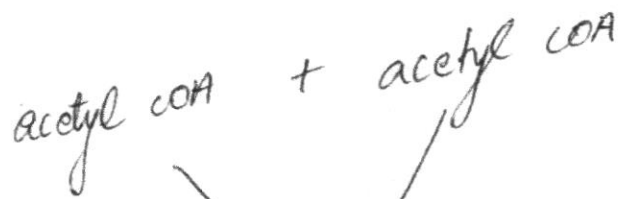
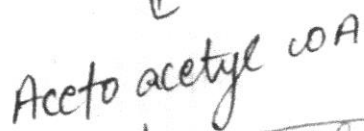


②

②

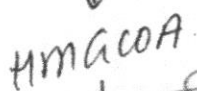


Thiolase

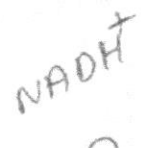
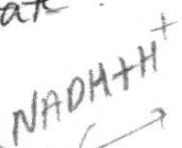
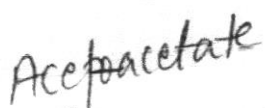
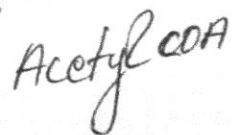


Hmg CoA synthase

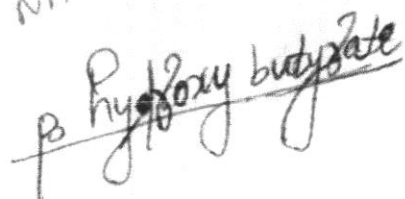
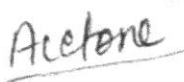
Rate limiting enzyme

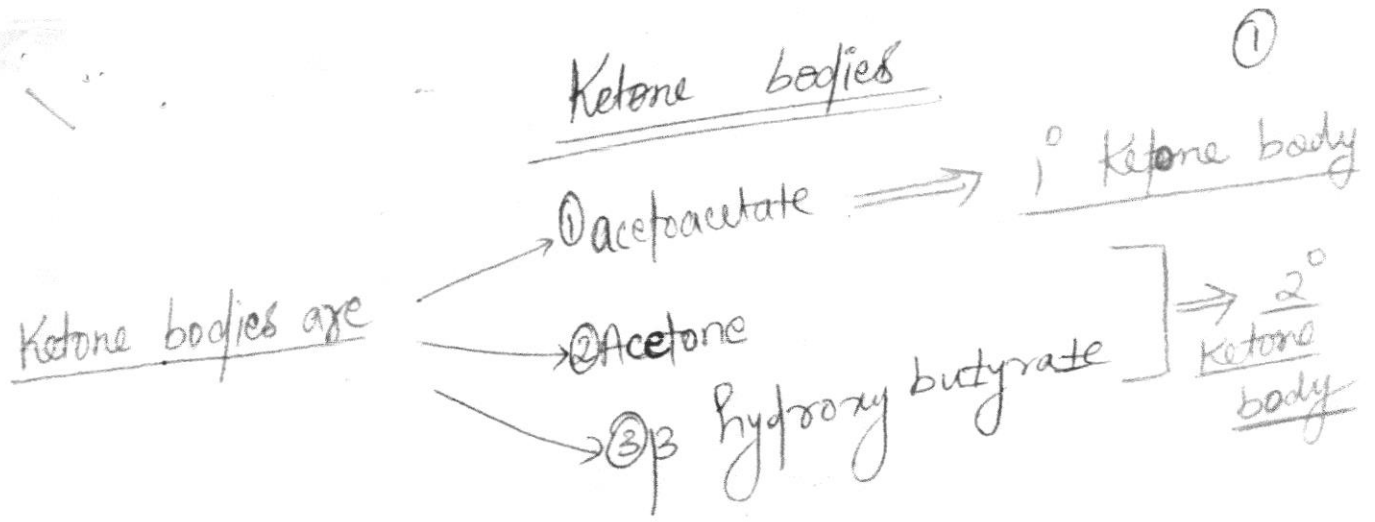


Hmg CoA lyase



spontaneous conversion i.e. non enzymatic





## Synthesis of Ketone bodies / Ketogenesis

- Site  $\rightarrow$  liver mitochondria
- Starting material  $\rightarrow$  Acetyl CoA from  $\beta$  oxidation
- Rate limiting enzyme  $\rightarrow$  HMG CoA synthase

