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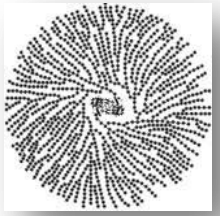
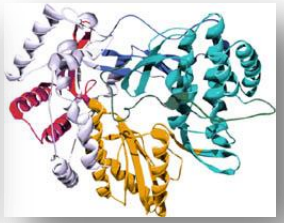
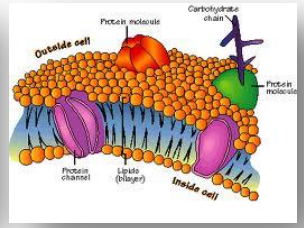
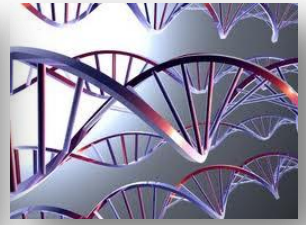
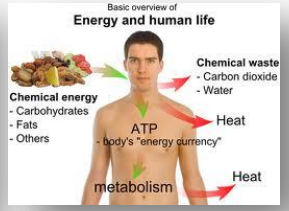
BIOC203W1

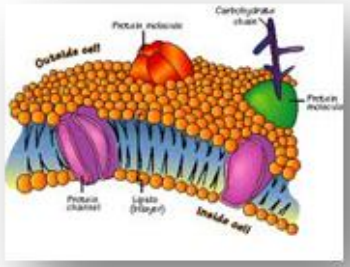
Biochemistry for Biologists

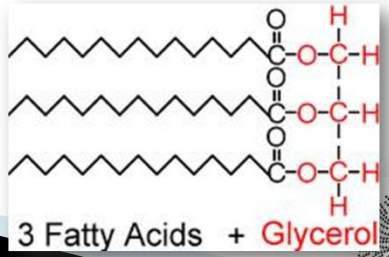



Dr MS Islam
Sr. Lecturer of Biochemistry
School of Life Sciences, Westville Campus

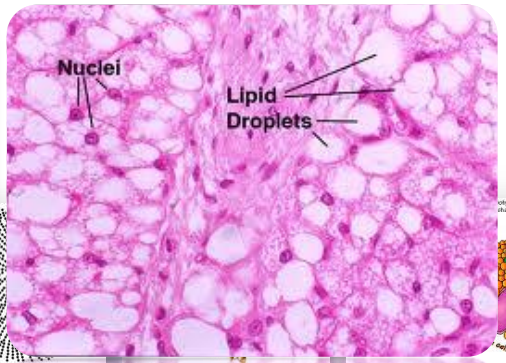
Importance of lipids?

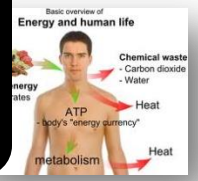


- Lipids play roles both in energy metabolism and in aspects of biological structure and functions
- The great bulk of lipid in most organisms is present in the form of triglycerides
- A mammal may contain 5-25% of its body weight as lipid and 90% of this is present in the form of triglycerides.
- Most of this fat is stored in adipose tissue.
- Triglycerides are derived from two major sources:
  1. The diet digestion, absorption and transport of fat to adipose tissue
  2. The mobilisation of fat stored in adipocytes



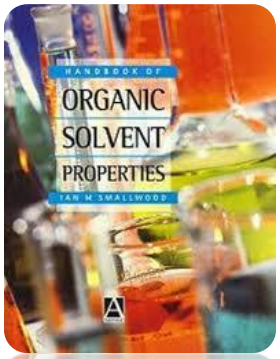
Triglycerides



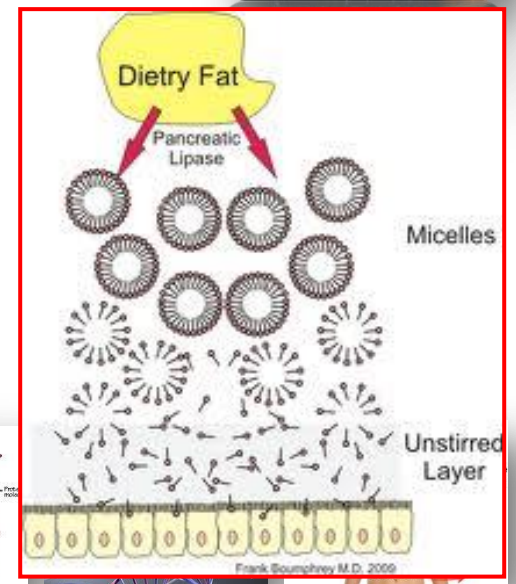


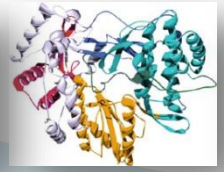
Page 10 in Handouts

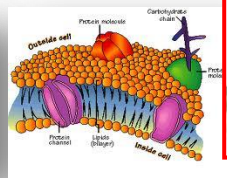
Digestion of fats



- An adult man ingests about 60-100g of fat per day.
- As you know, triglycerides constitute more than 90% of dietary fats and the rest is made up of phospholipids, cholesterol, cholesterol esters, and free fatty acids.
- Lipids are organic molecules and mainly soluble in organic solvents
- On the other hand, the lipid digesting enzyme e.g. pancreatic lipase or lipo-protein lipase can only work in the aqueous environment
- Although the lipids will be hydrolyzed into smaller constituents, the products tends to aggregate to larger complex that make poor contact with the cell surface and reduce the rate of absorption.



