Reactions of Beta oxidation

- Sequential removal of two carbon unit at a time removed as acetyle coA
- Repeating sets of four reactions catalyzed by four enzymes result in the final degradation of a fatty acid into acetyl CoA, FADH2, NADH +H
- After every set a molecule of acetyle CoA and a fatty acyl CoA two carbon shorter than the previous one is formed
- The number of times the reactions set is repeated is calculated as (n/2)-1
- In the end the number of acetyle CoA moleclues formed is calculated as follows n/2
- And number of reducing equivalent formed is calculated as (n/2)-1
- Where n is the number of carbon atoms of fatty acid

- Theses reactions are :
- 1.Dehydrogenation
- 2. Hydration
- 3. Dehydrogenation
- 4.thiolysis

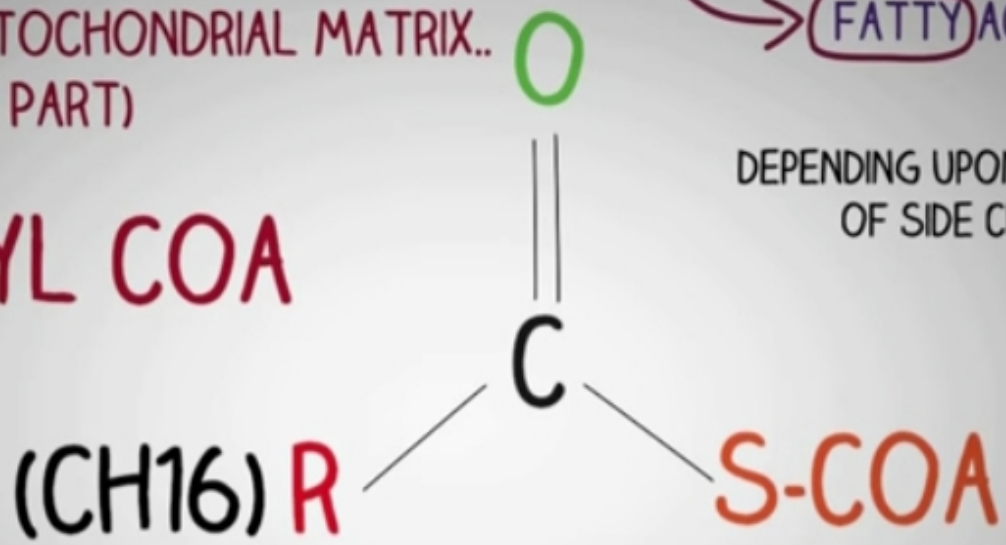
FATTY ACID

FATTY ACEYL COA

WHAT HAPPENS IN THE MITOCHONDRIAL MATRIX..
(COMPLEX PART)

DEPENDING UPON LENGTH
OF SIDE CHAIN

PALMITOYL COA



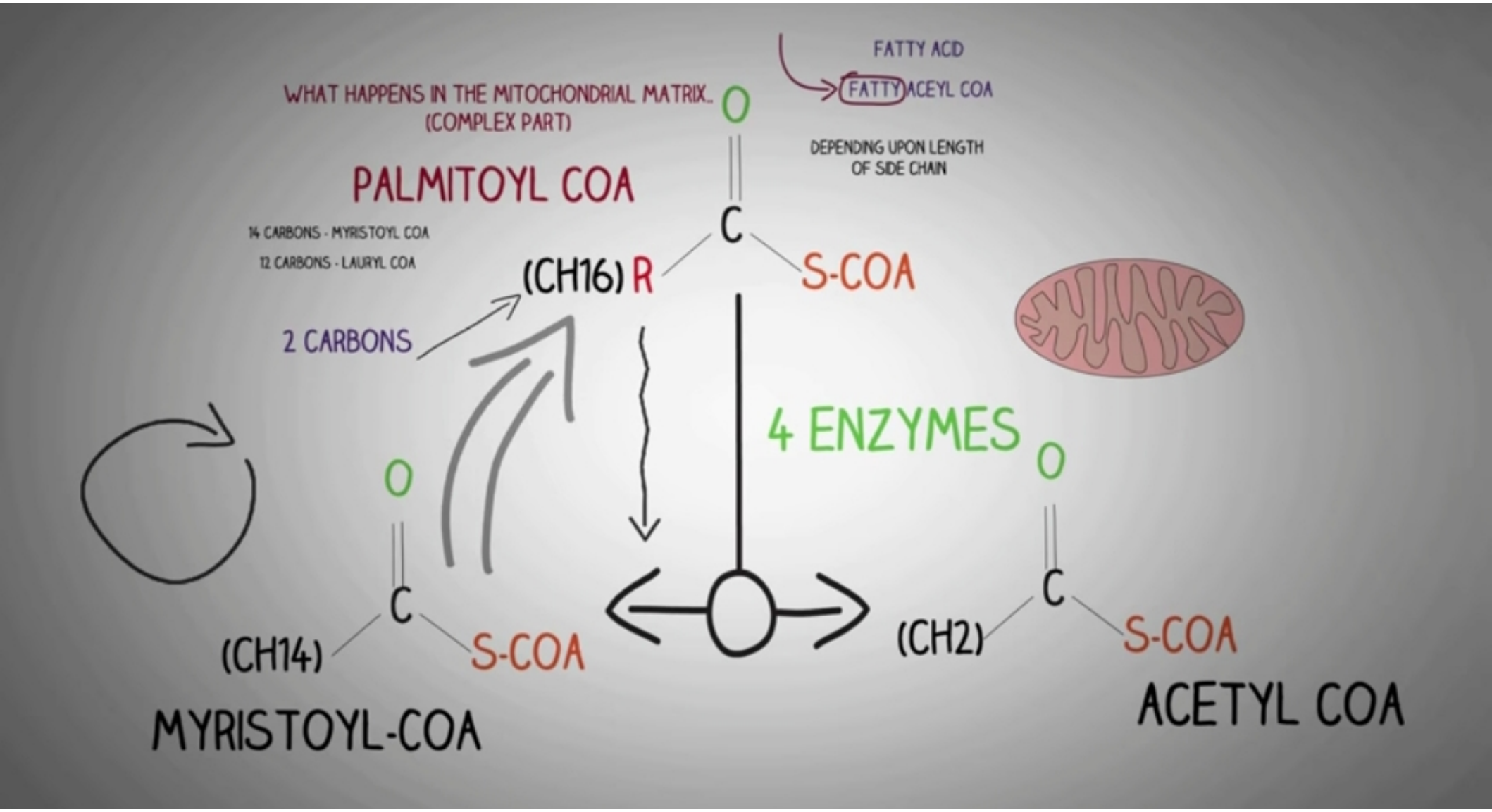
(COMPLEX PART)

