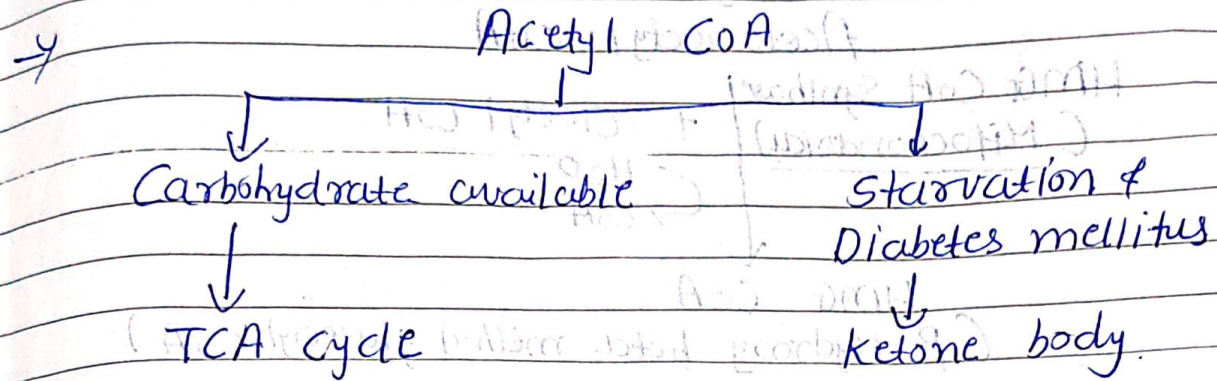
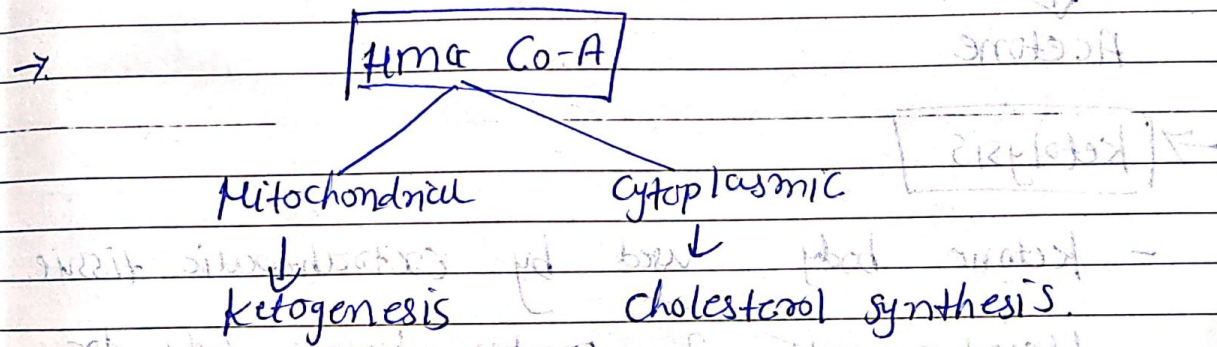
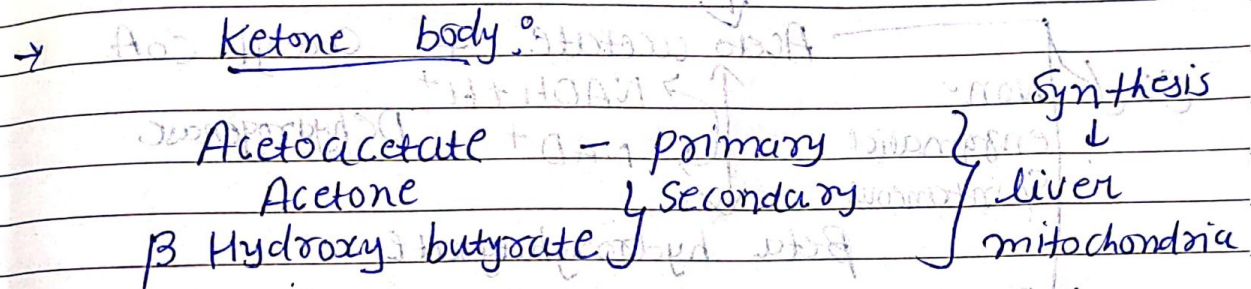


