BB 422/622

OUTLINE:

Introduction and review
Transport
Glycogenolysis
Glycolysis
Other sugars
Pasteur: Anaerobic vs Aerobic

Exam-1 material

Fermentations

Exam-2 material

Pyruvate
- pyruvate dehydrogenase (ox-decarbox; S-ester)

Krebs' Cycle
- How did he figure it out?
- Overview
- 8 Steps
  - Citrate Synthase (C-C)
  - Aconitase (=, -OH)
  - Isocitrate dehydrogenase (ox-decarbox; =O)
  - Ketoglutarate dehydrogenase (ox-decarbox; S-ester)
  - Succinyl-CoA synthetase (sub-level phos)
  - Succinate dehydrogenase (=)
  - Fumarase (-OH)
  - Malate dehydrogenase (=O)
- Energetics
- Regulation
- Summary

Oxidative Phosphorylation
- Energetics (−0.16 V needed for making ATP)
- Mitochondria
- Transport (2.4 kcal/mol needed to transport H^+ out)
- Electron transport
  - Discovery
  - Four Complexes
    - Complex I: NADH → $CoQH_2$
    - Complex II: Succinate → $CoQH_2$
    - Complex III: $CoQH_2$ → Cytochrome C (Fe^{2+})
    - Complex IV: Cytochrome C (Fe^{2+}) → H_2O
- Chemiosmotic theory: Phosphorylation
  - ATPase
  - Mitchell Hypothesis
  - Binding-Change Model
  - Connection to the proton motive force
  - Net ATP production
  - Regulation

Exam-2 material

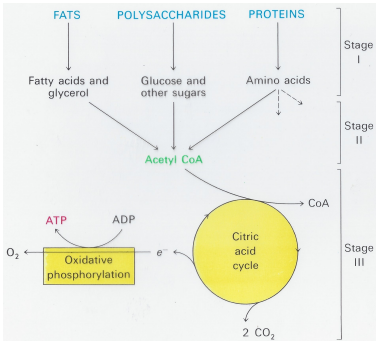
Exam-3 material

Catabolism: Lipid Degradation
- Digestion and storage
- FOUR stages lipid catabolism
  - Mobilization from adipose tissues
  - Activation of fatty acids
  - Transport into mitochondria
  - Oxidation
    - Saturated
    - Unsaturated
    - Odd-chain
- Ketone Bodies
- Oxidation in other organelles

Catabolism: Nitrogenous
- Digestion
- Inside of cells
  - Protein turnover
    - Ubiquitin
    - Proteosome
- Urea Cycle
- Amino-acid Degradation
- Nucleotide Degradation

Ketone Bodies

Fates of Acetyl CoA



(HMG-CoA) 3-Hydroxy-3-methyl-glutaryl CoA ← **Acetyl CoA** ← Fatty acids

Amino acids

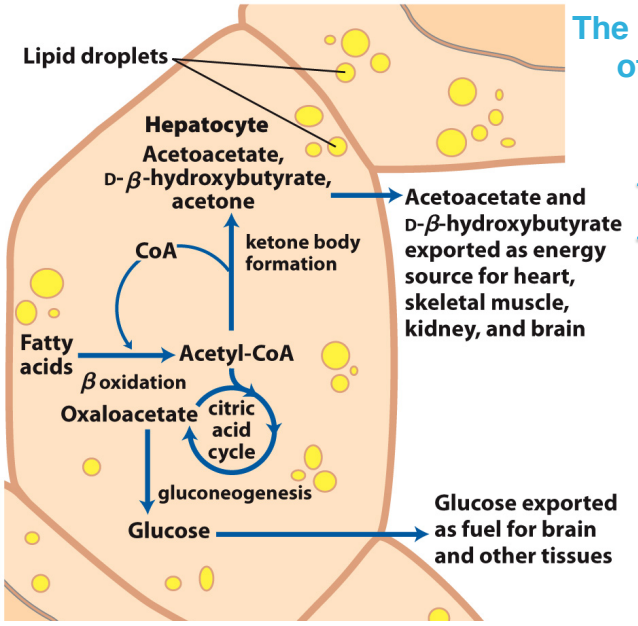
CO_2

Cholesterol

Ketone bodies

1. Oxidation
2. Lipid catabolism
3. Amino acid catabolism

Ketone Body Degradation



The Liver Is the Source of Ketone Bodies

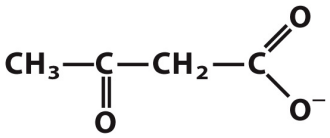
Ketone Bodies

Ketone Body Degradation

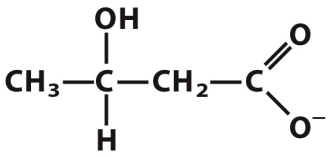
- Entry of acetyl-CoA into citric acid cycle requires oxaloacetate.
- When oxaloacetate is depleted, acetyl-CoA is converted into ketone bodies in the LIVER.
  - frees coenzyme A for continued β oxidation
- Three forms of ketone bodies can leave the liver: acetone, acetoacetate, and β-hydroxybutyrate.
- 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