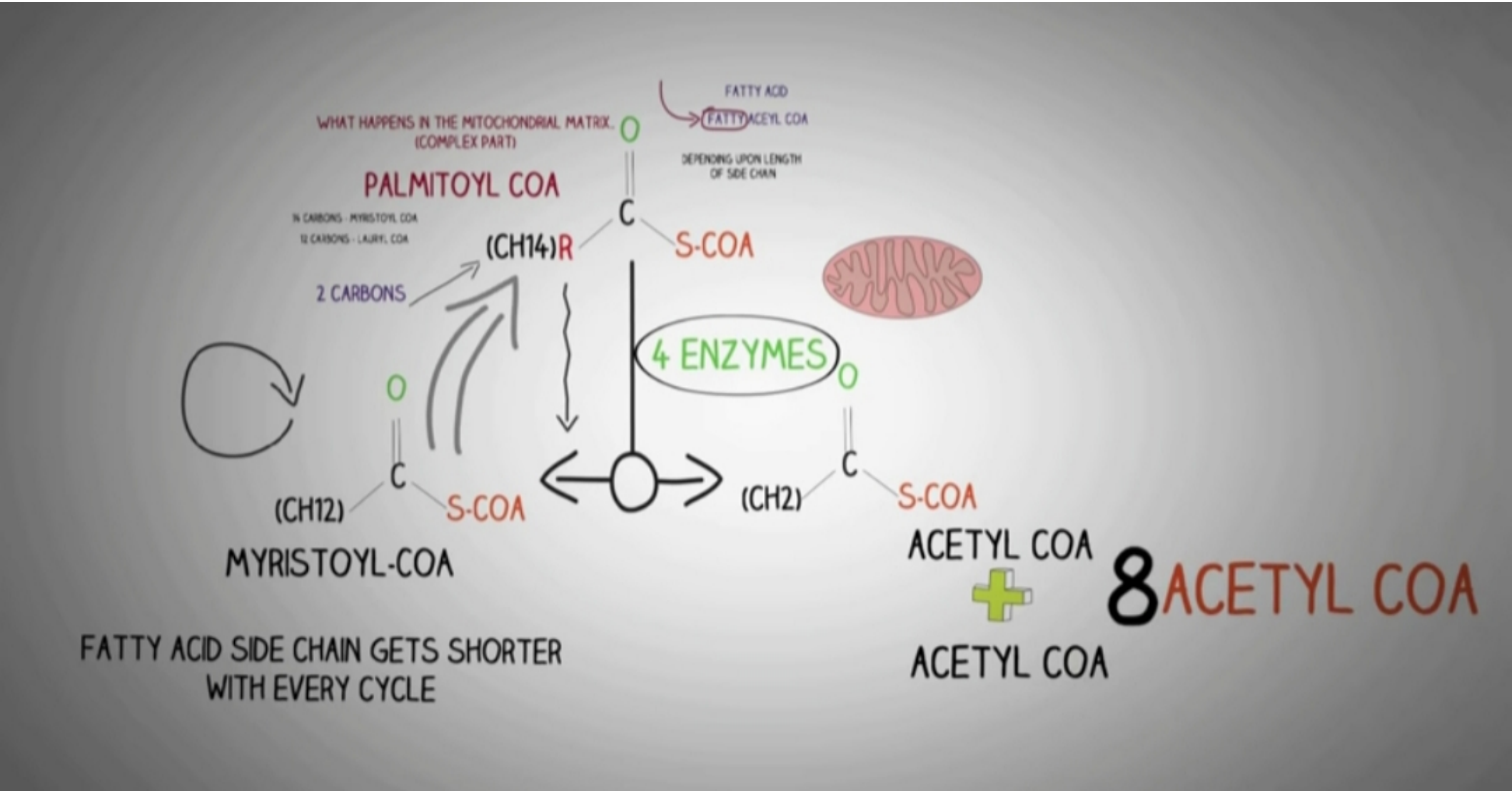
PALMITOYL COA

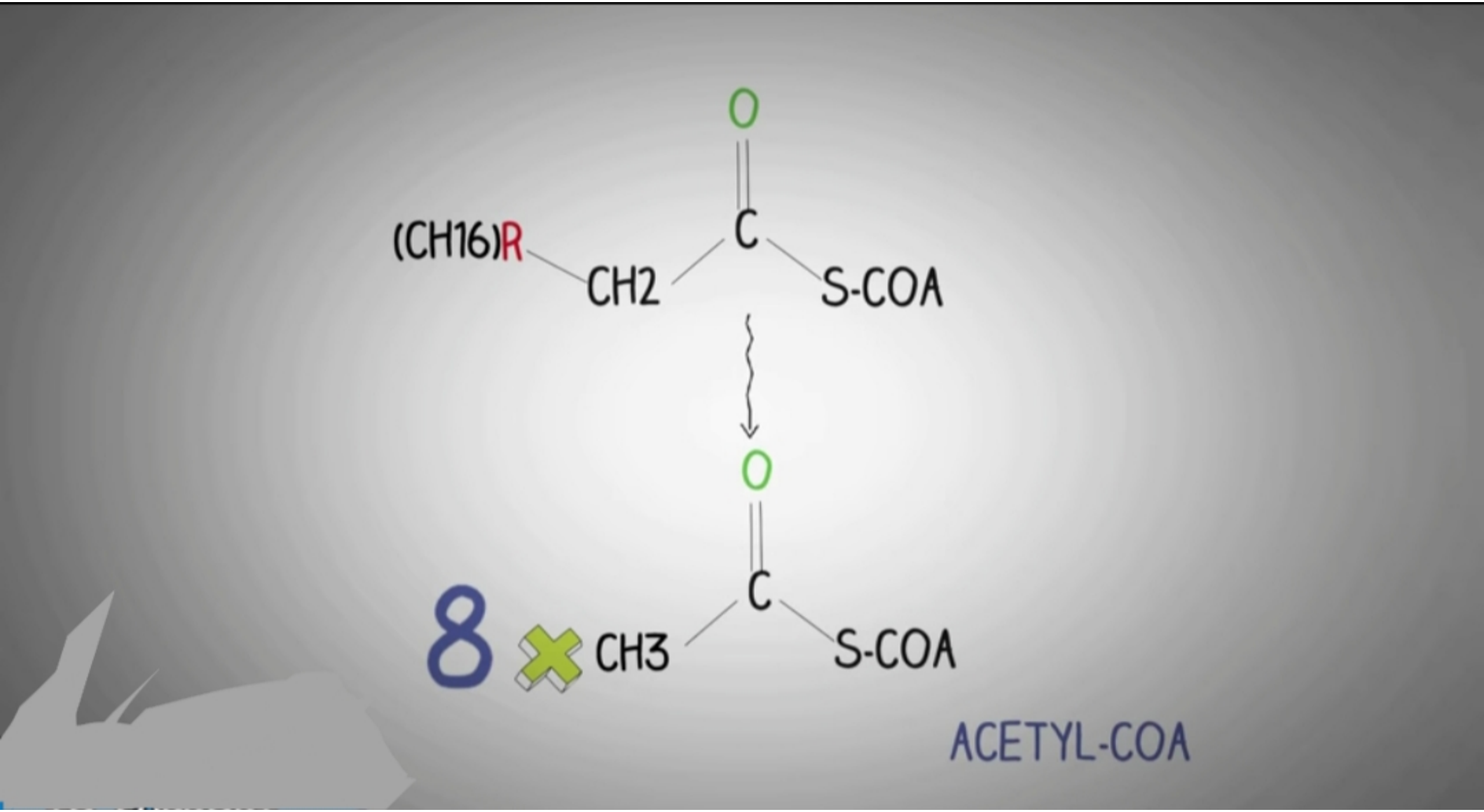
14 CARBONS - MYRISTOYL COA

12 CARBONS - LAURYL COA

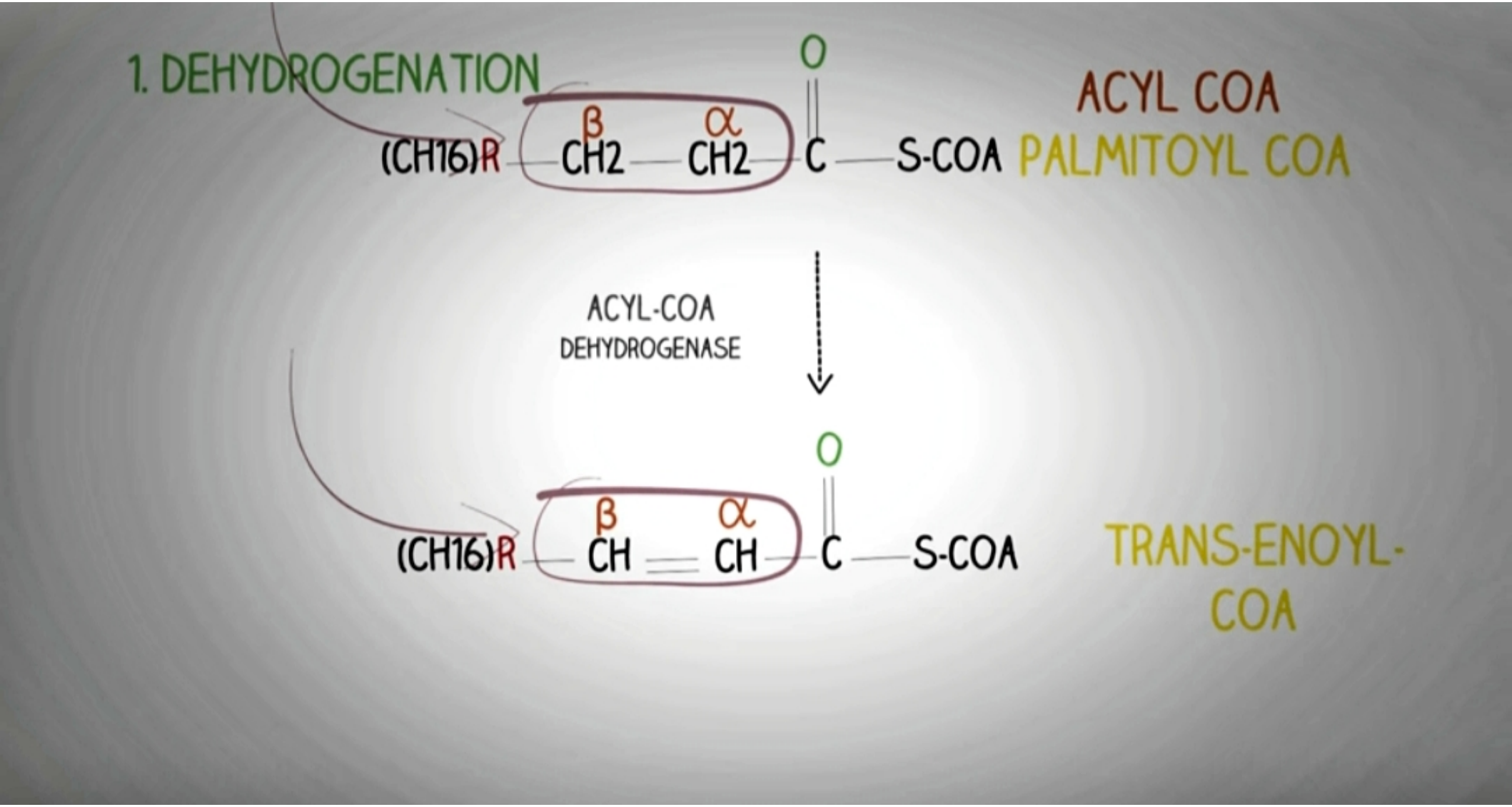
(CH16) R


WHAT HAPPENS IN THE MITOCHONDRIAL MATRIX..
(COMPLEX PART)
PALMITOYL COA
14 CARBONS - MYRISTOYL COA
12 CARBONS - LAURYL COA
FATTY ACID
FATTY ACEYL COA
DEPENDING UPON LENGTH
OF SIDE CHAIN
O
C
(CH16) R
S-COA
2 CARBONS
4 ENZYMES
O
C
(CH14)
S-COA
MYRISTOYL-COA
O
C
(CH2)
S-COA
ACETYL COA