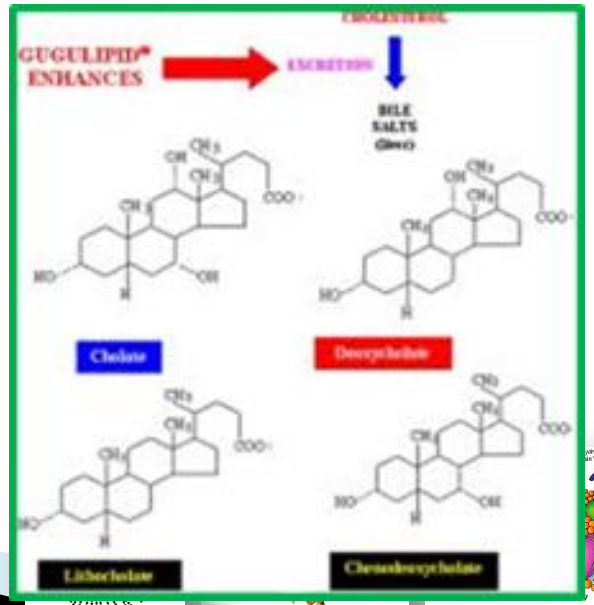


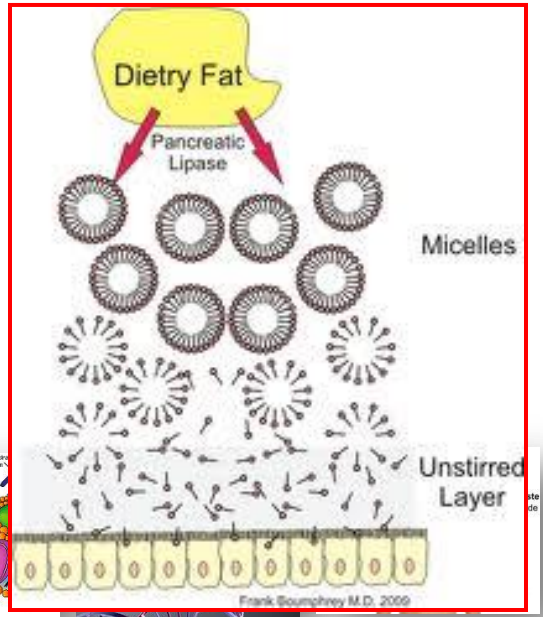


Page 10 in Handouts

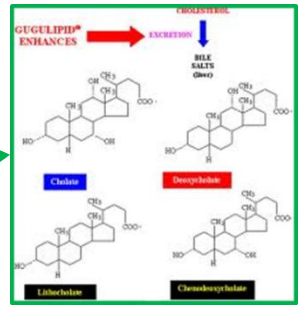
Digestion of fats

- This problem is overcome by some detergent like materials e.g. **bile acids and bile salts** which can create a favorable environment for both lipids and lipid digesting enzymes.
- Bile acids composed of 24C atoms containing 2-3 hydroxyl groups and side chain with carboxylic acid group (-COOH) which often conjugate by an amide bond with glycine or taurine to for glyco-cholic or tauro-cholic acid, respectively.

