Metabolism of lipids IV:

Ketone bodies

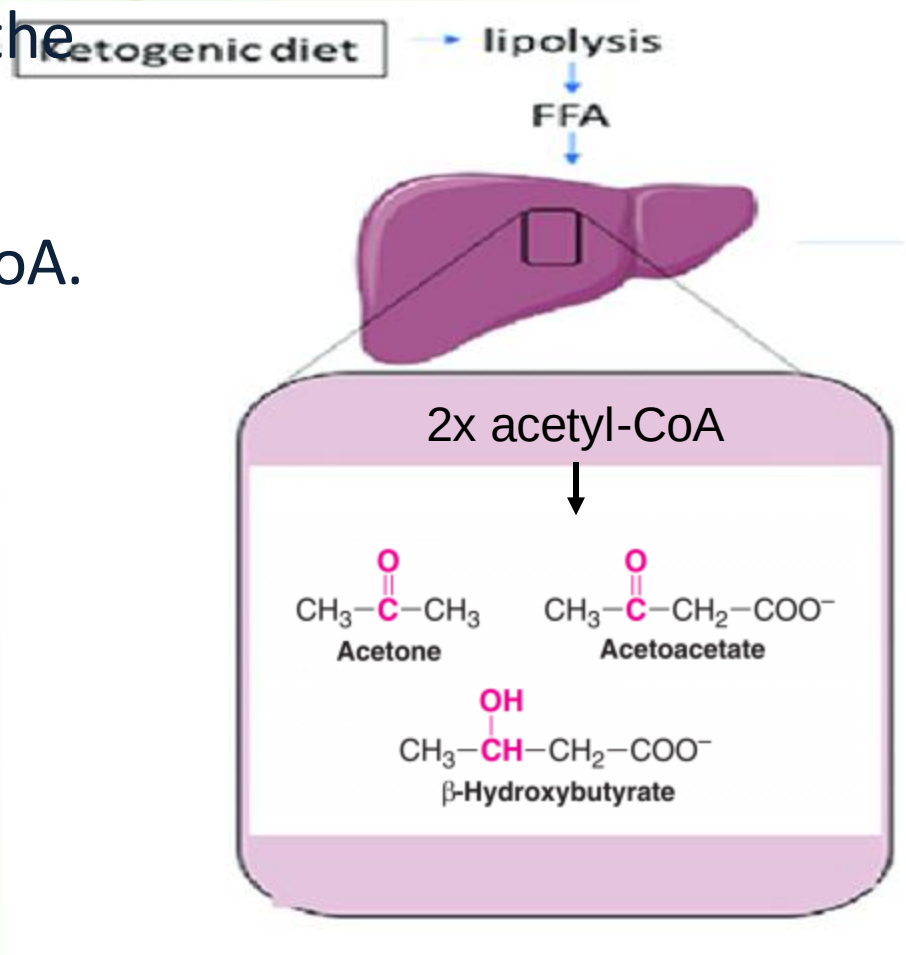
Prof. Mamoun Ahram

Resources

- This lecture
- Lippincott's Biochemistry, Ch. 16
- Diabetic, alcoholic and starvation ketoacidosis
  - https://derangedphysiology.com/main/cicm-primary-exam/required-reading/acid-base-physiology/acid-base-disturbances/Chapter%20617/diabetic-alcoholic-and-starvation-ketoacidosis
- Deep Dive – Alcoholic Ketoacidosis
  - https://aomcfoamed.com/2020/01/14/deep-dive-alcoholic-ketoacidosis/
- Alcoholic Ketoacidosis: Mind the Gap, Give Patients What They Need
  - https://www.emra.org/emresident/article/alcoholic-ketoacidosis/

