Ketone Bodies

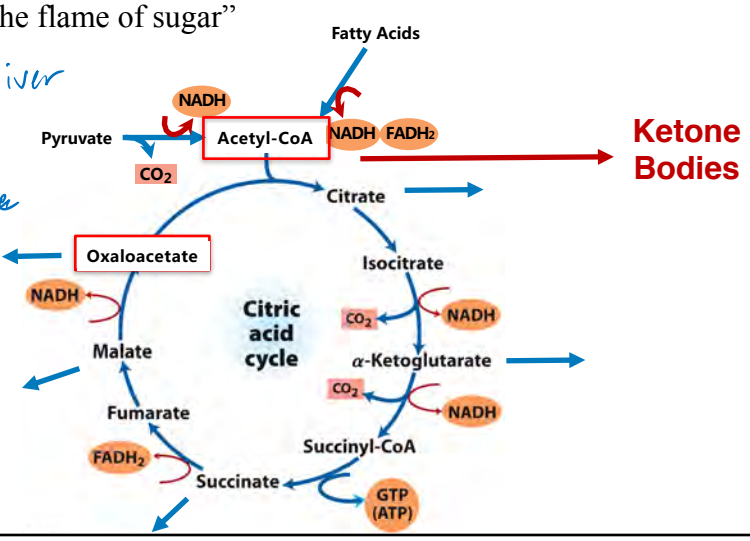
Fatty Acid Degradation

Ketone Bodies

"Fat burns in the flame of sugar"

made by liver

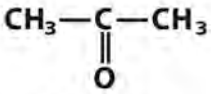
Used by heart, muscle adapted brain



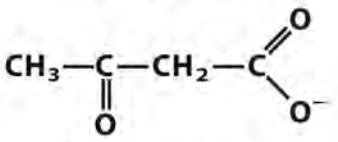
Fatty Acid Degradation

- Entry of acetyl-CoA into citric acid cycle requires oxaloacetate.
- When oxaloacetate is depleted, acetyl-CoA is converted into ketone bodies.
  - frees coenzyme A for continued β oxidation
- Three forms of ketone bodies can leave the liver: acetone, acetoacetate, and β-hydroxybutyrate.
- Therefore, the anabolism of Ketone Bodies is connect to catabolism of fatty acids and sugars
- For now, we will discuss Ketone Body catabolism

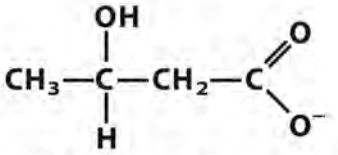
Ketone Bodies



Acetone



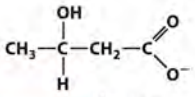
Acetoacetate



D-β-Hydroxybutyrate

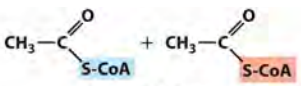
Fatty Acid Degradation

Ketone Bodies as Fuel



D-β-Hydroxybutyrate

1. Make CoA derivatives
2. Oxidize alcohol
3. Thiolase reaction



2 Acetyl-CoA

Fatty Acid Degradation

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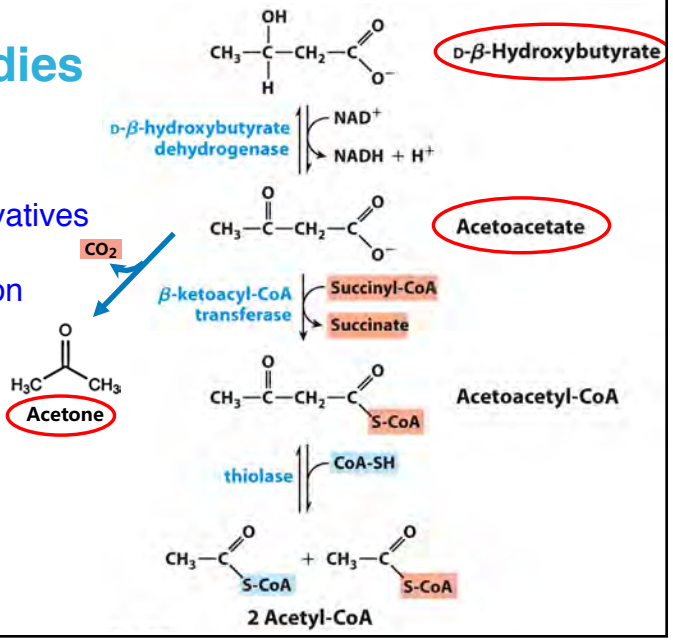
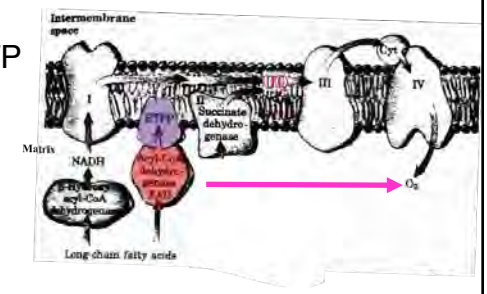