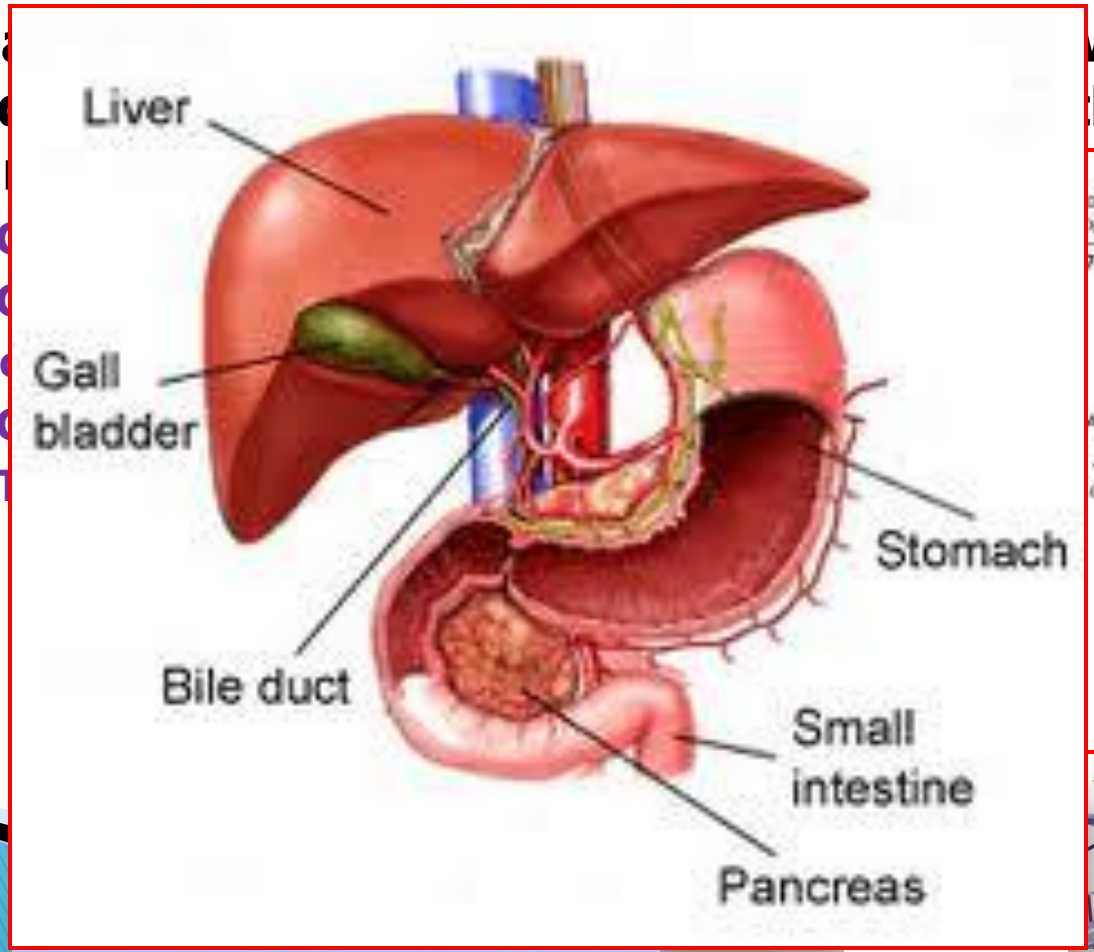


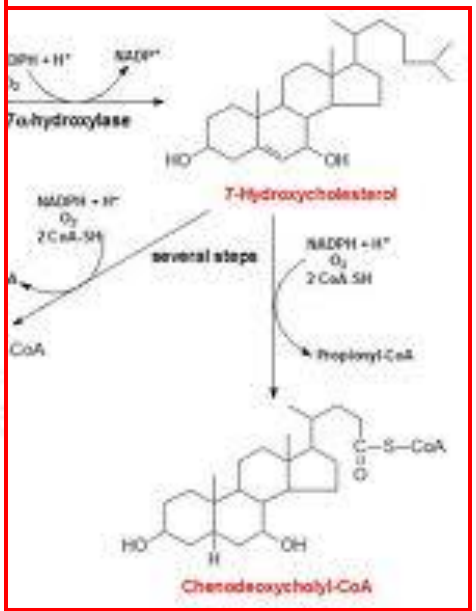


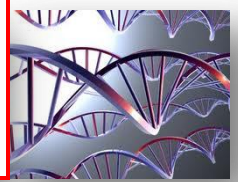
Digestion of fats

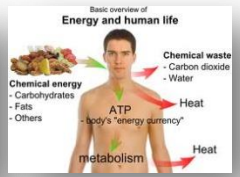


- **Bile acids and bile salts** are produce in the liver from cholesterol and transport to the gall bladder via bile duct for deposition and further necessary actions.
- There a… which work on lipi… the small intesti…
  - C…
  - C…
  - C…
  - C…
  - T…

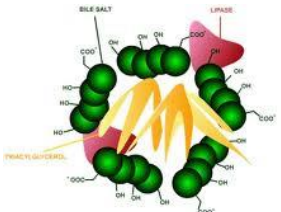


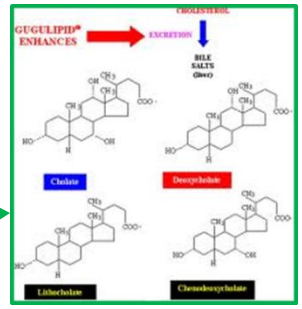




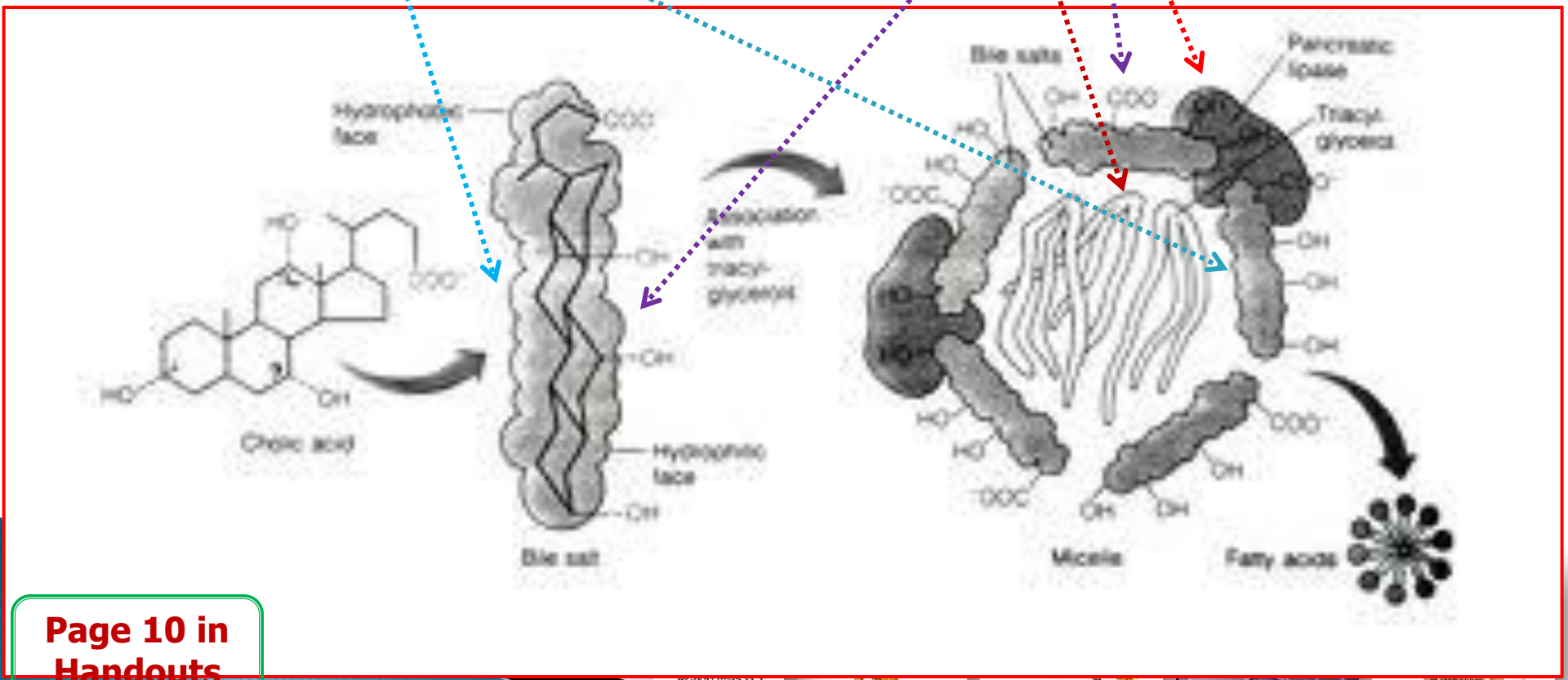


Digestion of fats



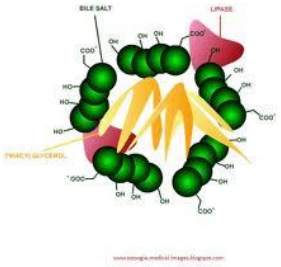


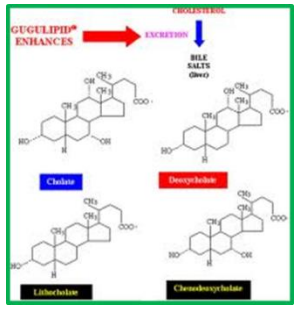
- **Bile acids and bile acids** contain both **hydrophilic** and **hydrophobic** surface allow them to dissolve in an oil-water interface which emulsifies **triglycerides** to form bile salt micelle (1 um) to digest it by enzyme **lipases**.



