, producing NADH at #2 C (-7.5 kcal).
c: **activates two carbon acetyl fragment** by attaching to CoASH

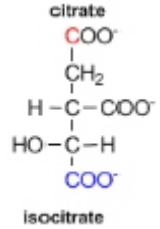
CoA: adenine-3-PO_4, 5- pyroPO_4-pantothenic acid-$NHCH_2CH_2SH$ (a thiol) (p. 256)
Forms *thioester*, a high energy bond, capable of donating to substrate (oxaloacetate)

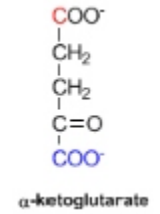
TCA cycle: (p. 261)

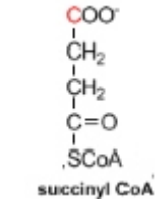
step	process	molecule	by product
1	**acetylation:** Acetyl CoA transfers acetyl group to oxaloacetate (C-4) *via CH_3 end*	citrate	
2	**dehydration, rehydration:** citrate (tertiary alcohol) **isomerized** to isocitrate, with oxidizable secondary alcohol	isocitrate	
3	**oxidation, decarboxylation:** 2° hydroxyl on isocitrate is **oxidized**, making **NADH**, creates unstable molecule, **decarboxylates** (drives rxn) yielding α-ketoglutarate. (first decarboxylation)	α-ketoglutarate	CO_2 NADH
4	**oxidation, decarboxylation, form thioester:** α-ketoglutarate is similar to pyruvate: an α-keto acid, similar to formation of acetyl CoA: oxidation, makes NADH, decarboxylation (makes CO_2) and CoA thioester high energy bond (succinyl CoA).	succinyl CoA	CO_2 NADH
5	**thioester split, phosphorylation of GDP:** Thioester bond used to **PO_4yllate GDP**, release succinate and CoASH. GTP PO_4yllates ADP (only direct ATP in cycle)	succinate	GTP
6	**oxidation: Succinate α,β carbons dehydrogenated, forming $FADH_2$** (not enough energy to form NADH) and fumarate	fumarate	$FADH_2$
7	**hydration: fumarate is hydrated** to form malate	malate	
8	**oxidation: malate (a secondary alcohol) is oxidized** to form oxaloacetate, producing **NADH**. Serves as acceptor of acetyl group from acetyl CoA	oxaloacetate	NADH

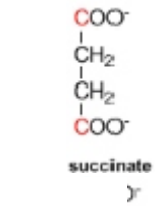










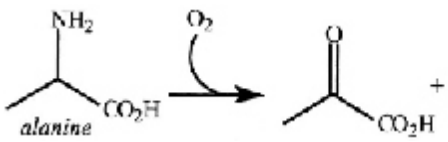


FAT CATABOLISM: BETA OXIDATION, FEEDS INTO TCA (p. not in text???):

beta oxidation: (Steps 2-4 = TCA 6-8, succinate to oxaloacetate) occurs in mitochondria

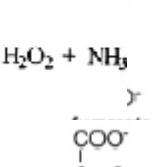
	Reaction	Details	Product
1.	**Activation:**	**FA +CoASH** condensed using **ATP to AMP + PPi**	**CoA-S-FA**
2.	**Dehydrogenation:**	α, β carbons dehydrogenated, make	**$FADH_2$**
3.	**Hydration:**	water added to double bond, making	**β OH CoA-S-FA**
4.	**Oxidation:**	NAD used to oxidize β OH to	**carbonyl**
5.	**Thioester creation:**	acetyl CoA splits off, new CoASH attached **acetyl CoA**	

(Mnemonic: DHOT)



PROTEIN CATABOLISM: 3 of 20 AA deaminated, feed to TCA

deamination or transamination to α keto acid



TCA CYCLE IS AMPHIBOLIC

It can either 'burn' glucose, etc, or its intermediates can be used for synthesis:

succinyl CoA is used to synthesize amino acids and heme
citrate to acetyl CoA (reverse reaction from usual), used for fatty acid synthesis

Replenishment of intermediates possible by carboxylation of glycolytic intermediates.