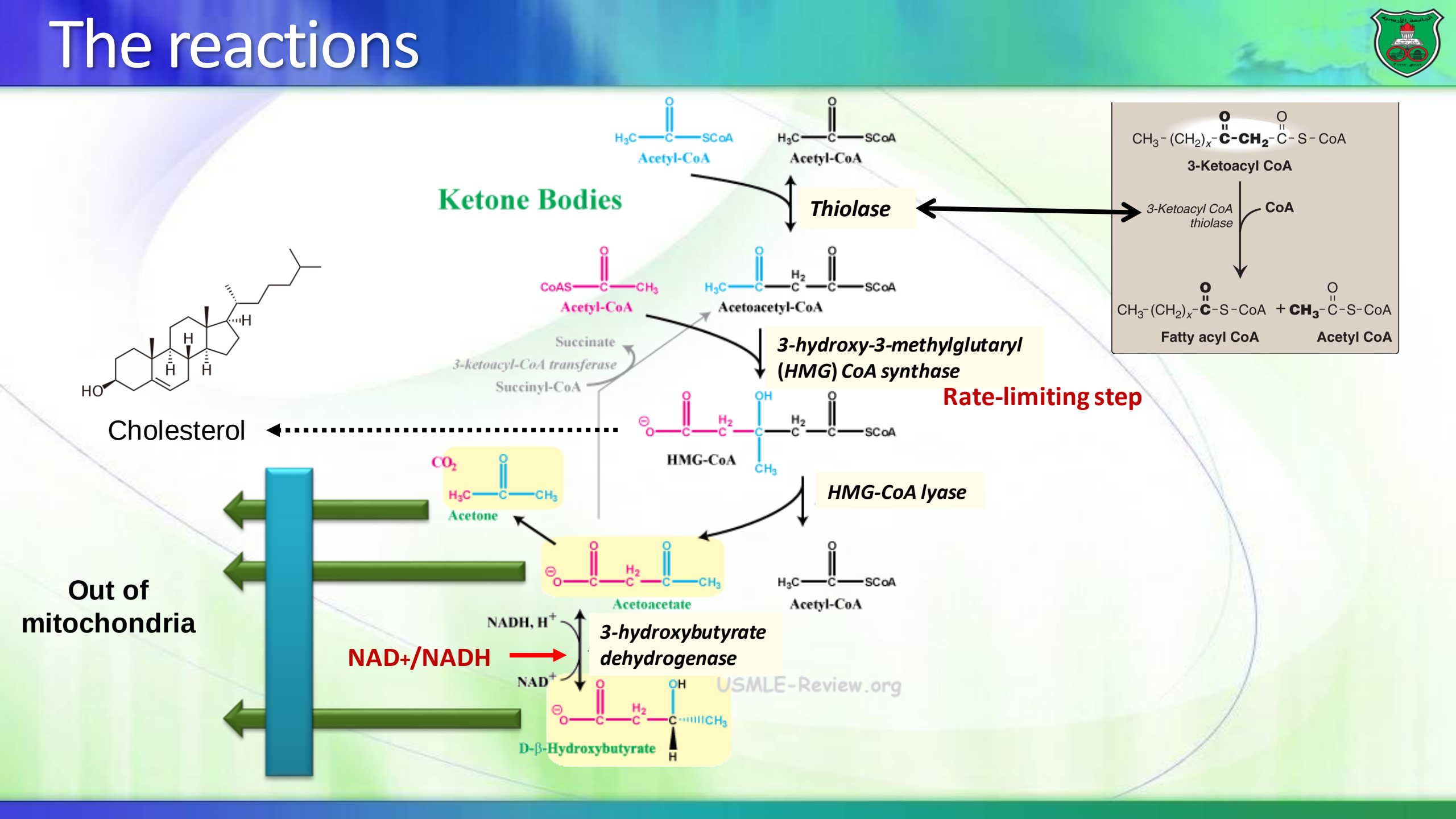
What are ketone bodies?

- Ketone bodies are produced from 2 acetyl-CoA in the liver for other tissues (e.g. muscle, heart, brain, …etc., but not RBC and liver) to use as a source of energy in case of starvation by re-forming acetyl CoA.
- They are acetoacetate, 3-hydroxybutyrate (AKA β-hydroxybutyrate), and acetone (volatile)
- Advantages:
  - Soluble (no carrier is needed)
  - Fast
  - Spare glucose