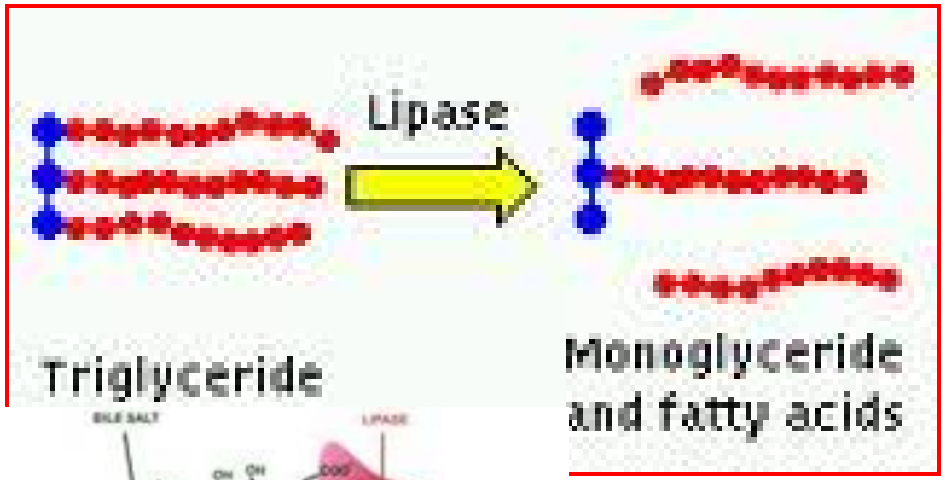
Page 10 in Handouts

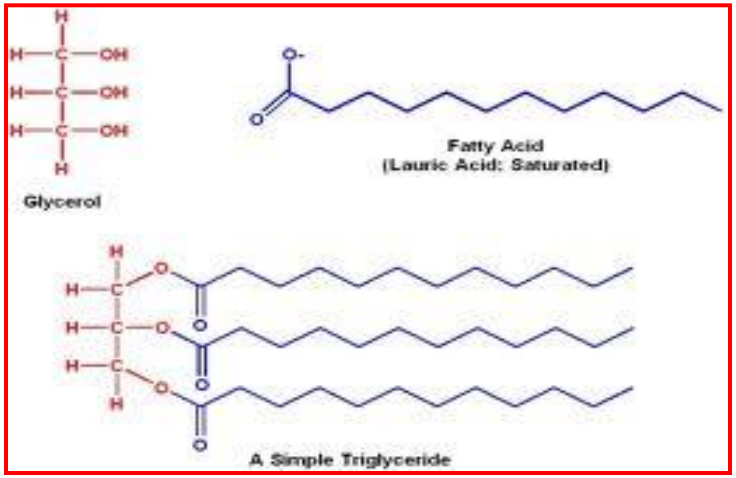
Digestion of fats

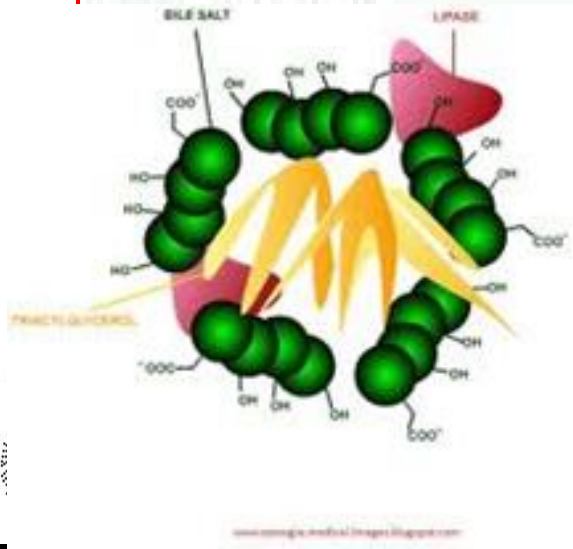


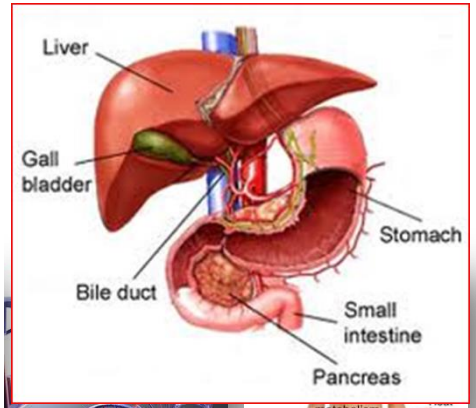


- **Finally, the digestion of triglycerides is done by the pancreatic lipase enzyme in the duodenum of small intestine to form monoglycerides and free fatty acids**