# metabolism of ketone bodies.

→ Oxidation of fat  
↓  
Carbohydrate required



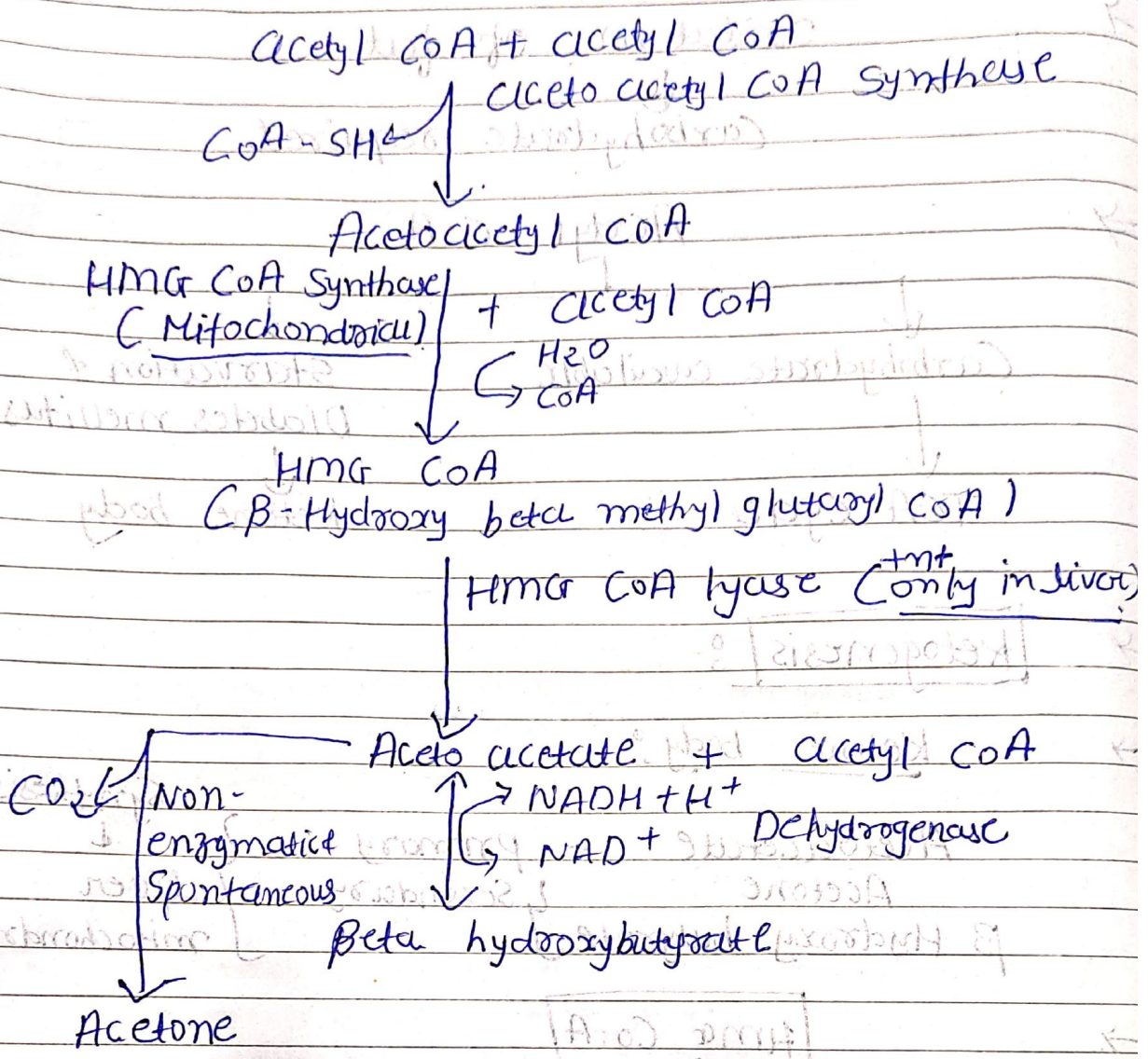
→ ketogenesis :-



→ Acetoacetate → ketogenic amino acid  
↓  
leucine  
lysine  
tyrosine  
phenylalanine

→ Hmc-CoA lyase - present only in liver.

