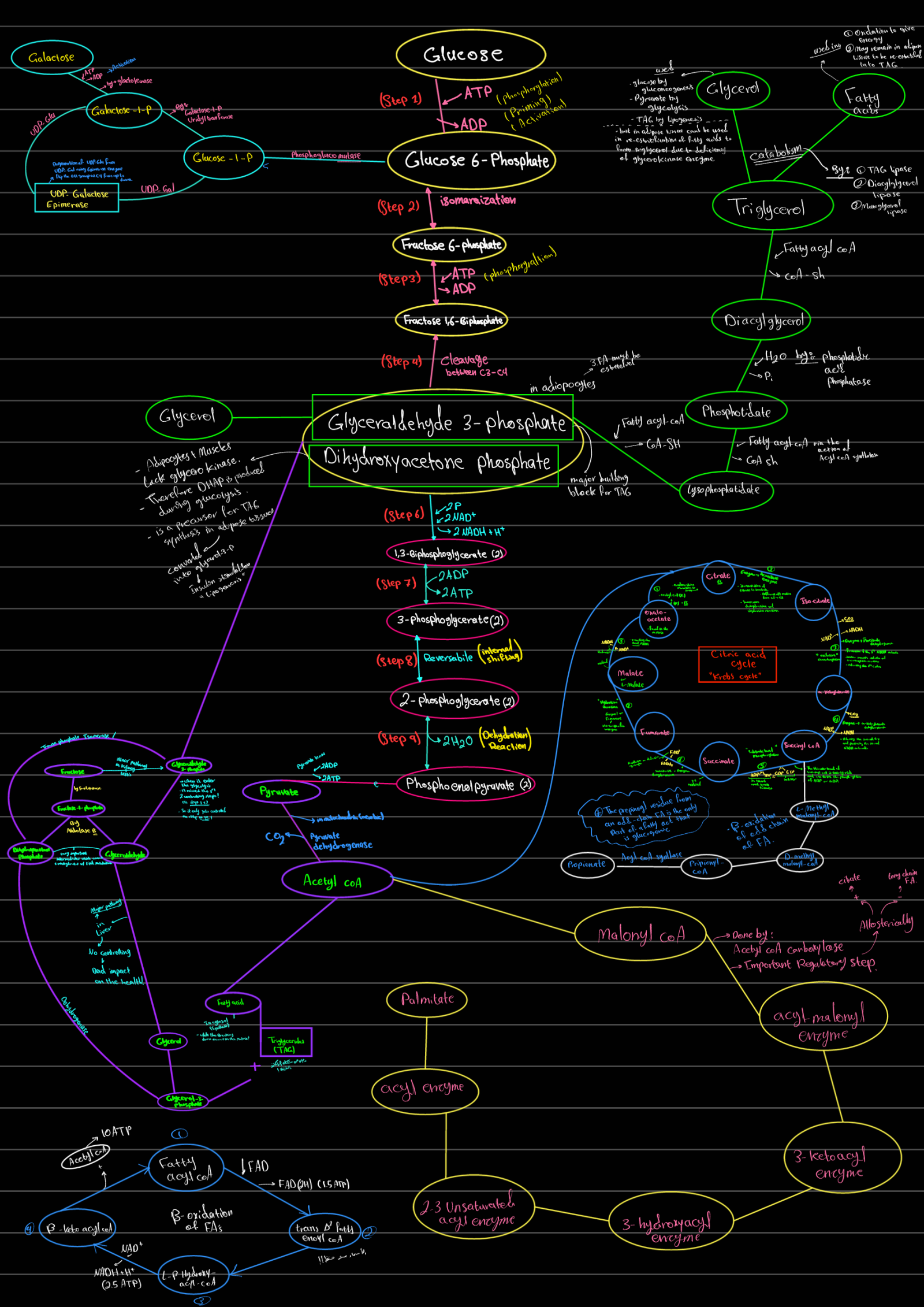