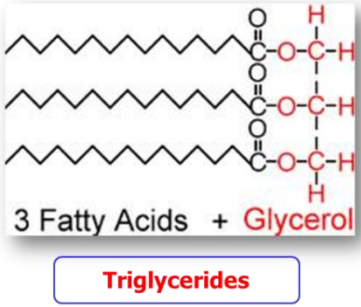




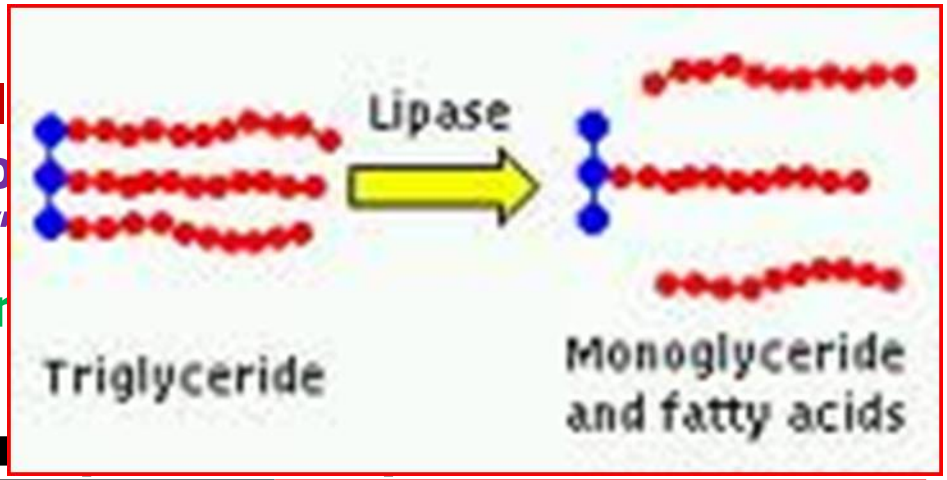


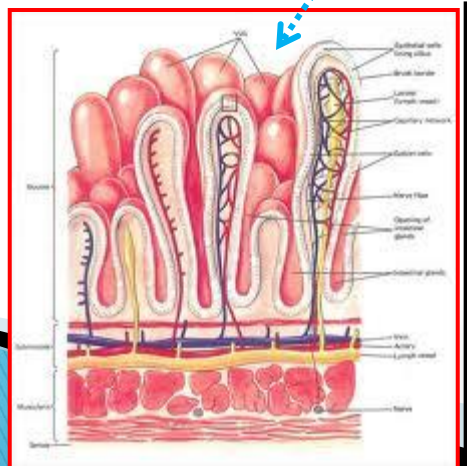


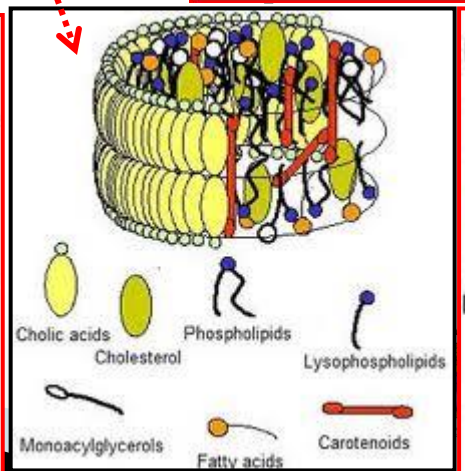
Digestion of dietary fats

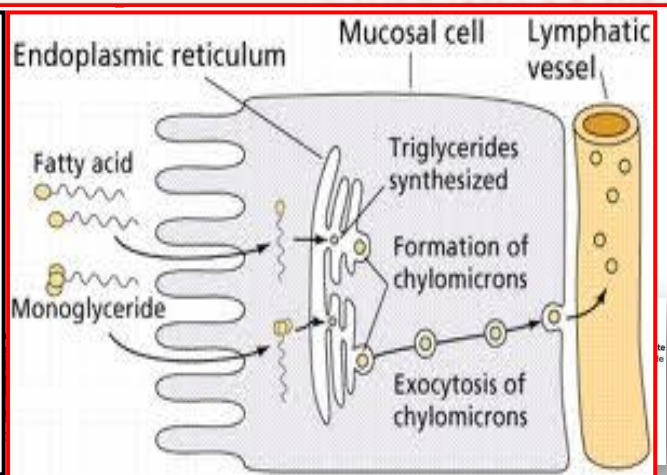


- The products of TG digestion, mainly monoglyceride and long chain fatty acids must be stabled before they can be absorbed via the small intestinal epithelium.
- This stabilization is achieved
  present in the bile salts micel
  monoglycerides, lysophospho
  acids to form "mixed micelle"
- Then absorb from the small i
  bile salts remain in the small
- Then digested lipids are take