Fatty Acid Oxidation in Other Organelles

Fatty Acid Degradation

β Oxidation in Plants Occurs Mainly in Peroxisomes

- Mitochondrial acyl-CoA dehydrogenase passes electrons into respiratory chain via electron-transferring flavoprotein (ETFP).
  - energy captured as ATP

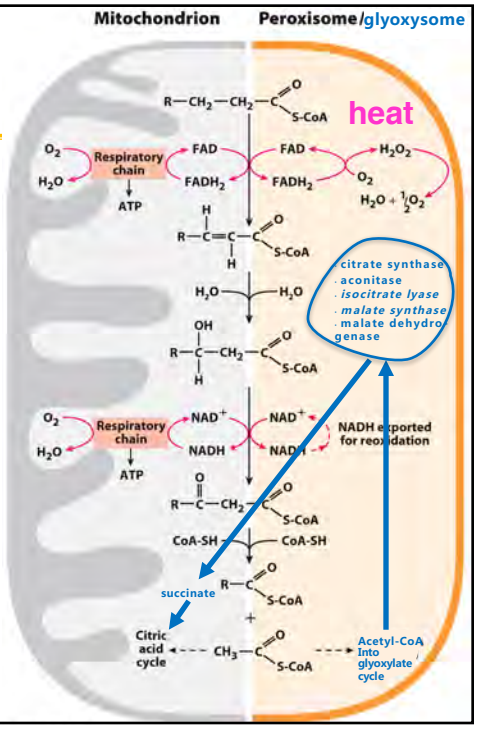


- Peroxisomal/glyoxysomal acyl-CoA dehydrogenase passes electrons directly to molecular oxygen and H_2O_2.
  - energy released as **heat**
  - hydrogen peroxide eliminated by catalase

Fatty Acid Degradation

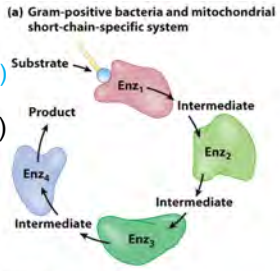
- Acetyl-CoA released from peroxisomal β oxidation is exported to cytosol and then imported to mitochondria.

- A peroxisome is also a glyoxysome when enzymes for glyoxylate cycle are present (e.g., germinating seeds).
- Acetyl-CoA released from peroxisomal β oxidation can be used in glyoxylate cycle.
- The glyoxylate cycle is found in most organisms, but not vertebrate animals.
- The glyoxylate cycle has an anabolic function to synthesize larger molecules from acetyl-CoA.



Fatty Acid Degradation

Fatty Acid Oxidation is Performed by a Single TriFunctional Protein (TFP)



- Hetero-octamer ($\alpha_4\beta_4$)
  - four α subunits
    - enoyl-CoA hydratase activity
    - β-hydroxyacyl-CoA dehydrogenase activity
    - responsible for binding to membrane
  - four β subunits
    - long-chain thiolase activity
- May allow substrate channeling between enzymes
- Associated with inner-mitochondrial membrane
- Processes fatty acid chains with 12 or more carbons
- Shorter chains processed by soluble enzymes in the matrix

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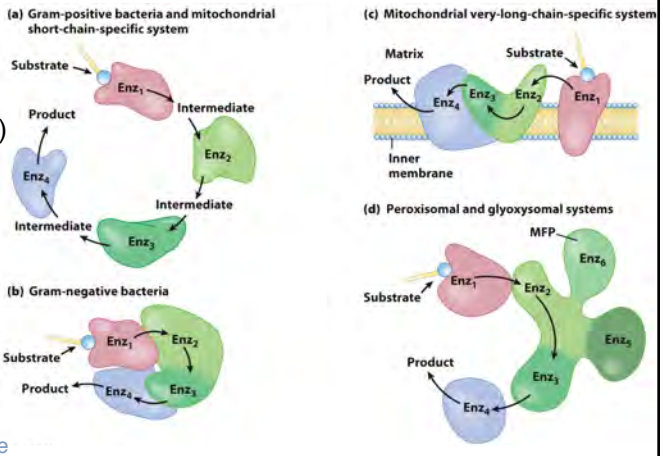

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Fatty Acid Degradation: Summary

We learned that:

- fats are an important energy source in animals
- two-carbon units in fatty acids are oxidized in a four-step β oxidation process into acetyl-CoA
- in the process, a lot of NADH and $FADH_2$ forms; these can yield a lot of ATP in the electron-transport chain
- Mono- and poly-unsaturated fatty acids require additional enzymes and lose an $FADH_2$ for every double bond and cost an NADPH for every pair.
- acetyl-CoA formed in the liver can be either oxidized via the citric acid cycle or converted to ketone bodies that serve as fuels for other tissues
- Other organelles can perform fatty-acid oxidation; during peroxisomal oxidation, fats can be oxidized to generate heat