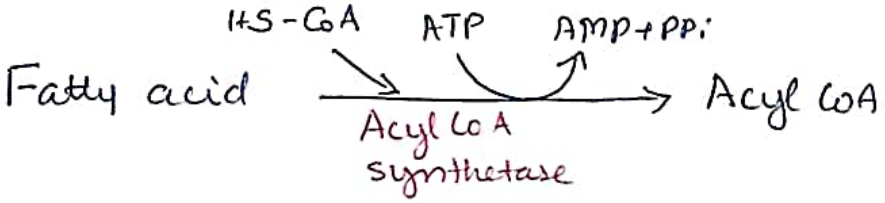
BETA OXIDATION OF FATTY ACIDS

* Major pathway by which f.a are oxidised in the body.
* Only type of oxidation of fatty acids which gives energy
* Oxidation occurs at β carbon; 2 carbon units are removed as acetyl CoA
* Fatty acids have to be first activated to Acyl CoA (in cytoplasm)
* β oxidation occurs in mitochondria

Activation of fatty acids



Acyl CoA synthetase (thiokinase) is located on outer mitochondrial membrane

So the reaction occurs in cytoplasm.

Palmitic acid is the most common fatty acid oxidised in the body

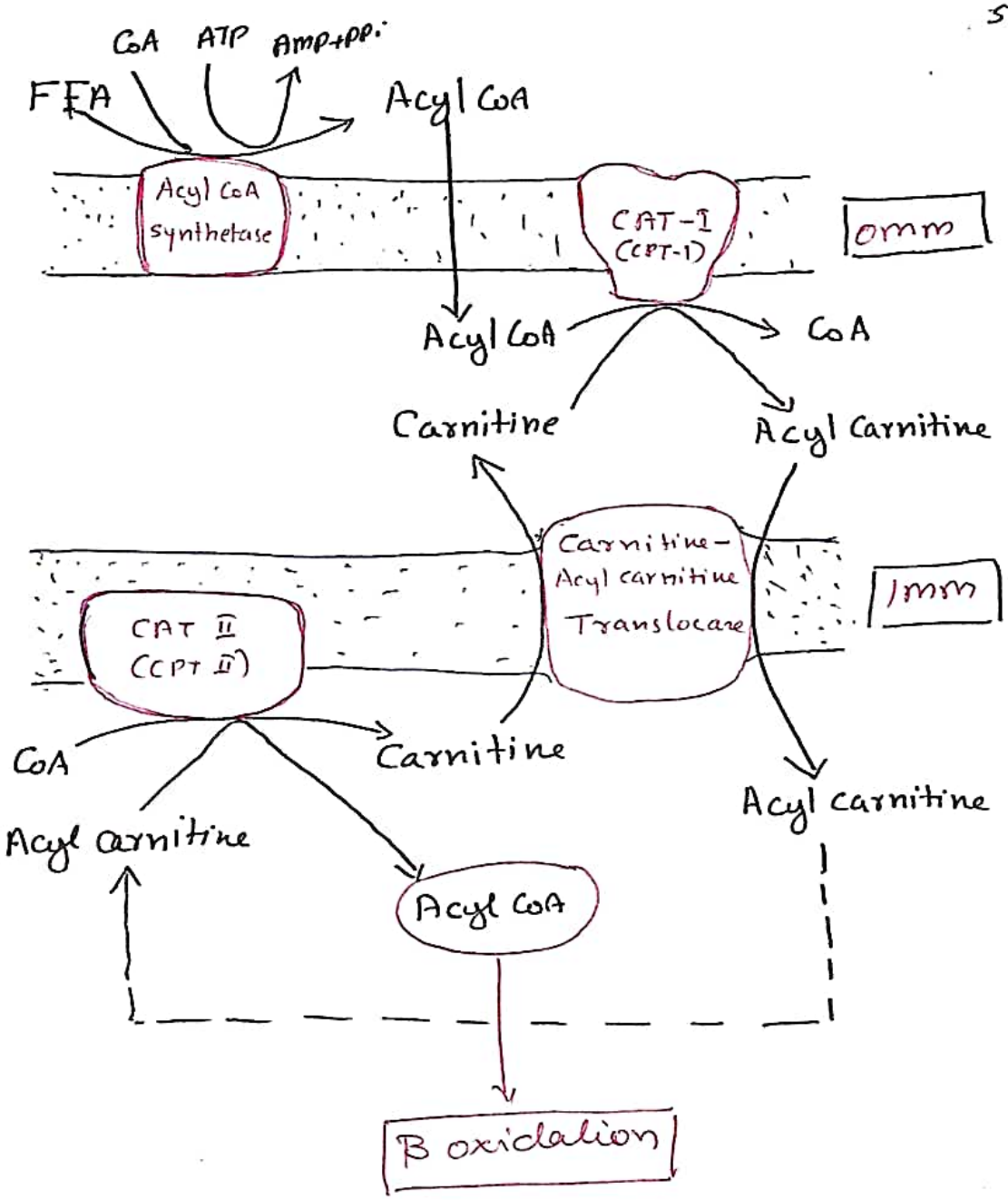
Transport into mitochondria

Steps of β oxidation occurs in mitochondria. So acyl CoA has to be transported to mitochondria