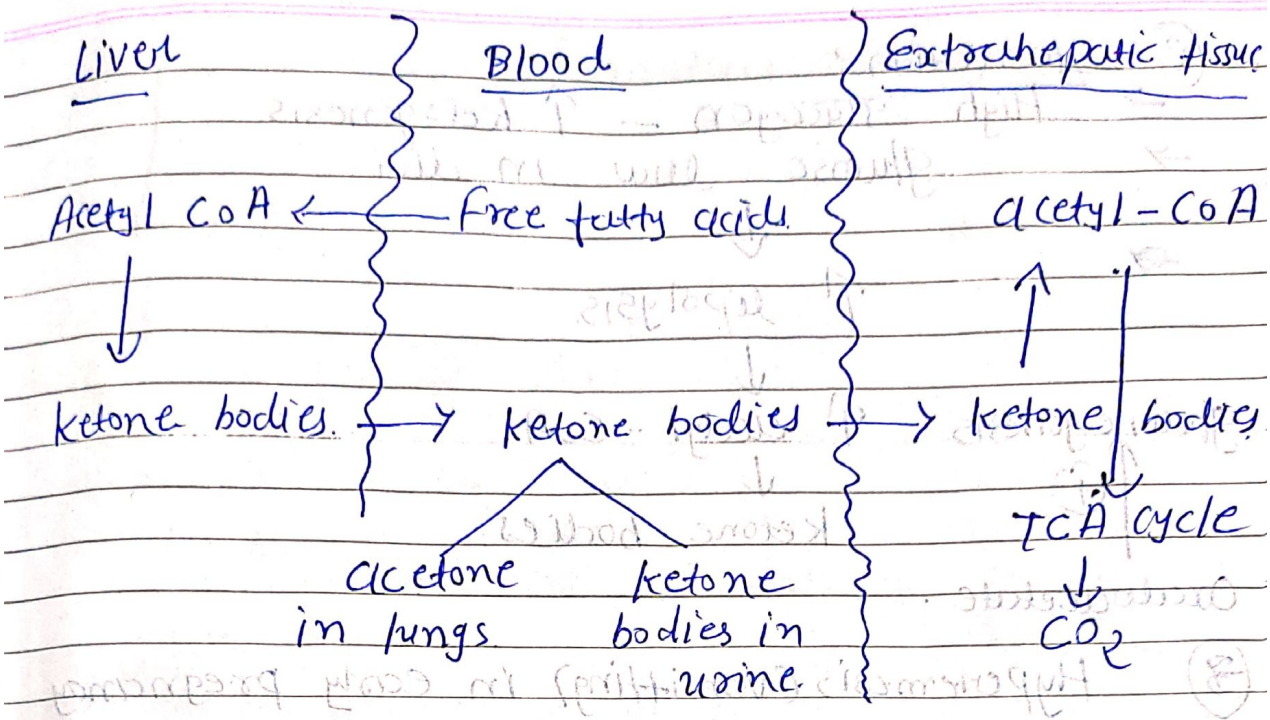
Metabolism of Ketone bodies



→ Ketolysis

- ketone body used by extrahepatic tissue.
- Heart muscle & Renal cortex prefer ketone bodies for fuel than glucose.
- Skeletal muscle & Brain use ketone body if glucose not available.

→ Acetoacetyl CoA + Succinyl CoA + thiophosphorase → Acetoacetyl CoA + Succinate ↓  
β oxidation pathway