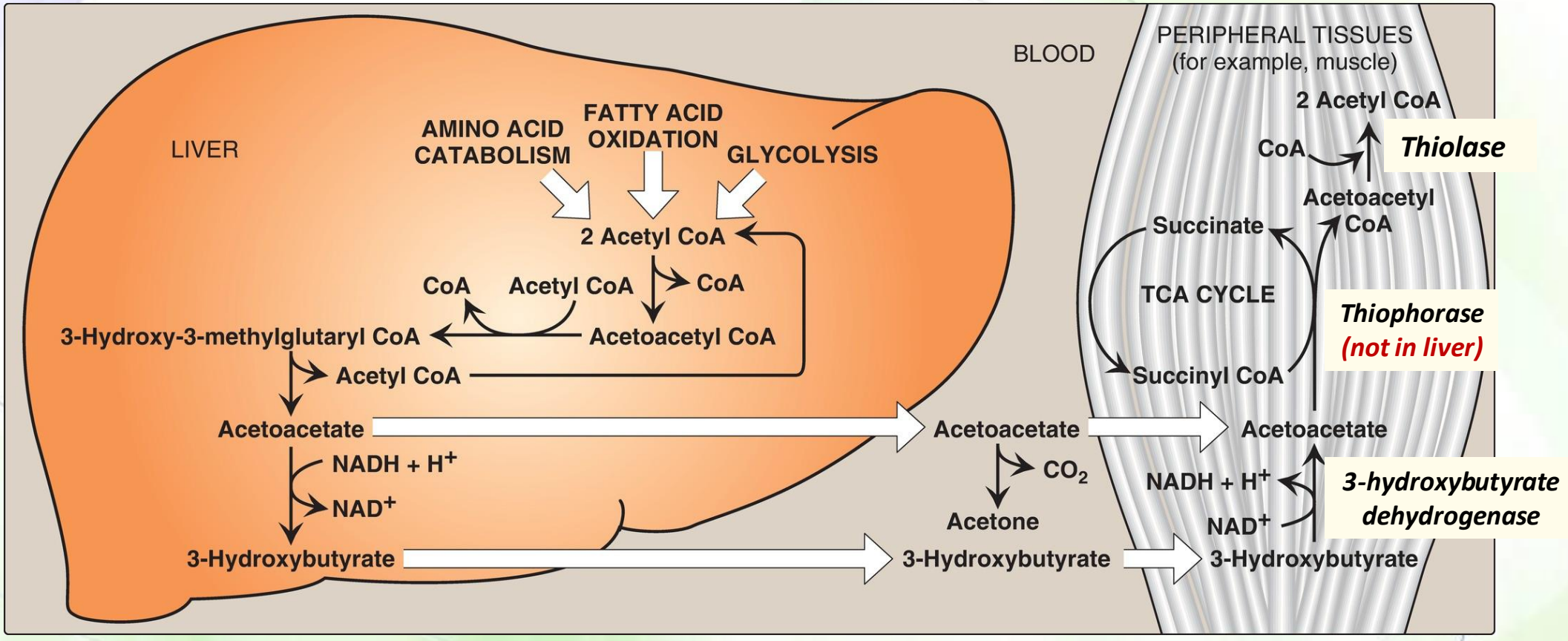


- **At wake-up time: 3-4% of energy**
- **Prolonged fasting: 30-40%**

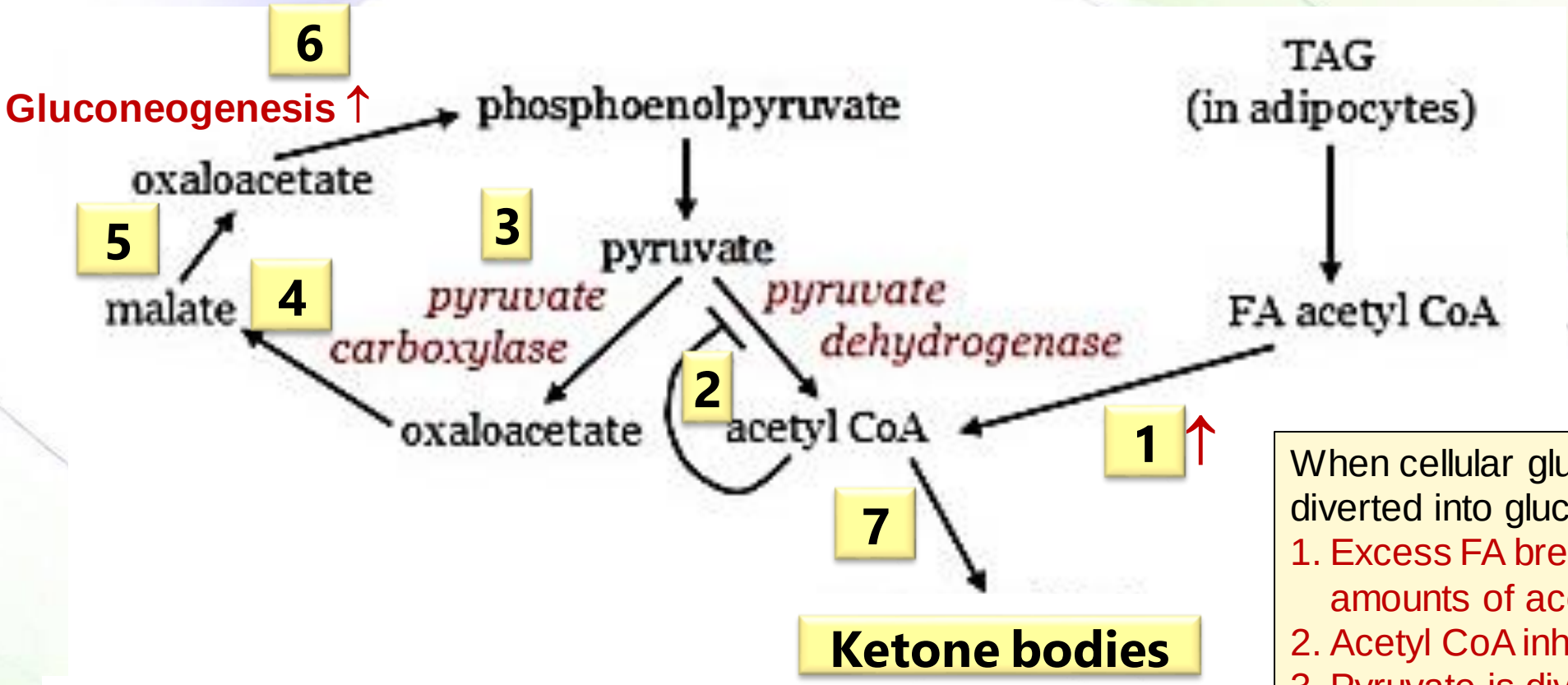
The reactions

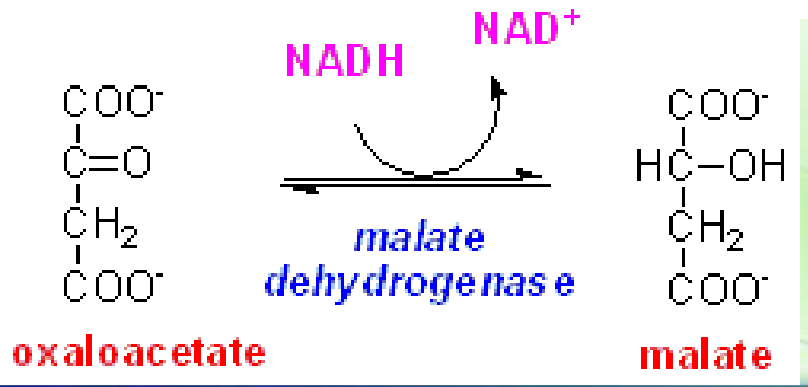


Use of ketone bodies



Under glucose-poor condition,



