



- ✓ What is the precursor for Ketone bodies formation – For ketone bodies formation, **Acetyl CoA is required.**
- ✓ From Where, this Acetyl CoA comes for ketone bodies formation –
  1. **Oxidation of fatty acid**
  2. **Oxidation of Pyruvate**

When glucose level declines in our body (During starvation condition)



Brain preferentially use glucose but during stress condition like starvation, brain can adapt to the use of ketone bodies like Acetoacetate and Beta- hydroxybutyrate.



But fatty acid cannot be utilised directly by brain

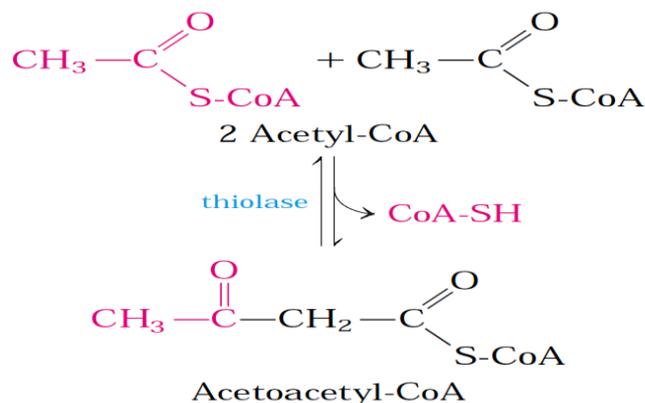


The reason is fatty acid can not cross blood brain barrier.

### Synthesis of ketone bodies

It involves 4 steps.

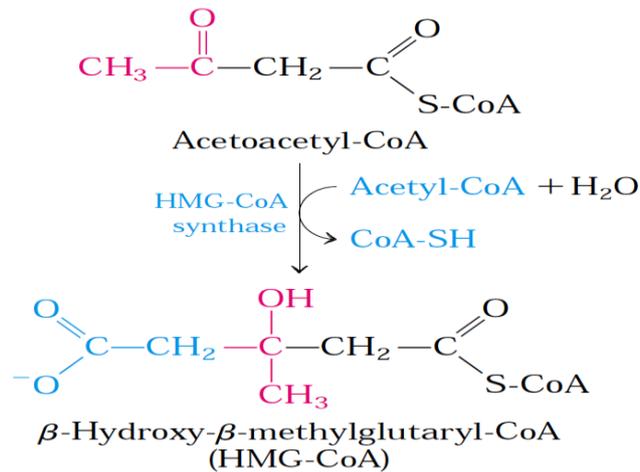
Step 1 is condensation of 2 molecules of acetyl CoA. Reaction is catalysed by thiolase enzyme. Product formed is Acetoacetyl CoA.



(Source-Lehninger)

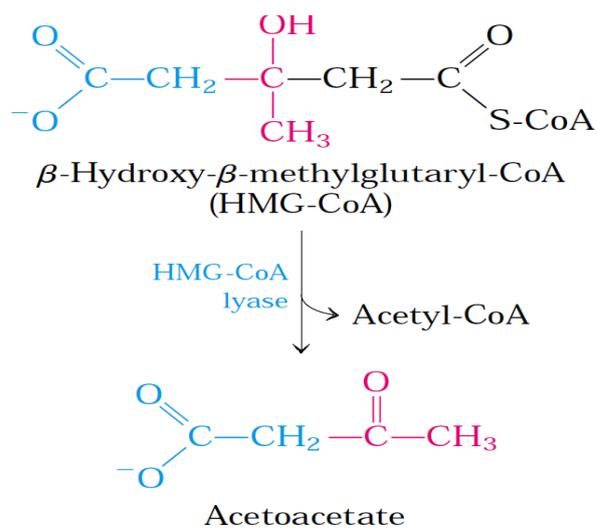
Step 2 involves combining of Acetoacetyl CoA with another molecule of acetyl CoA.

The reaction is catalysed by hydroxy-methyl glutaryl-CoA synthase (HMG-CoA synthase). Product formed is hydroxy-methyl glutaryl-CoA.



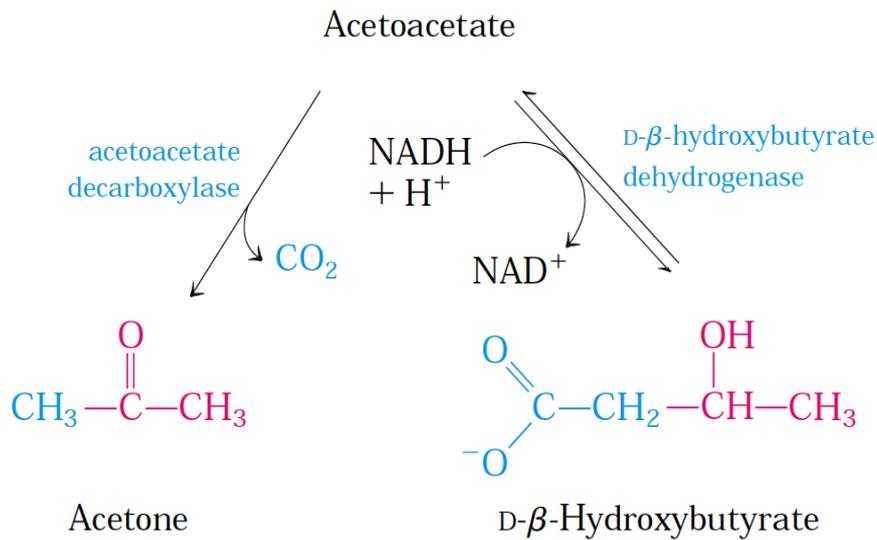
Source-Lehninger)

Step 3 involves Cleavage of hydroxy-methyl glutaryl-CoA by HMG-CoA lyase. It is present only in mitochondrial matrix.



Source-Lehninger)

Step 4 includes Acetoacetate and beta hydroxy butyrate.



Source-

Lehninger)

- ✓ Liver is only producer of ketone bodies for other tissues.
- ✓ Ketone bodies can be used as a fuel in all other tissues except liver because it has lack of an enzyme called **Beta-ketoacyl CoA transferase**.

Q. The question is why ketone bodies produced more during starvation condition.

Ans. Because starvation stimulates **GLUCONEOGENESIS** which depletes citric acid cycle intermediates, thus diverting acetyl CoA to Ketone body formation.

- ✓ **Acidosis**- When acetoacetate and beta hydroxy butyrate level increase in blood, the condition is known as Acidosis.
- ✓ Extreme acidosis can cause coma and sometimes death.
- ✓ In diabetic patients, ketone bodies formed crosses a limit above 3mg/100ml in blood and concentration above 125 mg in 24 hours. This condition is called **Ketosis**.
- ✓ When ketosis occurs with acidosis , the combined condition is called **Ketoacidosis**.