Short and Medium chain acyl CoA can cross the IMM and directly enter mitochondria

Long chain acyl CoA cannot cross IMM. They require **Carnitine**

Carnitine is β Hydroxy γ Trimethyl Ammonium butyrate. It is produced from Lys and Met ~~liver~~ in liver and kidney



→ Acyl CoA reaches the intermembrane space

→ Combines with carnitine to form acyl carnitine by the enzyme Carnitine Acyl transferase I (CAT-I) or Carnitine Palmitoyl transferase I (CPT-I) located on inner side of omm

S-22

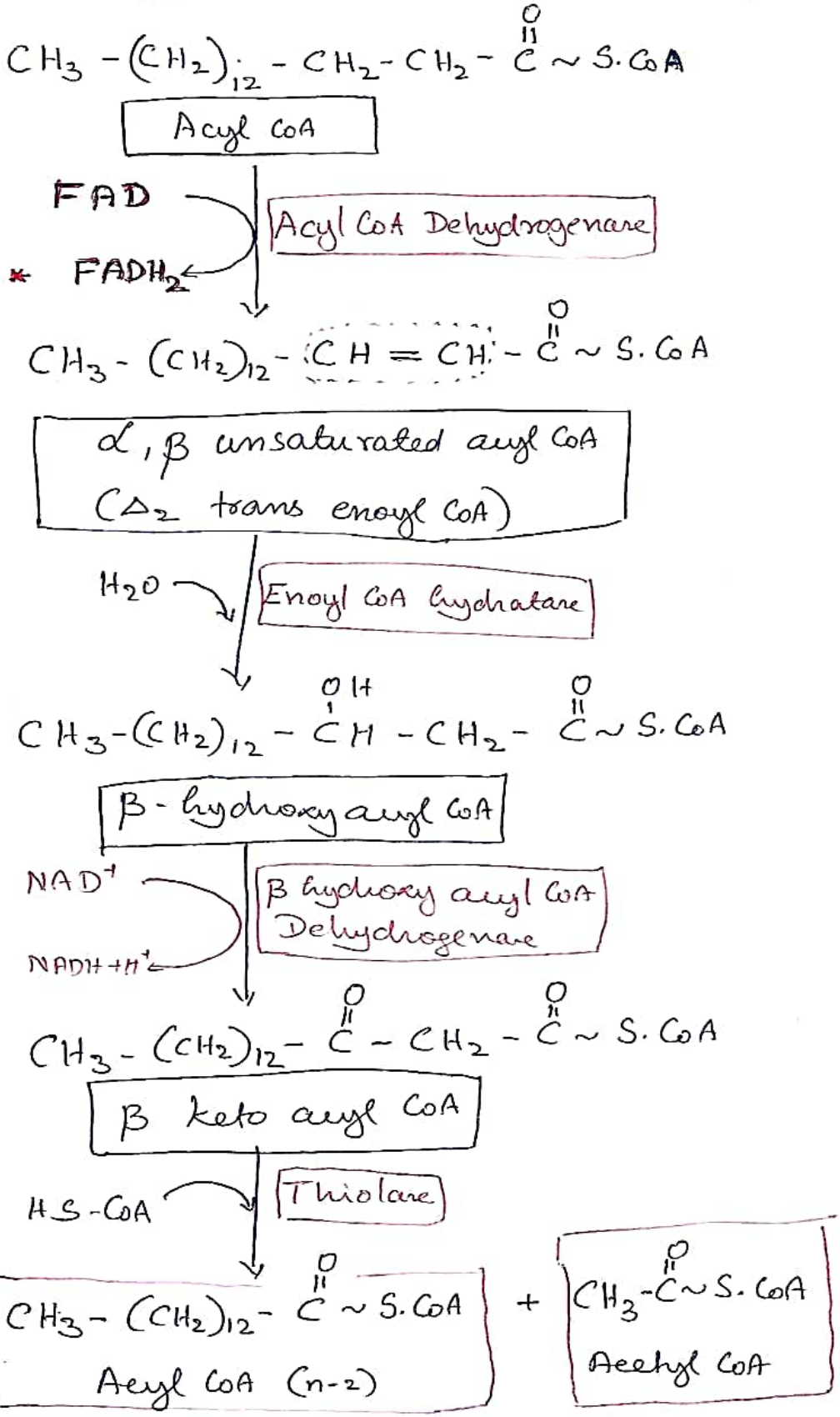
→ Acyl carnitine crosses IMM with the help of transmembrane transporter called "Carnitine - Acyl carnithe translocare"

→ Inside the mitochondria, acyl carnitine is converted to acyl CoA and carnitine by the enzyme CAT II or CPT II located on the inner side of IMM