ketone body - formation, utilization & excretion

→ Ketosis

Normal concentration

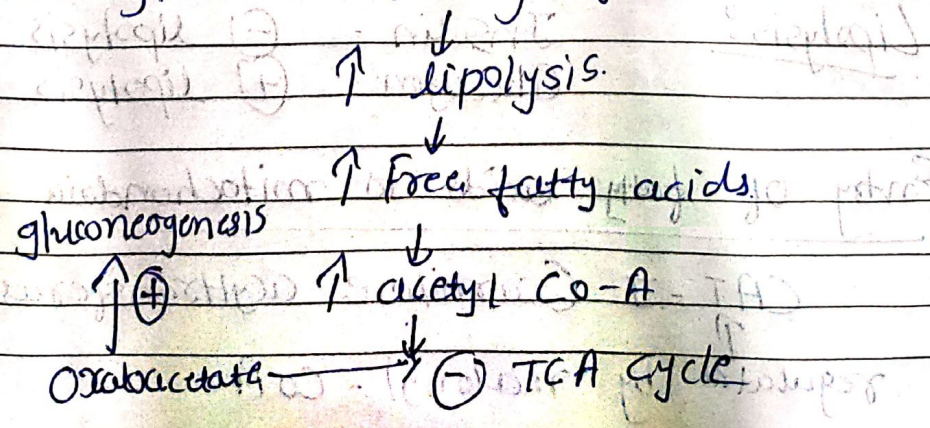
- Blood level  $\Rightarrow$   $< 1 \text{ mg/dl}$
- urine level  $\Rightarrow$  Not detectable

→ Ketosis  $\rightarrow$  Ketonemia  
 Ketonuria  
 Smell of acetone in breath

→ Causes ?

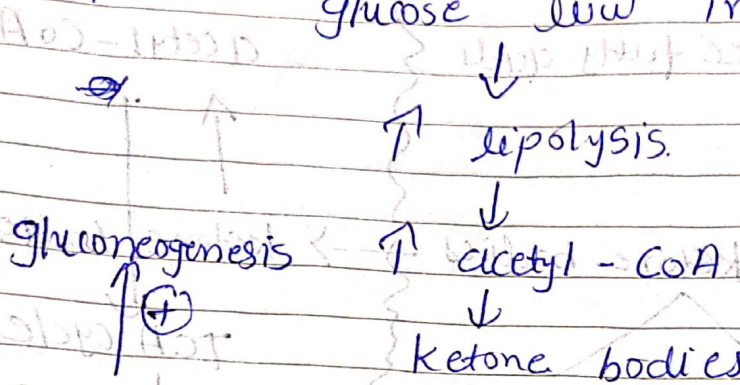
① Diabetes mellitus

- uncontrolled diabetes mellitus
- Deficiency of insulin



② Starvation:

→ High glucagon - ↑ ketogenesis  
→ glucose low in diet.

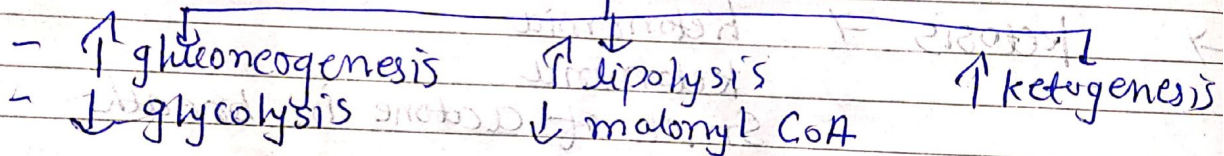


③ Hyperemesis (vomiting) in early pregnancy

→ Clinical aspect of ketogenesis:

Starvation & diabetes mellitus

↓  
↑ glucagon



→ Regulation of ketogenesis:

③ step

① Lipolysis:

Insulin - (-) lipolysis  
Glucagon - (+) lipolysis.