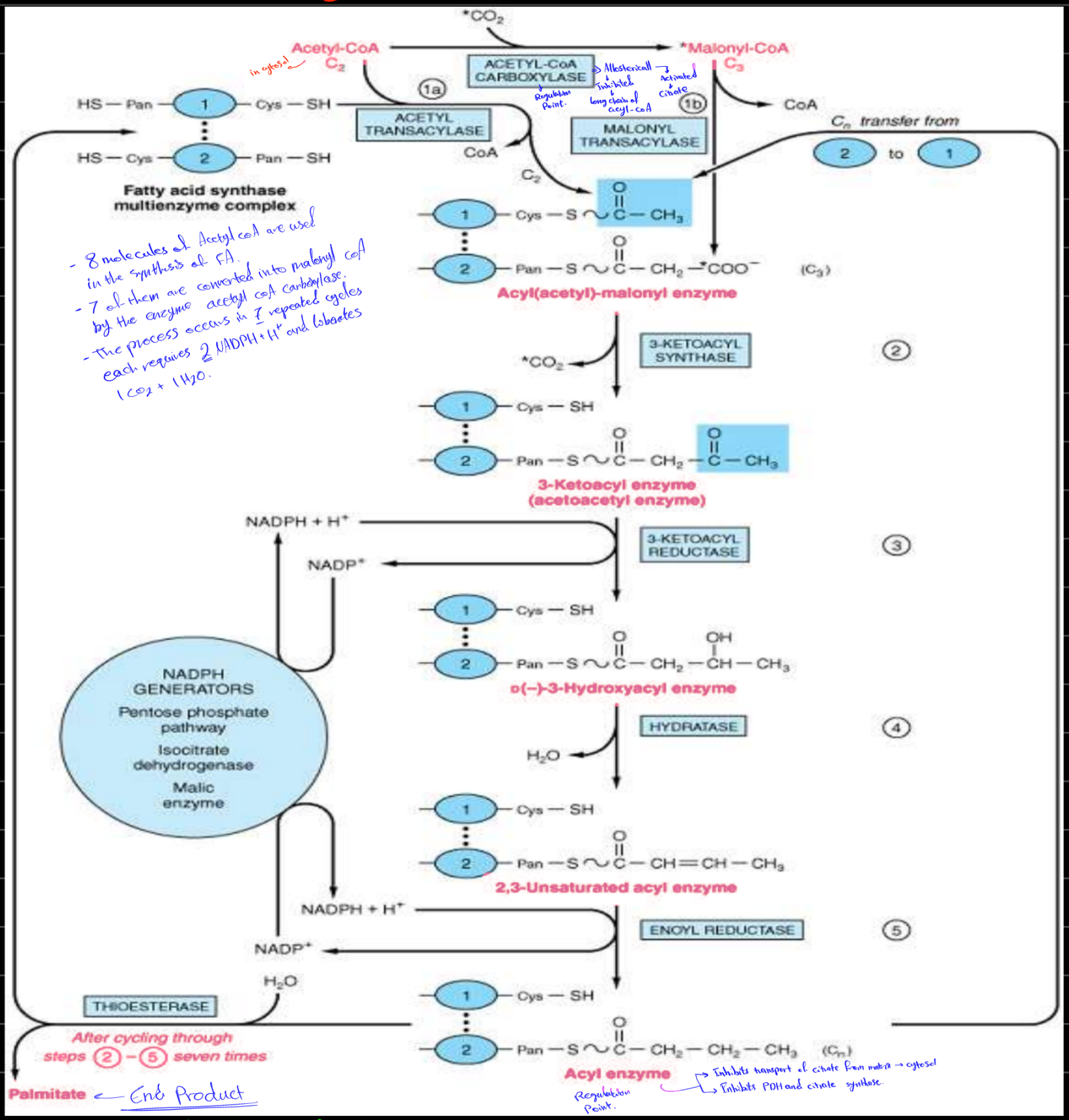