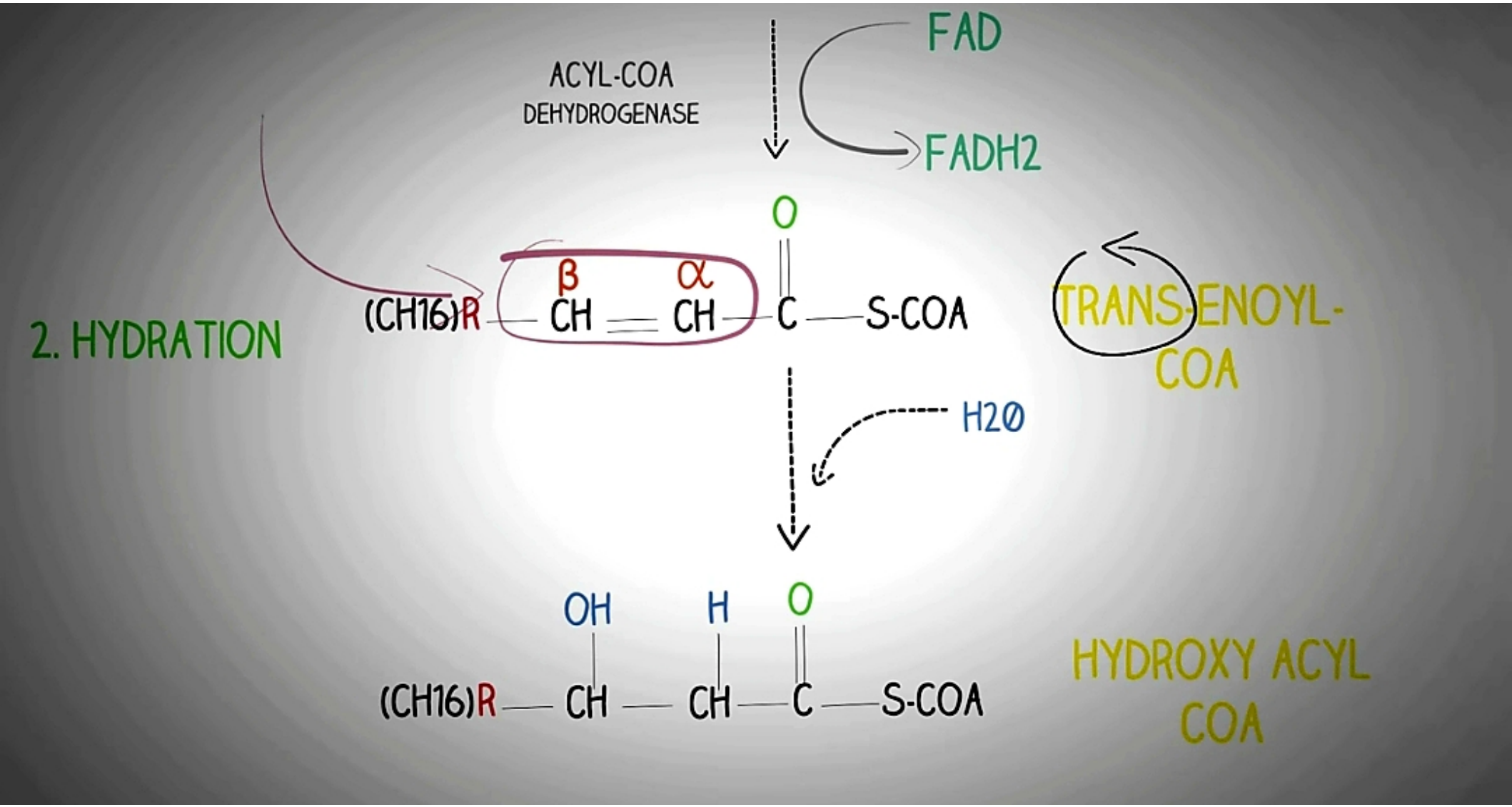

WHAT HAPPENS IN THE MITOCHONDRIAL MATRIX.
(COMPLEX PART)
PALMITOYL COA
16 CARBONS - MYRISTOYL COA
12 CARBONS - LAURYL COA
FATTY ACID
FATTY ACEYL COA
DEPENDING UPON LENGTH OF SIDE CHAIN
O
C
(CH14)R
S-COA
2 CARBONS
4 ENZYMES
O
C
(CH12)
S-COA
MYRISTOYL-COA
O
C
(CH2)
S-COA
ACETYL COA
ACETYL COA
8 ACETYL COA
FATTY ACID SIDE CHAIN GETS SHORTER
WITH EVERY CYCLE


O
(CH16)R
CH2
C
S-COA
O
8
CH3
C
S-COA
ACETYL-COA

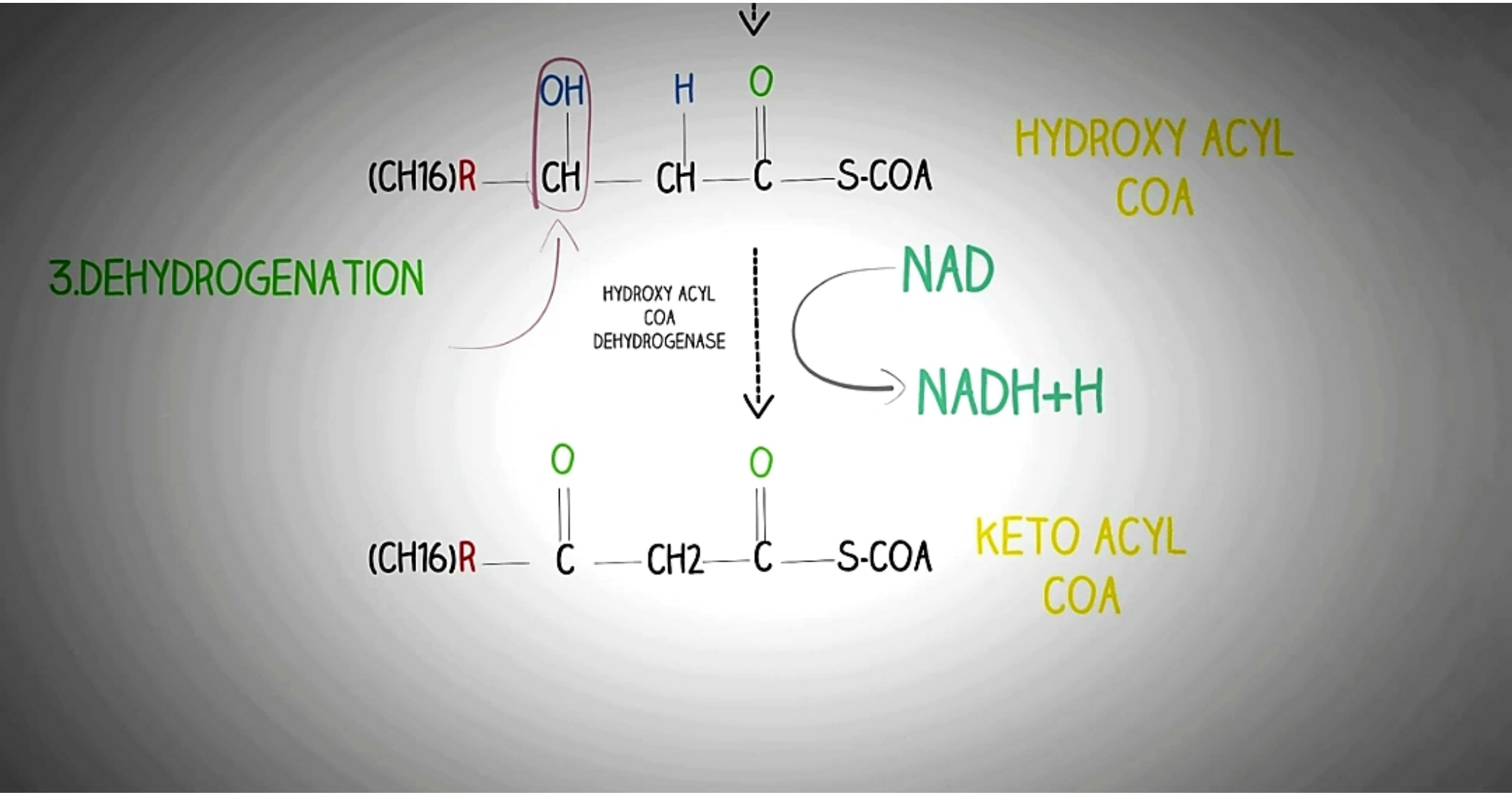
1-Dehydrogenation between carbon 2 and 3 in a FAD-linked reaction. Enzyme is acyl CoA dehydrogenase.


1. DEHYDROGENATION
O
β
α
(CH16)R
CH2
CH2
C
S-COA
ACYL COA
PALMITOYL COA
ACYL-COA
DEHYDROGENASE
O
β
α
(CH16)R
CH
CH
C
S-COA
TRANS-ENOYL-
COA