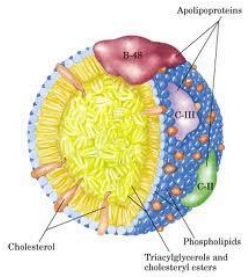




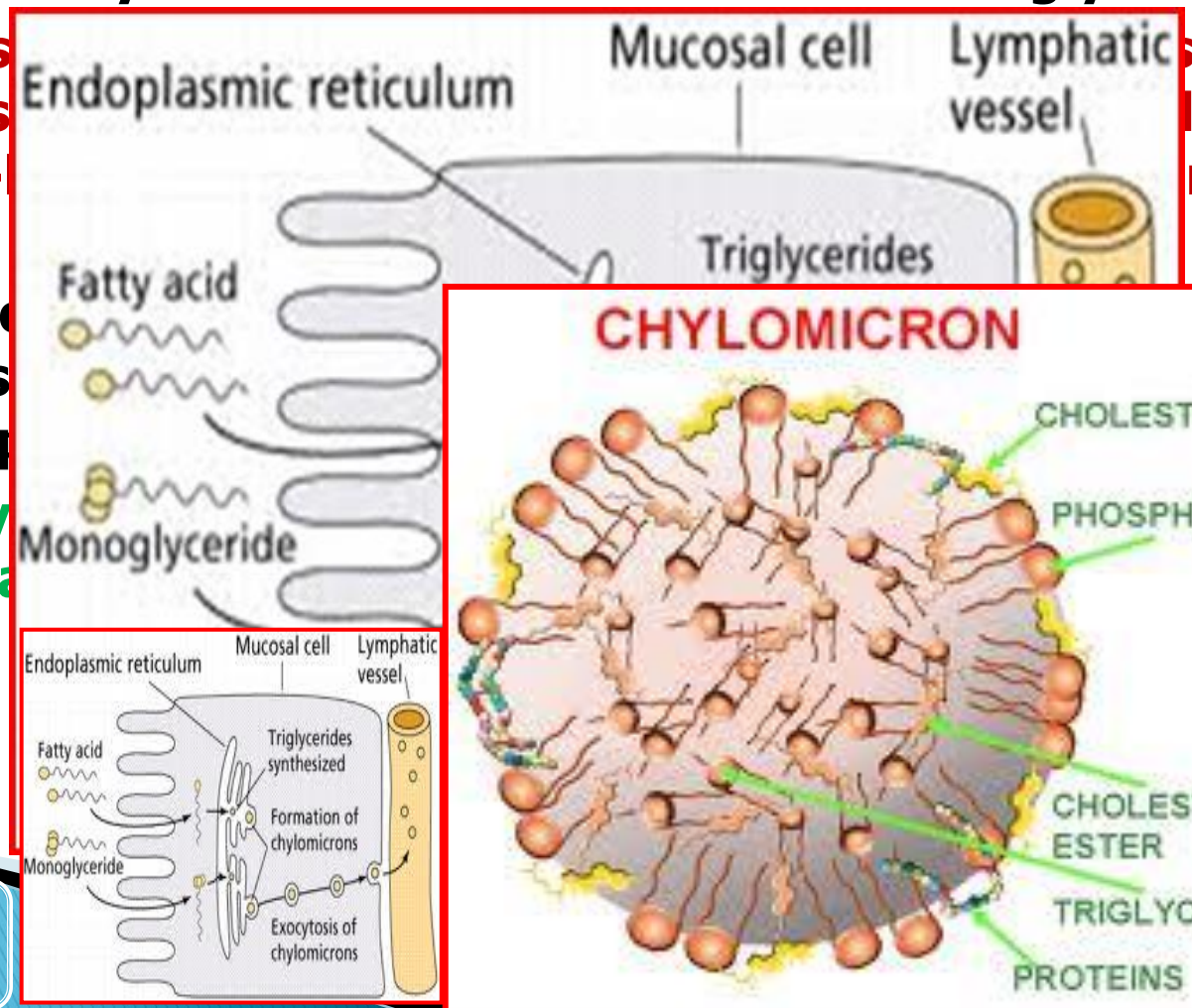


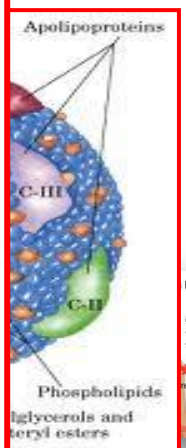


Chylomicron formation



- After absorption of fat into the small intestinal epithelial cells fatty acids are re-esterified to form triglycerides
- Subs… phos… some apo-… micron with …
- Chyl… , 8% phos… and 2% …
- They… er and a…





Page 11 in Handouts

Mobilization of fat

- The mobilization of fat is a hormone dependent process
- In feeding condition or consumption of high starchy foods



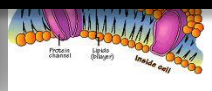
Blood glucose
Insulin

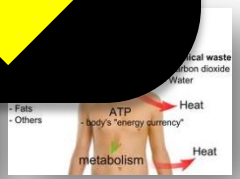
Glucagon
Adrenaline

Glycolysis
Glycogenesis
Fatty acid synthesis
Lipid biosynthesis

Fatty acid oxidation
Gluconeogenesis
Mobilization of fat







Mobilization of fat

- **In fasting condition** or when not eating for more than 3 h

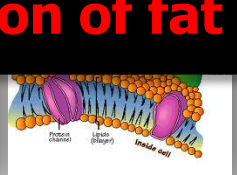
Blood glucose ↓
Insulin ↓

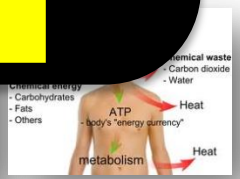
Glucagon ↑
Adrenaline ↑

→

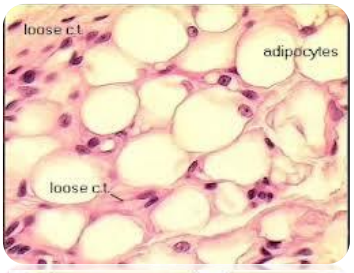
Glycolysis ↓
Glycogenesis ↓
Fatty acid synthesis ↓
Lipid biosynthesis ↓

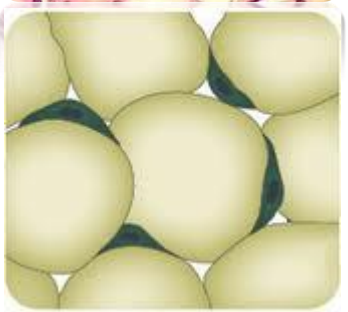
Fatty acid oxidation ↑
Gluconeogenesis ↑
Mobilization of fat ↑