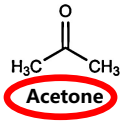
D-β-Hydroxybutyrate

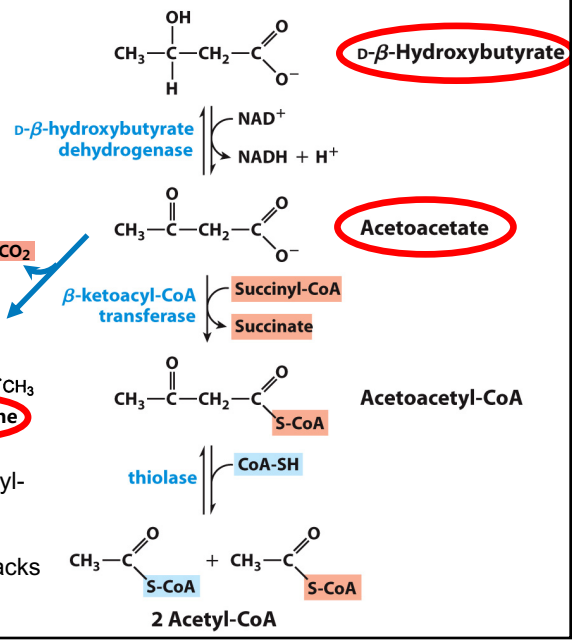
Ketone Body Degradation

Ketone Bodies as Fuel

(heart & muscle, brain if starving)

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





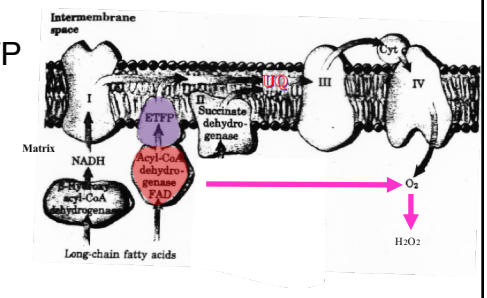
Notice the ingenious use of succinyl-CoA, which is a TCA cycle intermediate. If insufficient, this reaction does not happen and it backs up…….acidosis

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

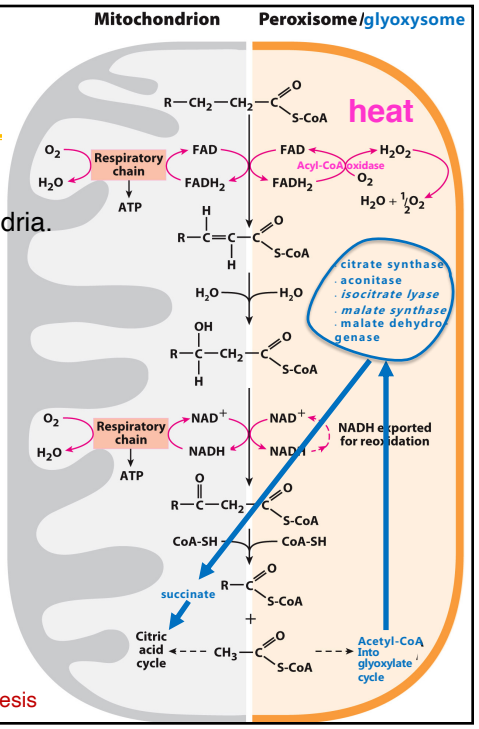


- Peroxisomal/glyoxysomal acyl-CoA oxidase passes electrons directly to molecular oxygen and H_2O_2.
  - energy released as **heat**
  - hydrogen peroxide eliminated by catalase

Fatty Acid Degradation

- Acetyl-CoA & NADH 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 made 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.

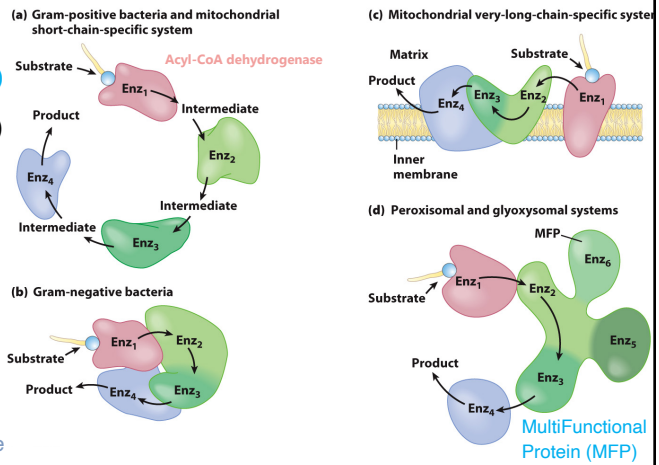
We'll come back to this when we discuss biosynthesis



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

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 at an odd carbon, and an NADPH for every double bond at an even carbon.
- 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