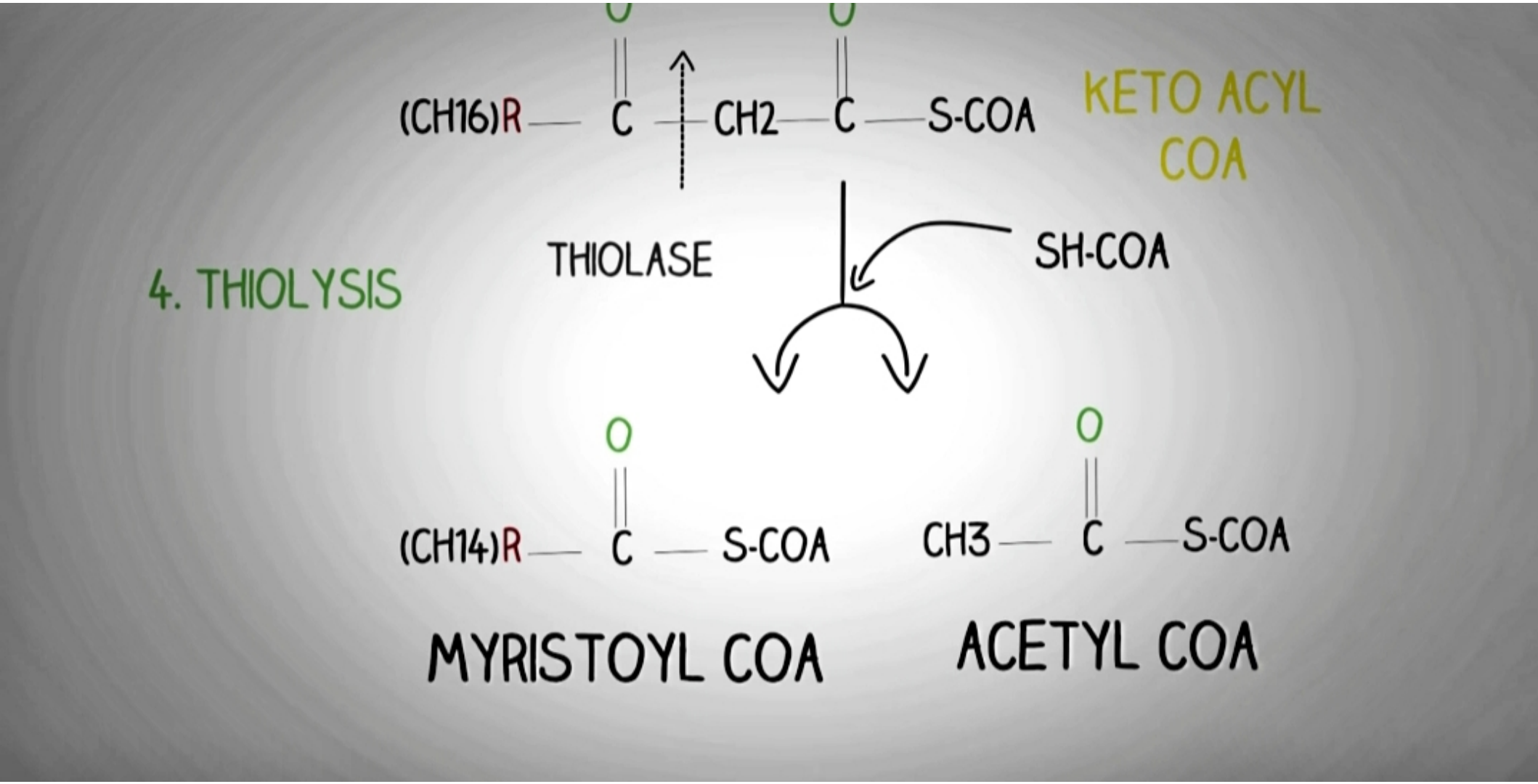
- 2. Hydration of the double bond by enoyl CoA hydratase


ACYL-COA
DEHYDROGENASE
FAD
FADH2
2. HYDRATION
β
α
(CH16)R — CH = CH — C — S-COA
O
TRANS-ENOYL-COA
H20
OH
H
O
(CH16)R — CH — CH — C — S-COA
HYDROXY ACYL COA

- 3-A second dehydrogenation in a NAD-linked reaction. Enzyme is 3-hydroxyacyl CoA dehydrogenase.


OH
H
O
(CH16)R
CH
CH
C
S-COA
HYDROXY ACYL COA
3.DEHYDROGENATION
HYDROXY ACYL COA DEHYDROGENASE
NAD
NADH+H
O
O
(CH16)R
C
CH2
C
S-COA
KETO ACYL COA

- 4-Thiolytic cleavage of the thioester by beta-ketoacyl CoA thiolase.


(CH16)R — C — CH2 — C — S-COA
KETO ACYL COA
THIOLASE
SH-COA
4. THIOLYSIS
(CH14)R — C — S-COA
CH3 — C — S-COA
MYRISTOYL COA
ACETYL COA

Types of fatty acyl CoA dehydrogenases

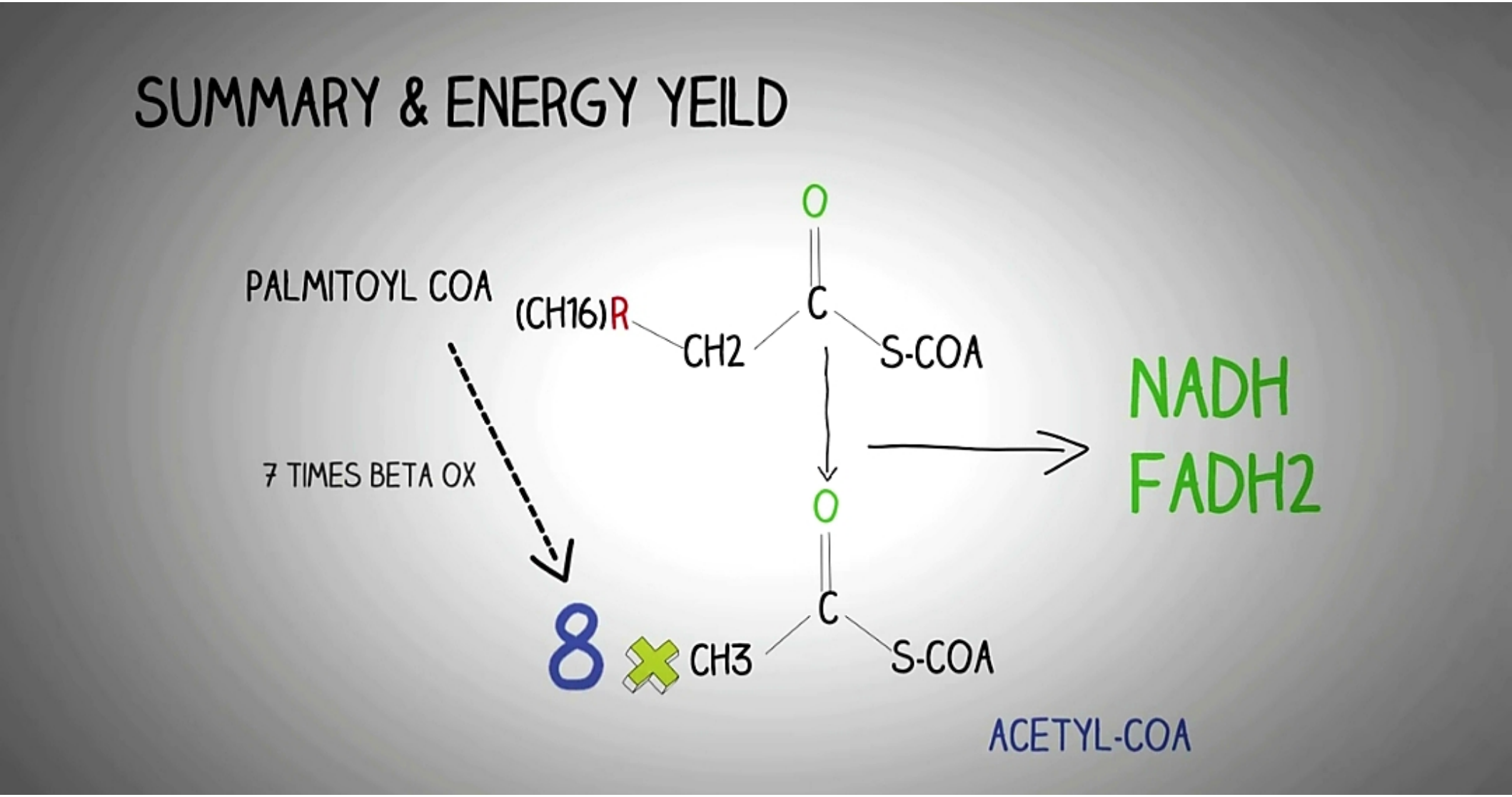
- Long chain fatty acyl CoA dehydrogenase (LCAD) acts on chains greater than C12.
- Medium chain fatty acyl CoA dehydrogenase (MCAD) acts on chains of C6 to C12.
- Short chain fatty acyl CoA dehydrogenase (SCAD) acts on chains of C4 to C6.
- MCAD deficiency is thought to be one of the most common inborn errors of metabolism.