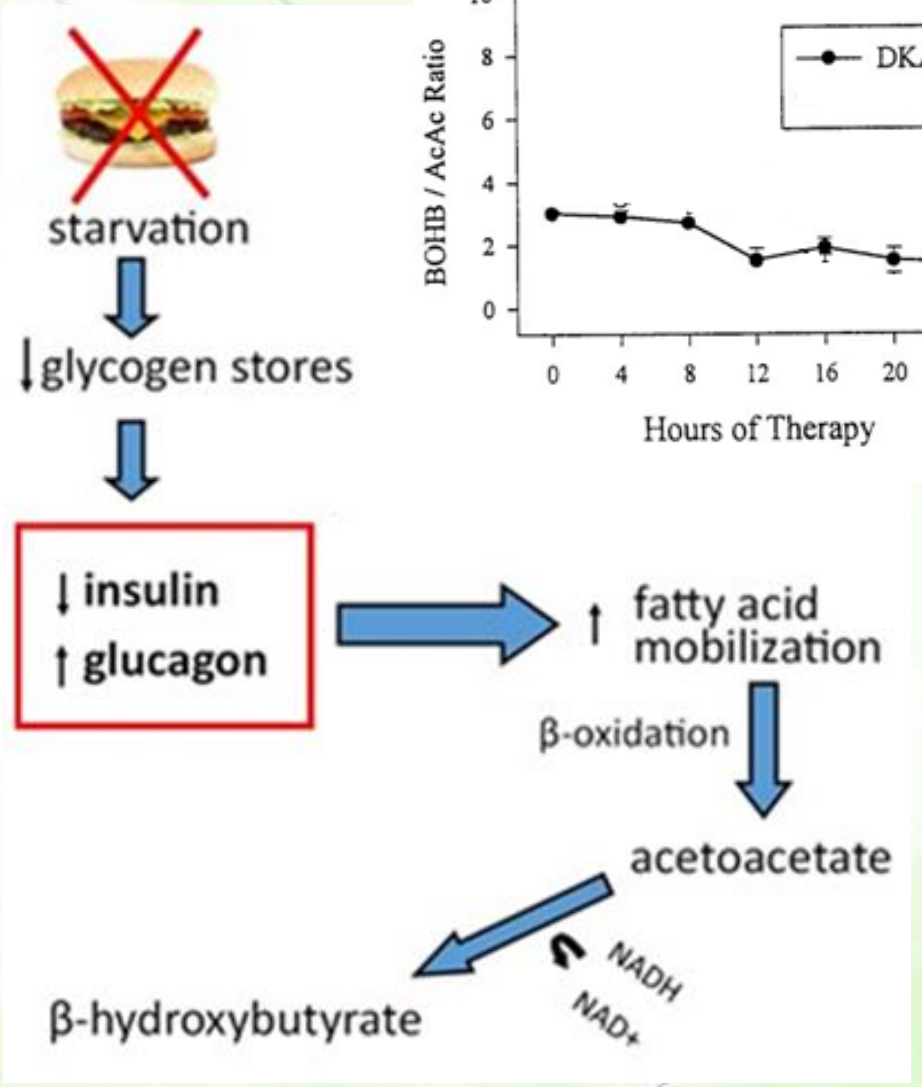


When cellular glucose is low, oxaloacetate is diverted into gluconeogenesis. In addition,

1. Excess FA breakdown produces large amounts of acetyl CoA.
2. Acetyl CoA inhibits pyruvate dehydrogenase.
3. Pyruvate is diverted toward oxaloacetate by pyruvate carboxylase.
4. Oxaloacetate is converted to malate,
5. and then back to oxaloacetate in the cytosol
6. Gluconeogenesis is activated and oxaloacetate is depleted.
7. Acetyl CoA is diverted into ketogenesis