## Steps of Ketogenesis

- ① Condensation
- ② Production of HMG CoA
- ③ Lysis
- ④ Reduction
- ⑤ Spontaneous decarboxylation



Ketosis

- (N) Ketone bodies present in blood  $< 1 \text{ mg/dl}$
- Rate of synthesis of ketone bodies exceeding the ability of extrahepatic tissues to utilize them  $> 1 \text{ mg/dl}$

Accumulation of ketone bodies  
 ↳ leads to  
 ① ketonemia  
 ② ketonuria  
 ③ smell of acetone breath  
 (also known as ketosis)

gives fruity odour in breath

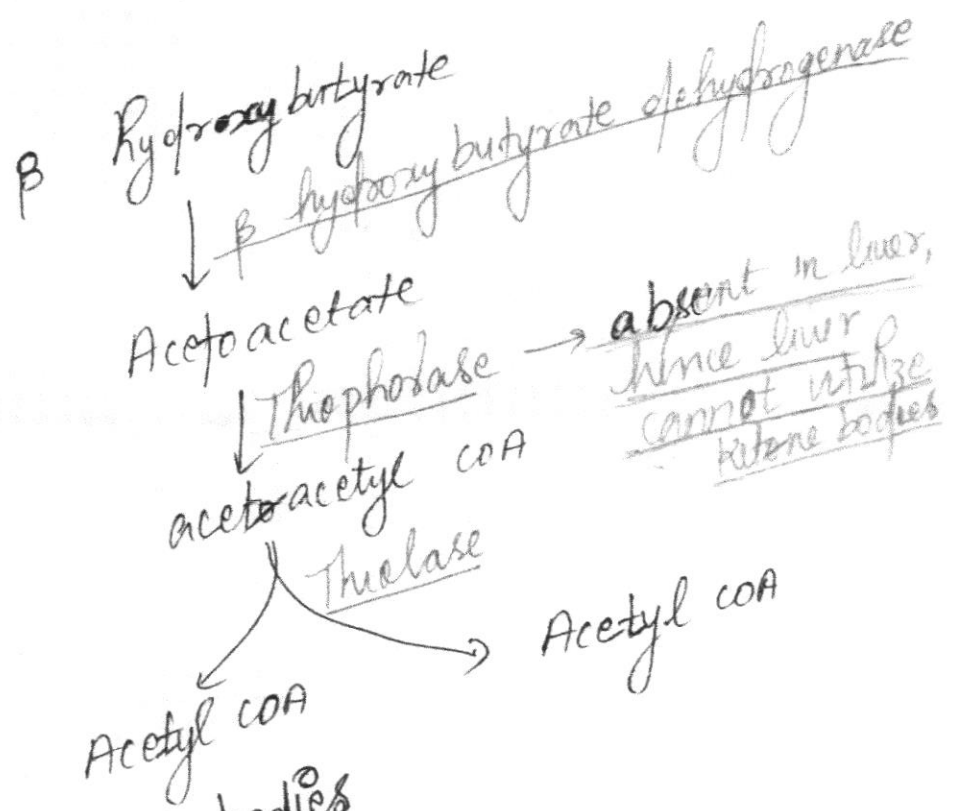
Causes of Ketosis

- ① Uncontrolled DM
- ② Starvation



## Degradation of Ketone bodies / also K/c/o Ketolysis

- Ketone bodies are degraded to acetyl CoA
- However, acetone cannot be catabolized further  $\rightarrow$  hence not used as a fuel source.