- Fate of acetyl CoA
- Oxidation by the citric acid cycle to CO_2 and H_2O.
- -In liver only, acetyl CoA may be used for ketone body synthesis.
- Fate of the $FADH_2$ and NADH + H+
- - $FADH_2$ and NADH + H+ are oxidized by the mitochondrial electron transport system, yielding ATP.

Regulation of Beta oxidation

- Beta-oxidation is regulated as a whole primarily by fatty acid availability; once fatty acids are in the mitochondria they are oxidized as long as there is adequate NAD+ and CoA.

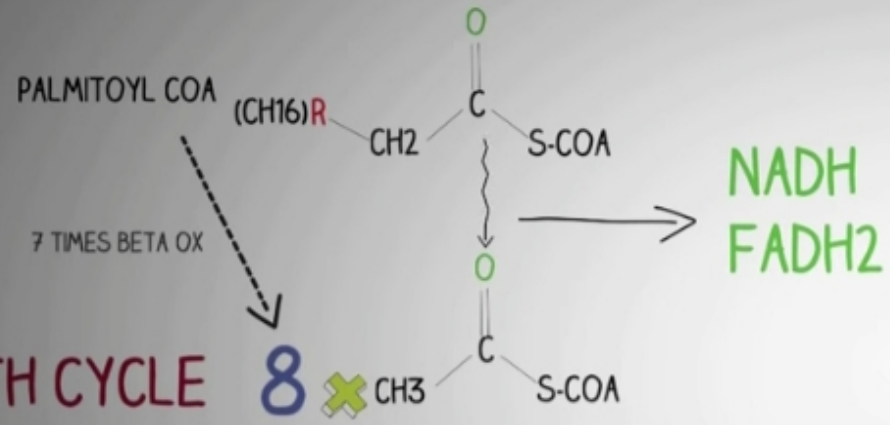
SUMMARY & ENERGY YEILD



Energy yeild from beta oxidation of palmitic acid

- Oxidation of one molecule of palmitoyl CoA to CO2 and water produces
- 8 acetyl CoA
- 7 NADH
- 7 FADH2

SUMMARY & ENERGY YEILD



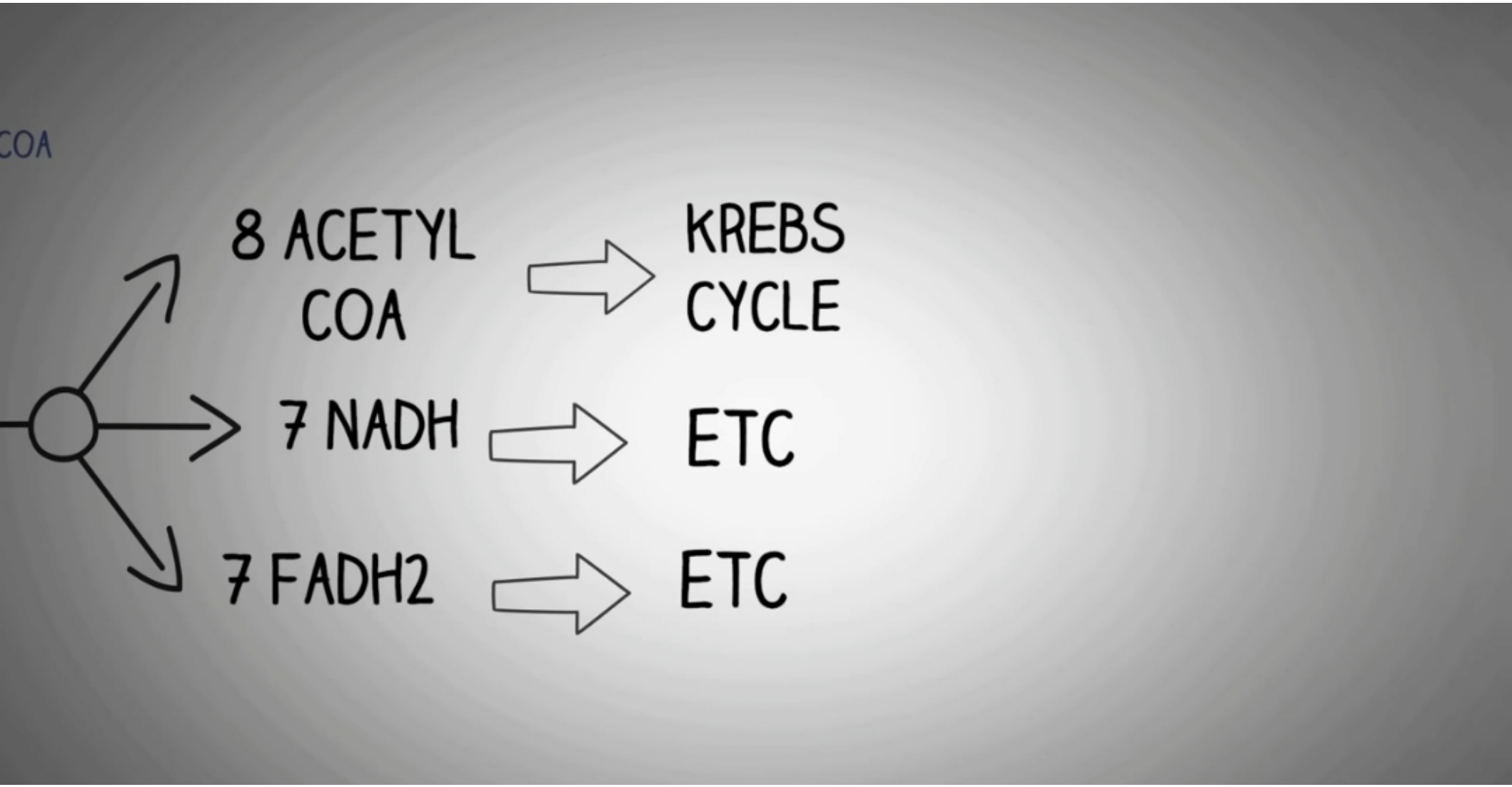
4 CARBON SIDE CHAIN LEFT
BROKEN DOWN INTO
2 ACETYL COA