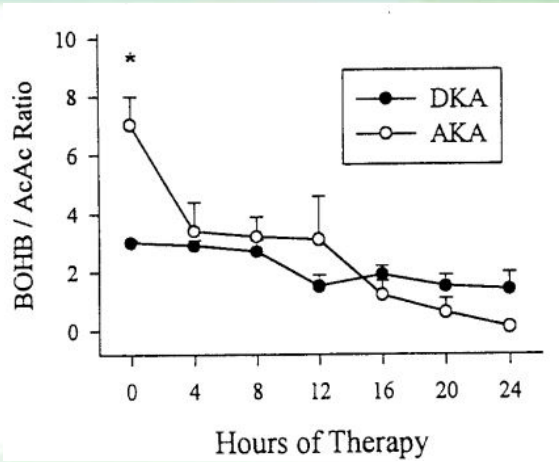
Diabetic ketoacidosis

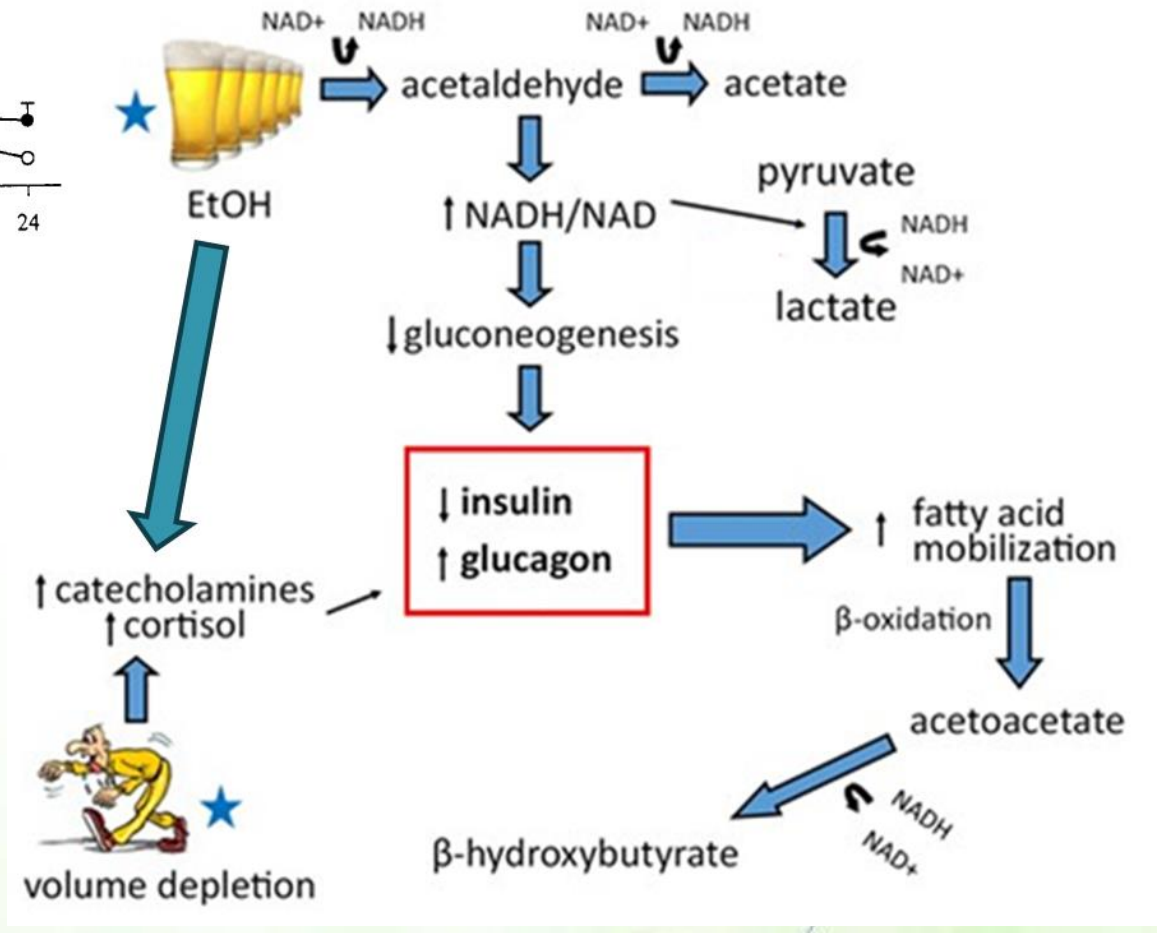
- Normally,
  - Levels of ketone bodies: <3 mg/dl
  - NAD+:NADH is 10:1
  - 3HB:AcAc is ~1:1
- Under uncontrolled diabetes,
  - Levels of ketone bodies: 90 mg/dl and urinary excretion of ketone bodies may be 5,000 mg/24 hours.
- The end-results:
  - Acidemia (ketoacidosis)
  - Dehydration
  - Fruity odor of breath



Alcoholic ketoacidosis

- There is also,
  - Acidemia (ketoacidosis)
- But,
  - 3HB:Ac is ~3:1
    - *The ratio gets back to 1:1 after a few hours*
  - *Gluconeogenesis is suppressed.*
  - *Pyruvate is converted to lactate leading to hypovolemia, heart failure, and sepsis.*





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