② Entry of fatty acids to mitochondria

- CAT - I (Carnitine acyltransferase I)  
↑  
regulated by malonyl-CoA

→ ↑ glucagon - ↓ malonyl-CoA - ↓ CAT-I activity  
 ↓  
 ↓ ket ↑ β oxidation

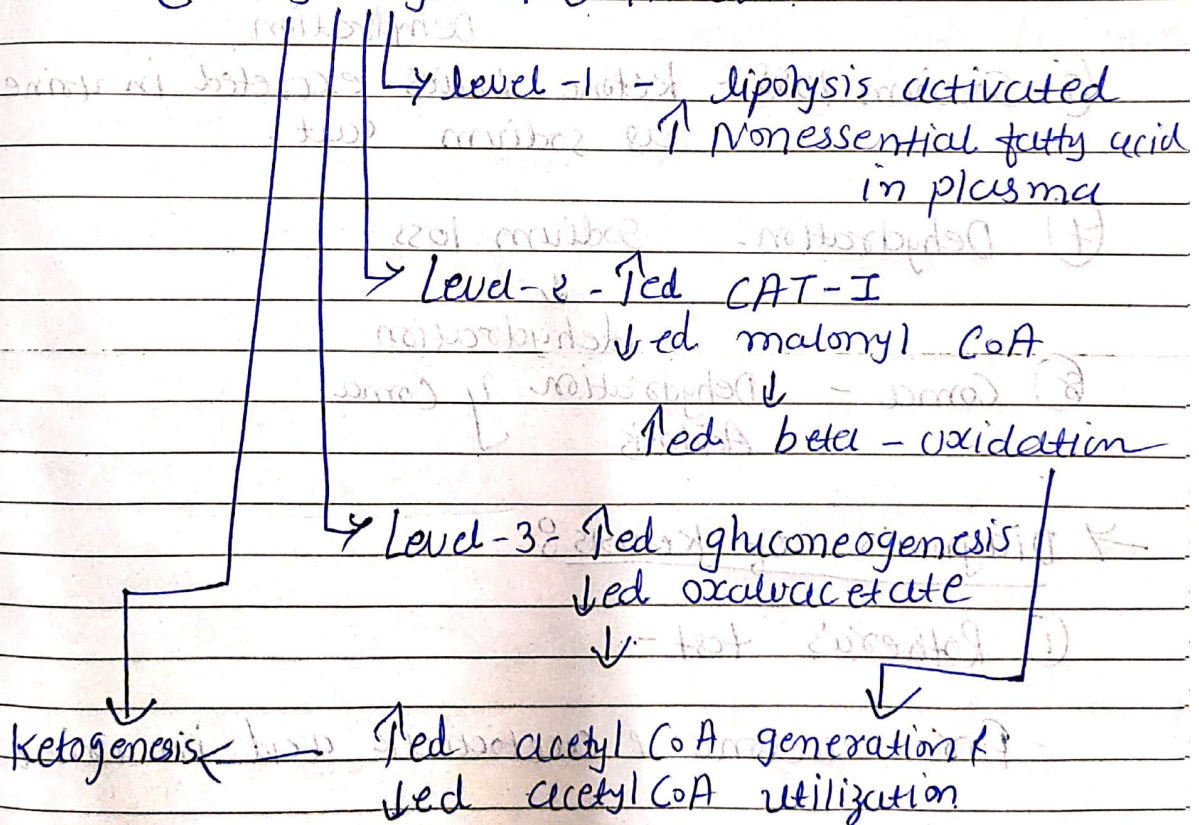
B) Oxidation of Acetyl-CoA

↑ acetyl CoA

↓ oxaloacetate availability for TCA cycle

↑ acetyl CoA → ketogenesis

→ Starvation / Diabetes mellitus  
 ( ↑ glucagon / ↓ insulin )



→ Salient feature of ketosis:-

- (1) Metabolic acidosis - ↑ acetoacetate  
↑ β-Hydroxybutyrate
- (2) Reduced buffers - Bicarbonate used up for buffering of ketone bodies
- (3) Kussmaul's respiration - acidotic breathing due to compensatory hyperventilation
- (4) Smell of acetone in patient's breath
- (5) Osmotic diuresis - Acetoneuria  
↓  
osmotic diuresis  
↓  
Dehydration
- (6) Sodium loss - ketone bodies excreted in urine as sodium salt.
- (7) Dehydration - Sodium loss  
↓  
Dehydration
- (8) Coma - Dehydration & Coma  
Acidosis

→ Diagnosis of ketosis:-

- (1) Rothera's test -  
- for acetone & acetoacetic acid in urine  
- purple color at junction of sodium nitroprusside & liquor ammonia in saturated ammonium sulfate sample.  
- strip test also available

(2) Gerhardt's test for acetoacetic acid:

- Not sensitive
- False positive test - salicylates

→ Differential diagnosis of ketosis:

Diabetes ketoacidosis → Benedict <sup>test</sup> positive  
Rothera test positive

Starvation → Benedict test negative  
Rothera test positive

→ management of ketoacidosis:-

- I.V. Insulin & glucose
- fatal hypokalemia occur
- I.V. bicarbonate
- maintenance of electrolyte & fluid balance