## Utilization of Ketone bodies

\* Ketone bodies being water soluble, transported in the blood to various extrahepatic tissues



↓  
This is how Ketone bodies serves as fuel source replacing glucose in starvation

② Uncontrolled DM

Insulin ⊖ lipolysis  
↓  
when there is insulin deficiency

↑ lipolysis

↑ fatty acid released due to lipolysis

↓  
more acetyl CoA formed which ~~enter~~ exceeds the citric acid cycle processing

+ oxaloacetate depleted due to gluconeogenesis

↓  
Acetyl CoA is diverted to Ketone body production

③ Hyperemesis gravidarum





① Starvation / prolonged fasting

Due to non availability of glucose, body depends on fatty acids for its energy requirement

mobilization of fatty acids from stored triglyceride in adipose tissue

oxidation of fatty acids

↓ ↓ acetyl CoA (overproduction) exceeding the capacity of citric acid cycle to process them

depletes oxaloacetate gluconeogenesis

both together acetyl CoA stops citric acid cycle

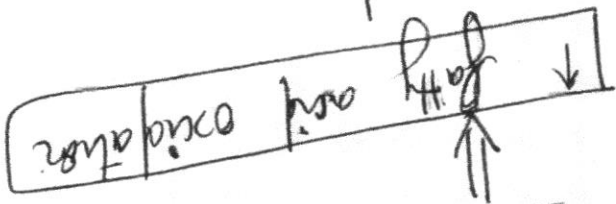
New acetyl CoA is diverted to ketone body production



Report of a experiment

mitochondria  
and carnitine which is transported across the  
long chain fatty acid  
from carnitine used  
forming

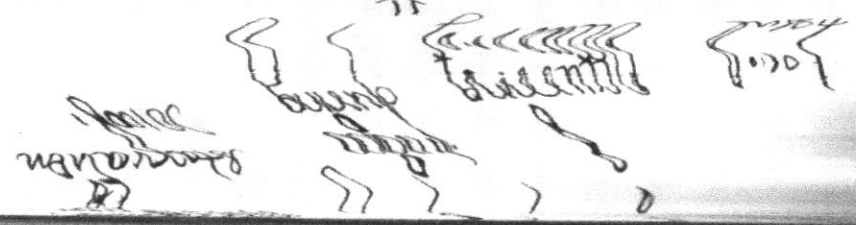
Synthesis of ketone  
bodies



Transferrase  
carnitine  
polymers  
CPT-I

The activity of this enzyme is in starvation.

Synthesis of ketone bodies  
FFA are



# (\*) Regulation of Ketone body metabolism (7)

glucagon  $\rightarrow$   $\uparrow$  Ketogenesis  
insulin  $\rightarrow$   $\downarrow$  Ketogenesis

1) Liberation of free fatty acid from adipose tissue occurring during starvation.

$\Downarrow$   
ffa are in turn used for synthesis of ketone bodies

2) CPT-I  $\rightarrow$  The activity of this enzyme is  $\uparrow$  in starvation.

Carnitine acetyltransferase I  
 $\downarrow$  palmitoyl

$\downarrow$  imp for fatty acid metabolism

Transfers  $\downarrow$  long chain fatty acid from coenzyme A to carnitine forming acyl carnitine which is transported across the mitochondria

$\Downarrow$   
 $\uparrow$  fatty acid oxidation

$\downarrow$   
 $\uparrow$  synthesis of ketone bodies



Revised for oxidation

3)

## concentration of oxaloacetate

- both starvation and uncontrolled  $\downarrow$  depletes the level of oxaloacetate



low level of oxaloacetate diverts the bulk of acetyl CoA to the synthesis of ketone bodies

$\Downarrow$   
overproduction of ketone bodies

## Features of Ketosis

### 1) metabolic acidosis

Acetoacetate  $\rightarrow$   $\beta$  hydroxybutyrate are acids  
 $\Downarrow$   
their accumulation causes

② Reduced buffers ( $\text{CO}_2$ ,  $\text{HCO}_3^-$  is used up for buffering of these acids)

Betsy

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MD, FRCOG, DNB, MICOG  
PRINCIPAL

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# Kussmaul's respiration

(9)



Acidotic breathing due to compensatory  
hyperventilation

(4) Osmotic diuresis → lead to dehydration

(5) Dehydration

→ Investigation

→ S. electrolytes

→ S. glucose

→ acid base parameters

→ Test for ketone bodies

→ Rotheras test

→ Gerhardt test

→ Rx of ketosis

- fluid replacement

- electrolyte infusion