→ Carnitine goes out through the translocase

→ Acyl CoA undergoes β oxidation

STEPS


CH3 - (CH2)12 - CH2 - CH2 - C ~ S.CoA
Acyl CoA
FAD
FADH2
Acyl CoA Dehydrogenare
CH3 - (CH2)12 - CH = CH - C ~ S.CoA
α, β unsaturated acyl CoA
(Δ2 trans enoyl CoA)
H2O
Enoyl CoA hydratare
CH3 - (CH2)12 - CH - CH2 - C ~ S.CoA
OH
β - hydroxy acyl CoA
NAD+
NADH + H+
β hydroxy acyl CoA Dehydrogenare
CH3 - (CH2)12 - C - CH2 - C ~ S.CoA
β keto acyl CoA
HS-CoA
Thiolare
CH3 - (CH2)12 - C ~ S.CoA
Acyl CoA (n-2)
+
CH3 - C ~ S.CoA
Acetyl CoA

The ~~cycles~~ reactions will repeat till the fatty acid is split into acetyl CoA molecules

ENERGETICS

→ Initial activation (Acyl CoA synthetase) needs 2 high energy phosphates (ATP → AMP)

→ In each cycle,

Acyl CoA DH → 1 $FADH_2$
β OH acyl CoA DH → 1 NADH
} 1.5 + 2.5 = 4 ATP

→ Acetyl CoA in TCA cycle → 10 ATP

Energy yield from palmitic acid

Acyl CoA synthetase : −2 ATP

7 cycles = 7 × 4 ATP = 28 ATP

8 Acetyl CoA = 80 ATP

Total = 106 ATP

Energetics of β oxidation of unsaturated fatty acids.

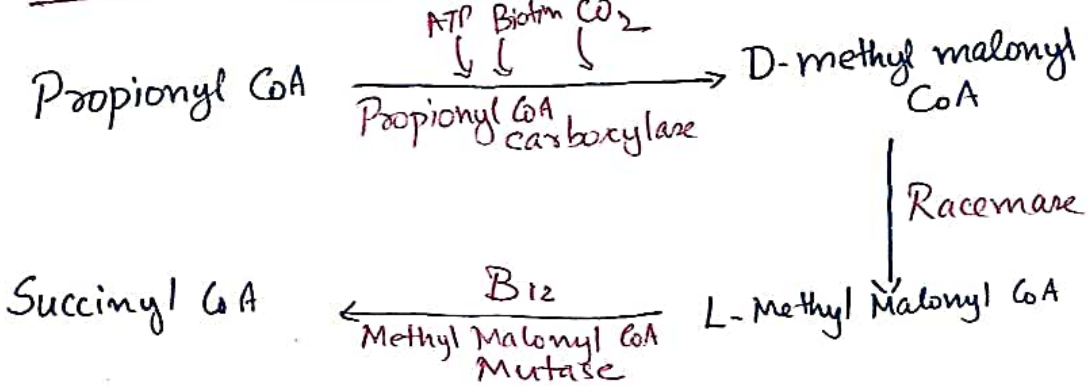
Similar to saturated fatty acids.
But, in the cycle where the double bond comes in ~~β~~ α, β position,
Acyl CoA dehydrogenase step does not operate. So $FADH_2$ will not be produced.

So the total energy production will be equal to that of the corresponding saturated fatty acid — No: of double bonds X 1 ATP

β oxidation of odd chain fatty acids

Fatty acids with odd number of C atoms are oxidised by β oxidation till a 3 C unit remains (Propionyl CoA)

Fate of propionyl CoA



Succinyl CoA enters TCA cycle and can be used for gluconeogenesis
∴ Propionyl CoA from odd chain fatty acids is the only gluconeogenic substrate from fatty acids.

β oxidation of VLCFA

VLCFA are oxidised in peroxisomes
The carbon chain is trimmed to make it a LCFA (Approx 18C). Then it is oxidised ~~in~~ in mitochondria.

Zellweger syndrome

Due to defect in peroxisomal β oxidation of VLCFA. This occurs due to a defective protein targetting.
Manifests as neurological damage

α oxidation & Refsum's disease

α oxidation occurs to fatty acids in which a branch / methyl group prevents β oxidation. Fatty acid is then oxidised and single carbon units are released till branching point is over

Eg: Phytanic acid
(Present in chlorophyll, milk and milk products)

Defective α oxidation of phytanic acid leads to Refsum's disease.

Enzyme deficient is α hydroxylase or phytanic acid oxidase.

Manifests as neurological damage

ω oxidation

When β oxidation is defective, the ω carbon is oxidised to $^{-}COOH$ - This causes dicarboxylic aciduria.

Jamaican vomiting sickness

Vomiting and hypoglycemia due to eating unripe fruit of akee tree.

It contains a toxin "Hypoglycin" which inhibit Short and Medium chain acyl CoA dehydrogenase