KB Facts

1. Produced by liver (mainly) - when OA becomes limiting
2. Primary (or very important) metabolic fuels of heart & skeletal muscle
3. Used by all organs (even brain) in times of starvation
4. Produced in excess in Diabetes Mellitus (also in Type I diabetes)
5. Ketogenesis = Mitochondrial reaction

Typical KBs

- Acetoacetate
- β-Hydroxybutyrate *
- Acetone **

* Not actually a ketone
** Fruity breath in diabetes

They can ↓ pH of blood from 7.4 to < 7 (e.g., 6.8) in diabetics

KB Formation - starts with β-ketothiolase running in reverse (of β-oxidation direction)

Go back and look at β KT step on page 18 - see similarity to citrate synthase (Claisen Reaction)
**KB Formation and Utilization**

**In Liver**
1. $\text{AcCoA}$
2. $\beta$-OH butyrate
3. $\text{AcCoA}$

$\beta$-OH butyrate cannot escape liver cell - must be converted to KB

$\text{AcCoA}$

**In Target Tissue (e.g. muscle)**
4. Aceto Acetyl CoA
5. Aceto Acetate

- Acetate Acetyl CoA
- NAD$^+$ NADH
- B-E butyrate DH

Follow numbers 1 - 6

**Diabetes Scenario**

- Pancreas β cells release insulin in response to food
- Insulin triggers Glucose uptake
- Insulin signaling defective:
  - Glucose not taken up from blood
  - Glycogen reserves very small

Liver cell (but all cells are defective in Glucose uptake)

**BLOOD**

In "out of control" diabetes

- [G] = 300+ mg / 100 mL (normal = 100 mg / 100 mL or 5 mM)
- [KB] = 15 - 25 mM (normal = <0.2 mM)
- pH as low as 6.8 (from 7.4)

Acidosis

Kidney tries to excrete H$^+$, [G]

Thirst ↑ to replace lost H$_2$O