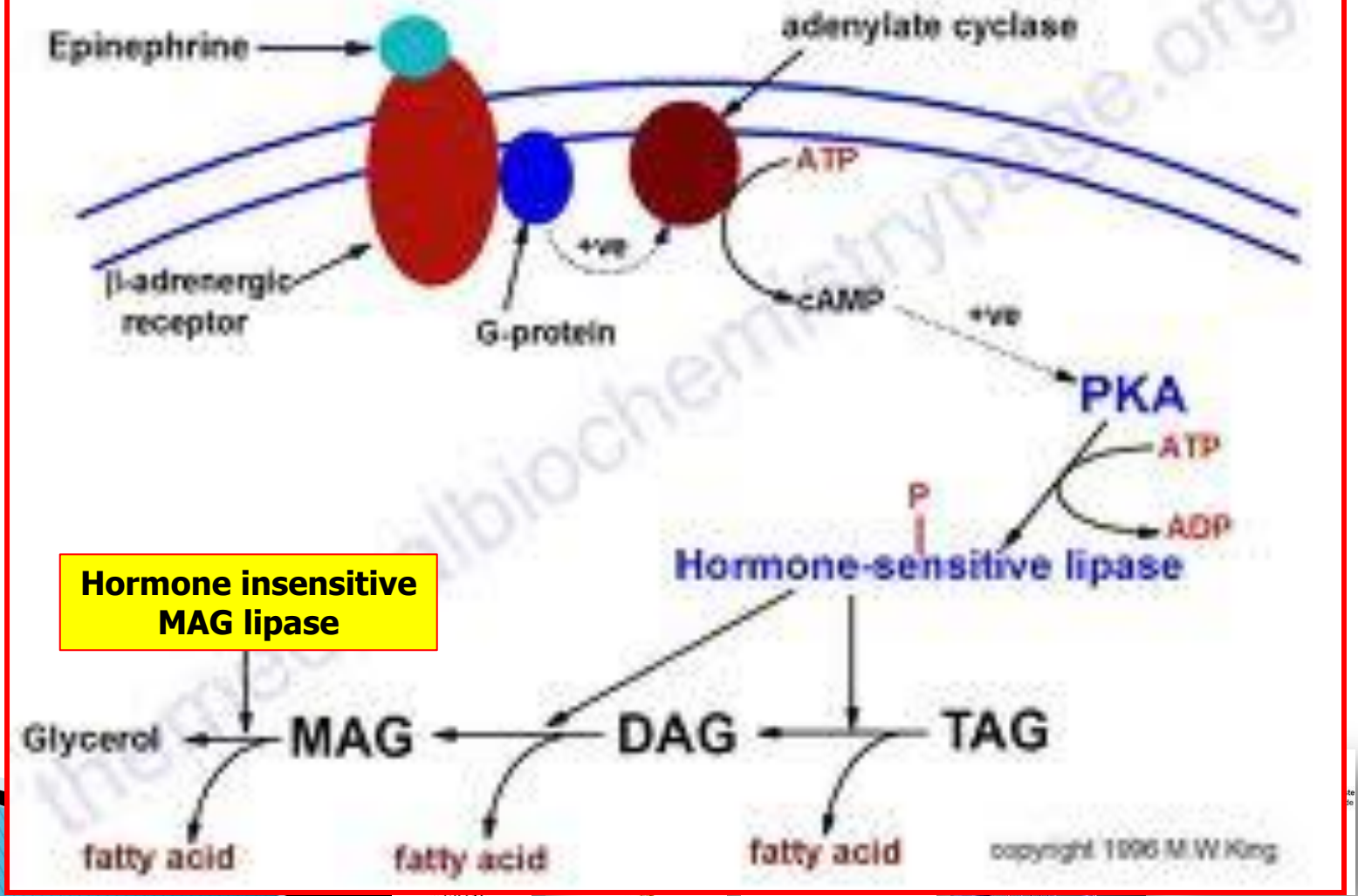


Mobilization of fat



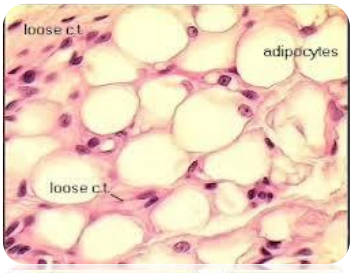


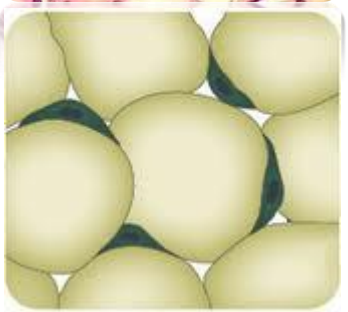
Hormone-Induced Fatty Acid Mobilization in Adipocytes