Galactose
ATP → ADP → Activation
by = galactokinase
Galactose - 1 - P
UDP-Glu
By: Galactose-1-p Uridyltransferase
Glucose - 1 - P
Phosphoglucomutase
Regeneration of UDP-Glu from UDP-Gal using Epimerase enzyme (by the OH group at C4 from up to down)
UDP- Galactose Epimerase
UDP-Gal
Glucose
(Step 1)
ATP
ADP
(phosphorylation)
(Priming)
(Activation)
Glucose 6- Phosphate
(Step 2)
isomarization
Fructose 6-phosphate
(Step3)
ATP
ADP
(phosphorylation)
Fructose 1,6-Biphosphate
(Step 4)
Cleavage between C3-C4
Glycerol
- Adipocytes & Muscles lack glycerokinase.
- Therefore DHAP is produced during glycolysis.
- is a precursor for TAG synthesis in adipose tissues
converted into glycerol-3-P
Insulin stimulates ↑ Gluconeogenesis
Glyceraldehyde 3- phosphate
Dihydroxyacetone phosphate
in adipocytes
3FA must be esterified
major building block for TAG
(Step 6)
2P
2NAD+
2 NADH + H+
1,3-Biphosphoglycerate (2)
(Step 7)
2ADP
2ATP
3-phosphoglycerate (2)
(Step 8)
Reversible (internal shifting)
2- phosphoglycerate (2)
(Step 9)
2H2O (Dehydration Reaction)
Phosphoenolpyruvate (2)
Pyruvate kinase
2ADP
2ATP
Pyruvate
in mitochondria (matrix)
CO2
Pyruvate dehydrogenase
Acetyl coA
used in
- glucose by gluconeogenesis
- Pyruvate by glycolysis
- TAG by lipogenesis
- but in adipose tissue can be used in re-esterification of fatty acids to form triglycerol due to deficiency of glycerokinase enzyme
Glycerol
Fatty acids
① Oxidation to give energy
② May remain in adipose tissue to be re-esterified into TAG
catabolism
By: ① TAG lipase ② Diacylglycerol lipase ③ Monoglycerol lipase
Triglycerol
Fatty acyl coA
coA - sh
Diacylglycerol
H2O by: phosphatidic acid phosphatase
Pi
Phosphotidate
Fatty acyl-coA via the action of Acyl coA synthase
CoA sh
Lysophosphatidate
Citrate
Iso-citrate
Oxalo-acetate
Malate
L-Malate
Citric acid cycle "Krebs cycle"
Fumarate
Succinate
Succinyl coA
L-Methyl malonyl-coA
D-methyl malonyl-coA
Propionate
Acyl-coA-synthase
Propionyl-coA
② The propionyl residue from an odd-chain FA is the only part of a fatty acid that is glucogenic
β-oxidation of odd chain of FA.
Fructose
Fructose-1-phosphate
Glyceraldehyde
Dihydroxyacetone phosphate
Aldolase B
Glycerol
Glycerol-3-phosphate
Dehydrogenase
Fatty acid
Triglycerides (TAG)
Malonyl coA
Done by: Acetyl coA carboxylase
Important Regulatory step.
Allosterically
citrate
Long chain F.A.
Major pathway in Liver
No controlling
Bad impact on the health
Palmitate
acyl enzyme
acyl-malonyl enzyme
3-ketoacyl enzyme
2-3 Unsaturated acyl enzyme
3-hydroxyacyl enzyme
Acetyl coA
10ATP
Fatty acyl coA
FAD
FAD(2H) (1.5 ATP)
β-keto acyl coA
β-oxidation of FAs
trans Δ Fatty Enoyl coA
NAD+
NADH+H+ (2.5 ATP)
L-β-Hydroxy-acyl-coA