7 CYCLES BETA OXIDATION

8 ACETYL COA

7 NADH

7 FADH2


COA
8 ACETYL COA
KREBS CYCLE
7 NADH
ETC
7 FADH2
ETC

ACETYL COA = 10 ATPS

NADH = 3 ATPS

FADH2 = 2 ATPS

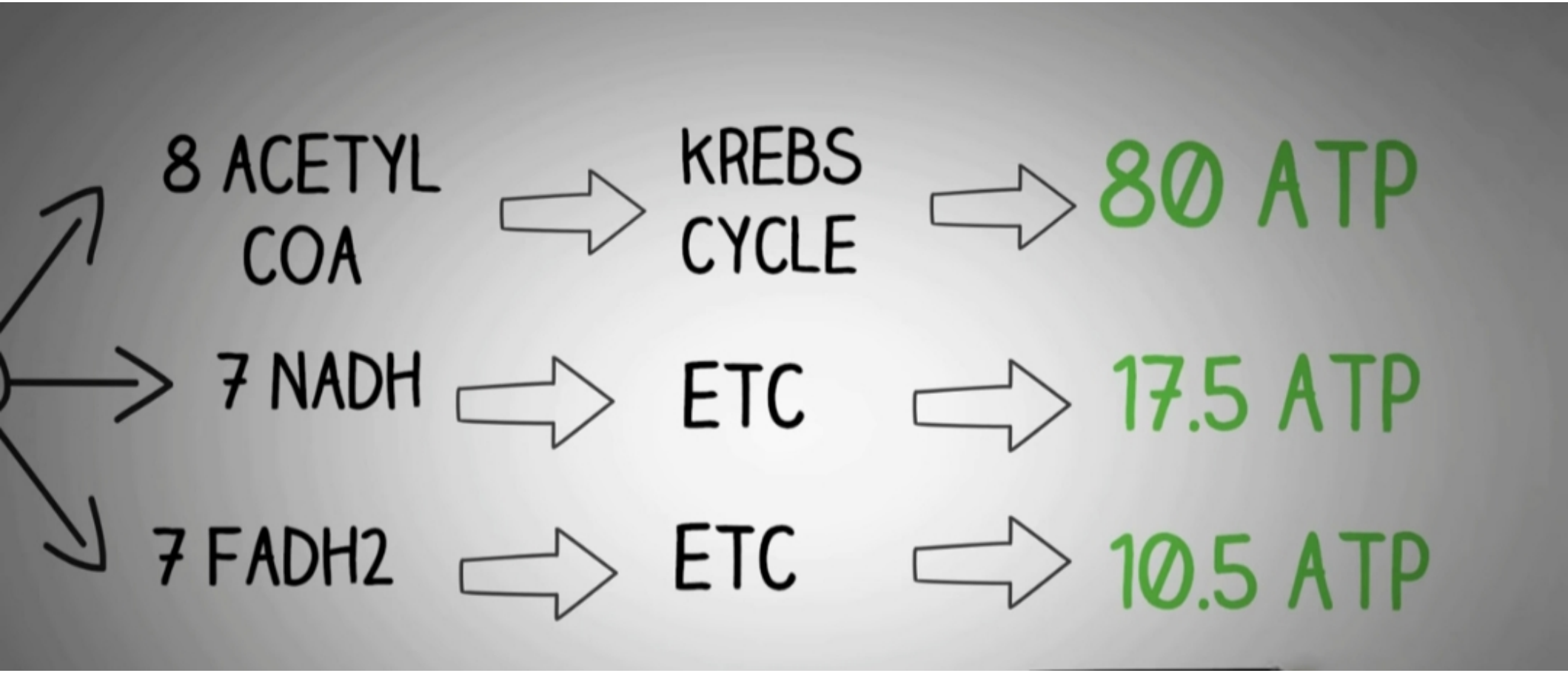
ACETYL COA = 10 ATPS

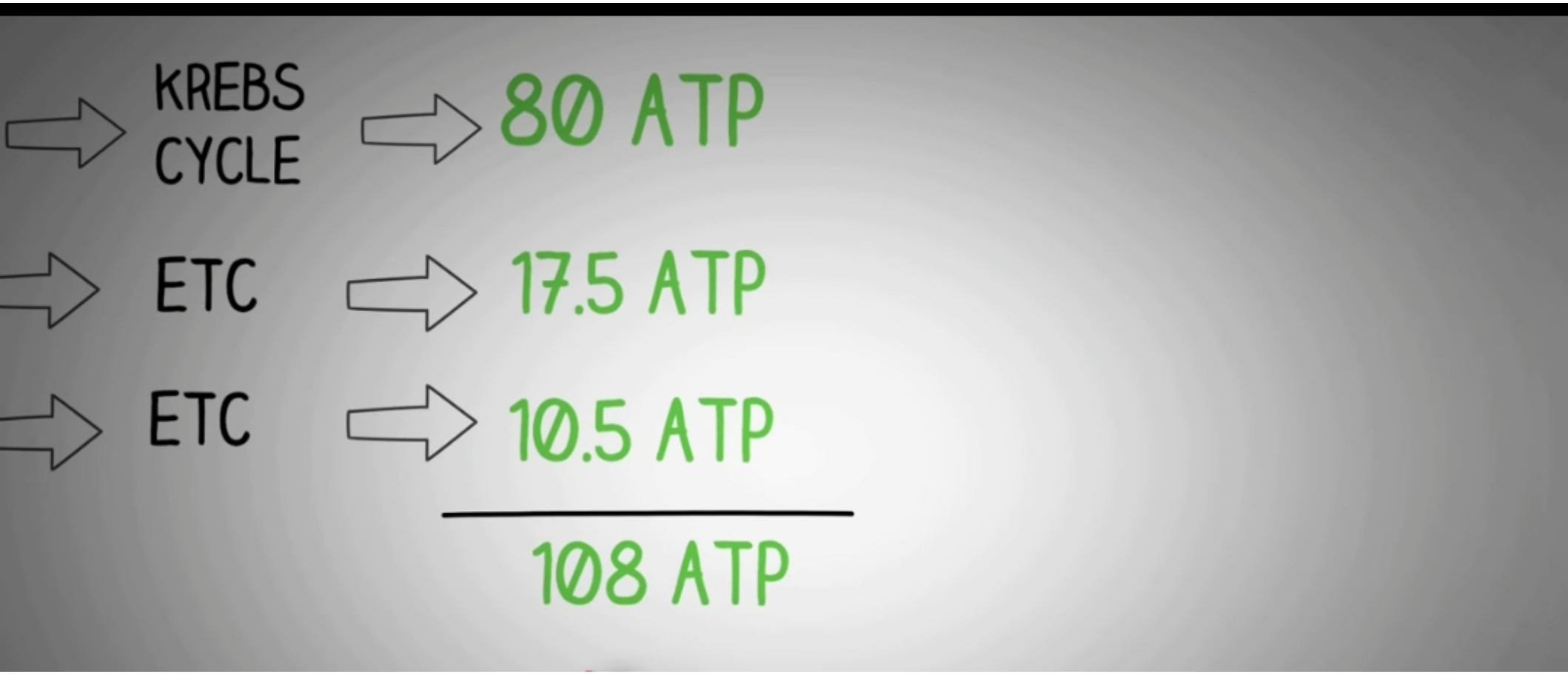
NADH = 2.5 ATPS

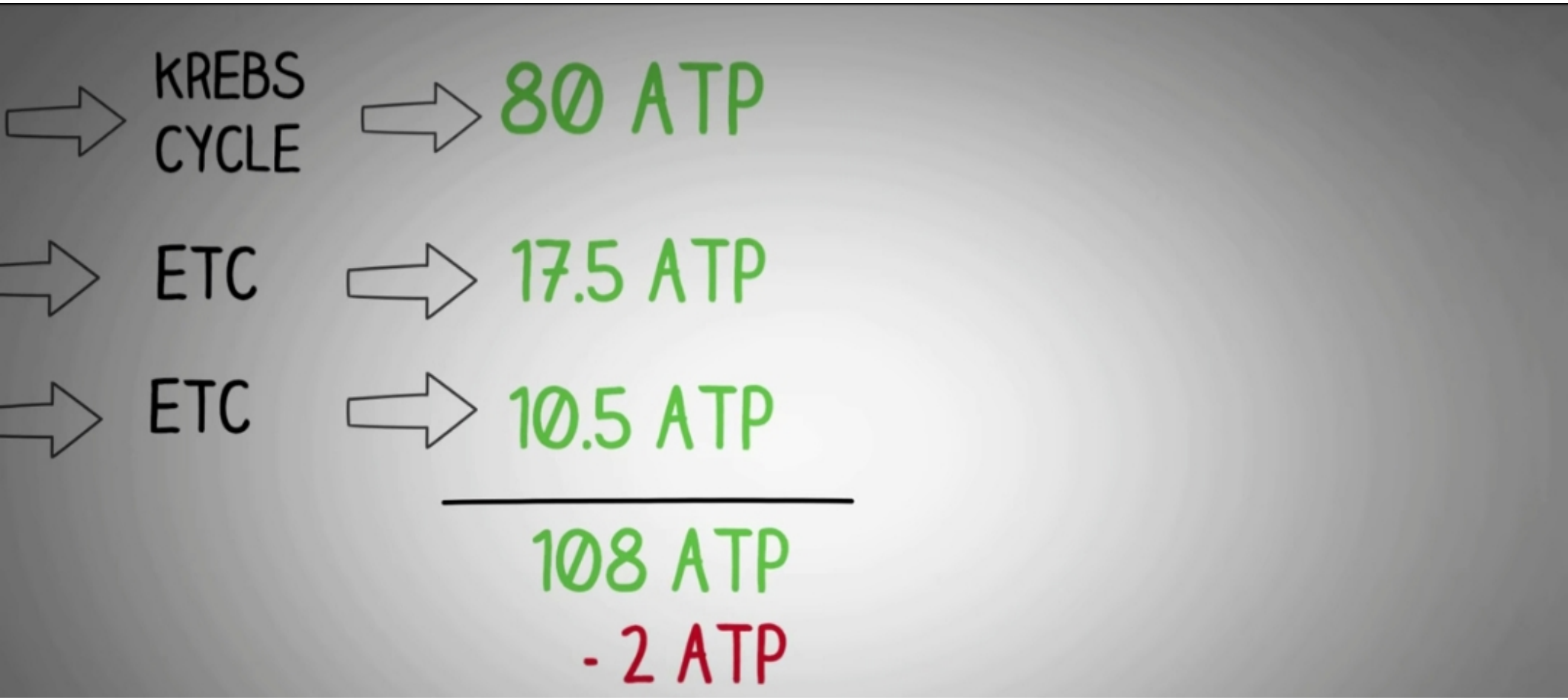
FADH2 = 1.5 ATPS

BECAUSE :

NOT ALL THE SUBSTRATE UTILIZED
SMALL ENERGY LOST IN TRANSPORT AND CARRIERS


8 ACETYL COA
KREBS CYCLE
80 ATP
7 NADH
ETC
17.5 ATP
7 FADH2
ETC
10.5 ATP


KREBS CYCLE
80 ATP
ETC
17.5 ATP
ETC
10.5 ATP
108 ATP


KREBS CYCLE
80 ATP
ETC
17.5 ATP
ETC
10.5 ATP
108 ATP
- 2 ATP

- 7 FADH2 = 2X 7 = 14 ATP
- 7 NADH = 3 X 7 = 21 ATP
- 8 Acetyl CoA = 12 x 8 = 96 ATP
- Total ATP = 131 ATP
- 2 ATP are utilized during the formation of acyl CoA . Therefore net yield is 129 ATP.

Other types of fatty oxidation

Oxidation of fatty acids with odd number of carbons

- Oxidation of fatty acids with odd number of carbons yield acetyl CoA and one molecule of propionyl CoA ---- a 3 C compound.
- Propionyl CoA is converted to Methylmalonyl CoA by carboxylase --- a biotin requiring enzyme.
- MMCoA is moved within the molecule by MMCoA mutase (vit.B12 coenzyme) to form succinyl CoA… gluconeogenic.

- Succinyl CoA enters TCA cycle and then yields energy.
- Deficiency of vit. B 12 results in urinary excretion of propionate and methylmalonate as mutase enzyme cannot function.

Oxidation of unsaturated fatty acids

- Less energy yield
- Less formation of reducing equivalents as unsaturated F.A are not highly reduced.
- The action of enoyl CoA isomerase is required to handle double bonds at odd-numbered carbons because beta-oxidation requires pre-existing double bonds at even-numbered carbons.

- If there is a double bond at an odd-numbered carbon (e.g., 18:1 9), the action of enoyl CoA isomerase is required to move the naturally occurring cis- bond and convert it to the trans- bond used in beta-oxidation.
- The product, with a trans- double bond, is a substrate for enoyl CoA hydratase, the second enzyme of beta-oxidation.

- In case of polyunsaturated fatty acids, e.g linoleic acid that is 18:2(9,12), NADPH- dependent Dienoyl CoA Reductase is required in addition to isomerase.

Beta oxidation in peroxisomes

- Fatty acids with 20 or more carbons (VLCFA) are first oxidized in the peroxisomes.
- The shortened fatty acid then goes to the mitochondria.
- The enzyme for initial dehydrogenation is FAD containing Acyl CoA oxidase.
- H2O2 is produced during the process which is toxic to cells and is therefore converted to H2O by Catalase.

- Zellweger syndrome ----- rare inherited disorder.
- Absence of peroxisomes.
- VLCFA cannot be oxidized
- Accumulation of VLCFA in brain, blood and other tissues like liver and kidney.

Omega oxidation

- Fatty acids undergo oxidation at the carbon atom farthest from the carboxyl carbon (ω carbon).
- Oxidation of carbon results in the formation of dicarboxylic acid.
- This dicarboxylic acid then undergoes beta oxidation.

Alpha oxidation

- This involves hydroxylation at alpha carbon.
- Seen in branched chain fatty acid, phytanic acid.
- Phytanic acid has methyl group on beta carbon and therefore it cannot be a substrate for acyl CoA dehydrogenase.
- Its alpha carbon is first of all hydroxylated by fatty acid alpha hydroxylase.

- Then it is decarboxylated and activated to its CoA derivative.
- This CoA derivative undergoes beta oxidation.

- Refsum disease ------ genetic disorder.
- Caused by a deficiency of alpha hydroxylase.
- There is accumulation of phytanic acid in the plasma and tissues.
- The symptoms are mainly neurological.
- Treatment involves dietary restriction of phytanic acid.