Fatty acid Synthesis



- 8 molecules of Acetyl coA are used in the synthesis of FA.
- 7 of them are converted into malonyl coA by the enzyme acetyl coA carboxylase.
- The process occurs in 7 repeated cycles each requires 2 NADPH + H+ and liberates 1 CO2 + 1 H2O.

Notes:

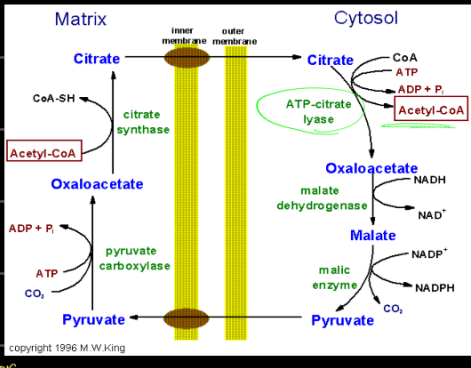
① Acetyl coA is always derived from glucose, never from FA. This is because Insulin after a meal drive lipogenesis not lipolysis from glucose.

② NADPH + H+ is provided by:
- Ⓐ Pentose phosphat pathway (Ribose-5-P)
- Ⓑ Action of cytoplasmic isocitrate dehydrogenase on Isocitrate.
- Ⓒ Action of malic enzyme on malate to produce pyruvate.

③ Every enzyme transfer CO2 ⇒ requires Biotin as a co-factor.

④ Translocation of acetyl-coA from matrix into cytosol occurs by:
- combining it w/ oxaloacetate and exit from the matrix.

-Acetyl coA may also pass through mitochondorial membrane into the cytosol in the form of acetyl carnitine by carnitone acetyl transferase, and Biotin as a co-factor.



Fate of palmitate:
- ① Esterification: Palmitate esterified w/ glycerol to form acyl glycerols or w/ Cholesterol to form cholesterol esters
- ② chain elongation: Palmitate may be elongated to form longer FA.
- ③ Destauration: synthesis of unsaturated FA. Palmitate may undergo destauration to form palmitoleic acid.
- ④ Sphingosine formation: it is formed by condensation of palmity coA and the amino acid serine.

Microsomal pathway for FA synthesis & main site for elongation for existing long chain, more than 16C.

(A) The elongated molecules are derived from:
① Palmitate: cytoplasmic pathway. ② FA of diet.

(B) The microsomal pathway needs malonyl CoA as acetyl donor and $NADPH+H^+$ as coenzyme

(C) Function: This system becomes active during myelination of nerves in order to provide C22 and C24 FAs which are present in sphingolipids.

Synthesis Of Unsaturated Fatty Acids:

A. Nonessential unsaturat ed fatty acids:

1. These are fatty acids which contain one double bond e.g. palmitoleic acid (16: 1) and oleic acid (18:1).
2. Synthesis of oleic acid (oleyl CoA) : It is synthesized - in the microsomes - from stearyl CoA (active stearic acid)

B. Essential fatty acid:

These are unsaturated fatty acids which contain more than one double bond.

Examples: linoleic acid and linolenic and arachidonic acid.

Functions:

a- They are Important for normal growth.

b- Synthesis of phospholipids

c- Prevention of atherosclerosis: Essential fatty acids combine with cholesterol forming esters which are rapidly metabolized by the liver. This prevents precipitation of free cholesterol along the endothelium of blood vessels ~ prevents atherosclerosis.

d- Synthesis of eicosanoid.

Regulation of lipolysis:

The key enzyme controlling lipolysis is Hormone sensitive triacylglycerol lipase (HSL):

-This enzyme is activated when phosphorylated by 3' 5'-cyclic AMPdependent protein kinase.

- In the presence of high plasma level of insulin and glucose, HSL is dephosphorylated, and become inactive. So during fasting → stimulation of lipolysis.

- Coffee contains caffeine and tea contains theophylline. Both inhibit phosphodiesterase enzyme → stimulation of lipolysis.

- Causes of excessive lipolysis: where there is a need for energy; starvation, diabetes mellitus, low carbohydrate diet, and in certain infectious disease as in tuberculosis (due to high catabolic state).

Types of fatty acid oxidation

- Fatty acids can be oxidized by:

1- β- oxidation- major mechanism, occurs in the mitochondrial matrix. 2-C units are released as acetyl CoA per cycle.

2- α- oxidation- predominantly takes place in brain and liver, one carbon is lost in the form of CO_2 per cycle.

3- ω- oxidation- minor mechanism, but becomes important in conditions of impaired β-oxidation

4- Peroxisomal oxidation- mainly for the trimming of very long chain fatty acids.

The remaining of the Lecture are the Oxidations (some few details) and the last few slides.