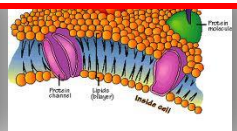


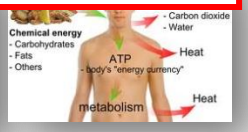
Page 12 in Handouts

Mobilization of fat



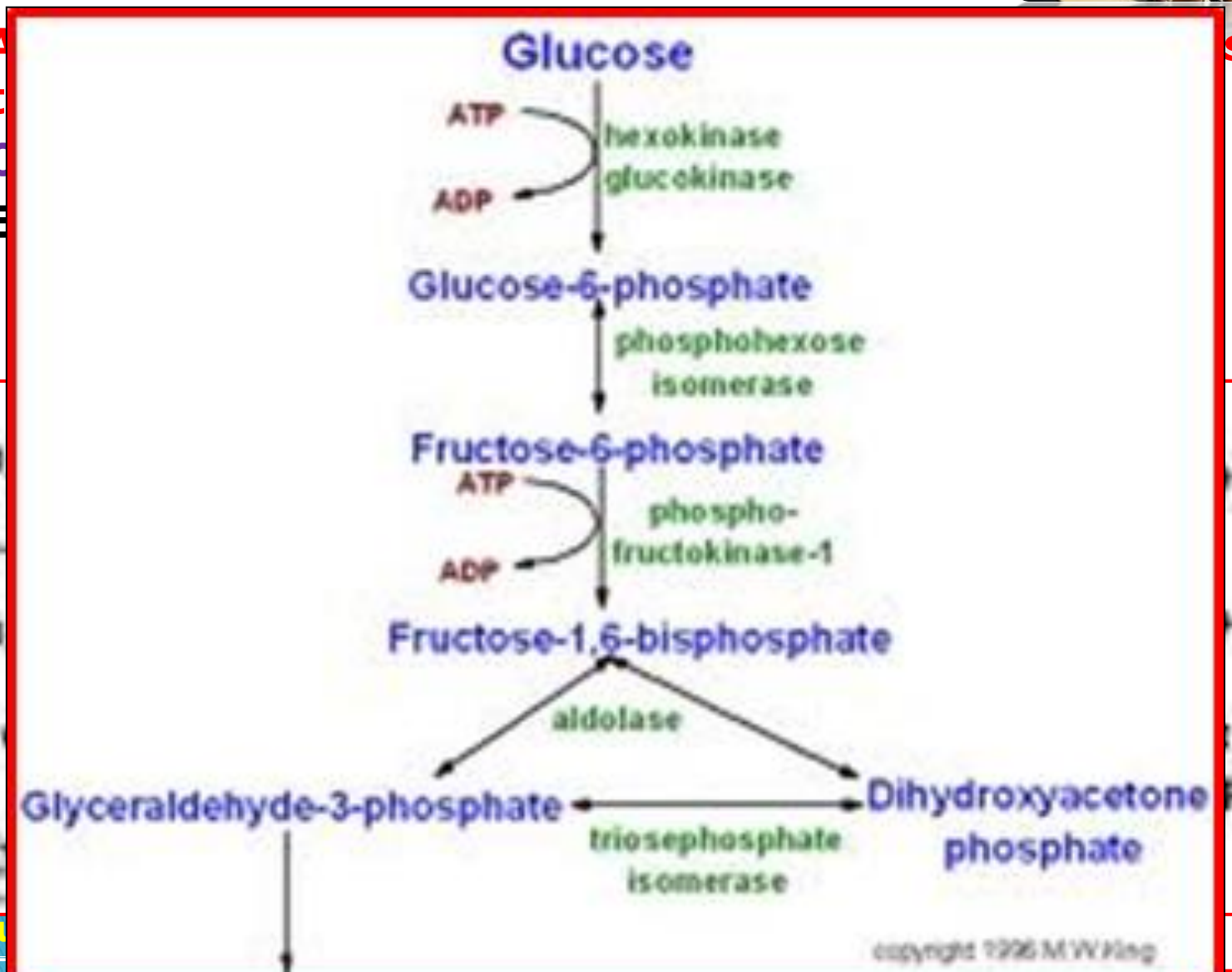


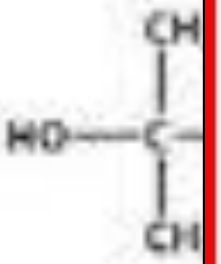




Oxidation of glycerol

- A … s in t…
- C…
- E…



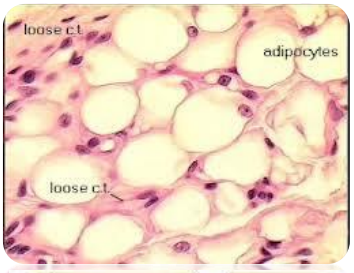


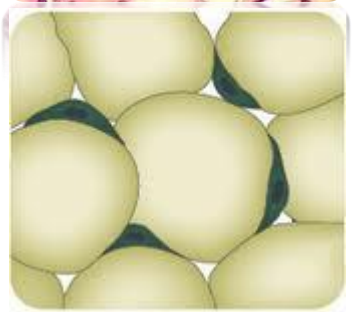
Glycer…

…yacetone …phate

Handou…

Beta oxidation of FAs

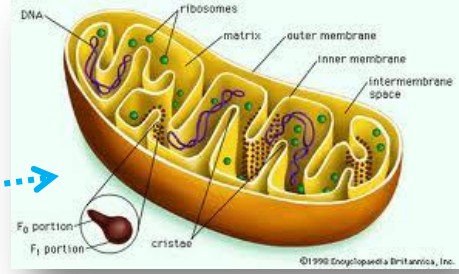




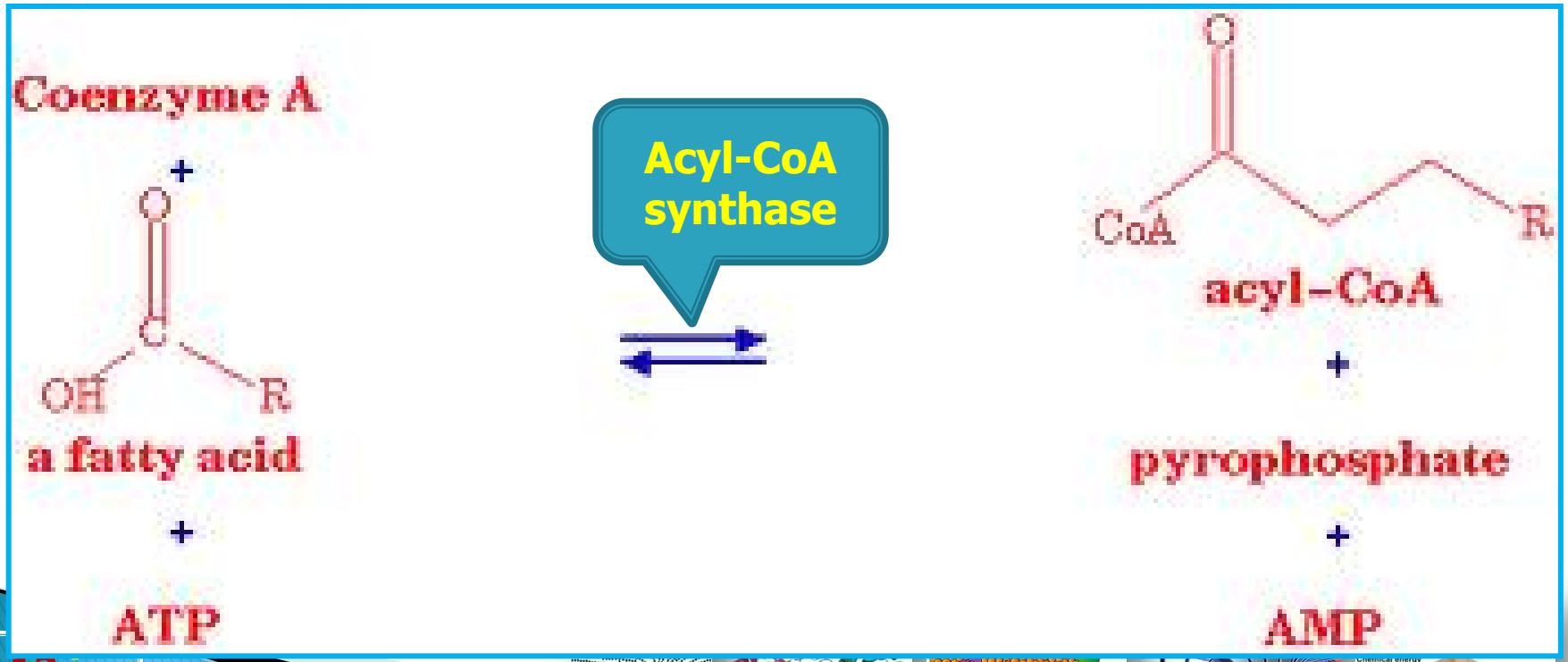
Hormone-Induced Fatty Acid Mobilization in Adipocytes

Epinephrine
adenylate cyclase
ATP
β-adrenergic receptor
G-protein
+ve
cAMP
+ve
PKA
ATP
ADP
P
Hormone-sensitive lipase
Hormone insensitive MAG lipase
Glycerol
MAG
DAG
TAG
fatty acid
fatty acid
fatty acid
copyright 1996 M.W.King

Beta oxidation of FAs

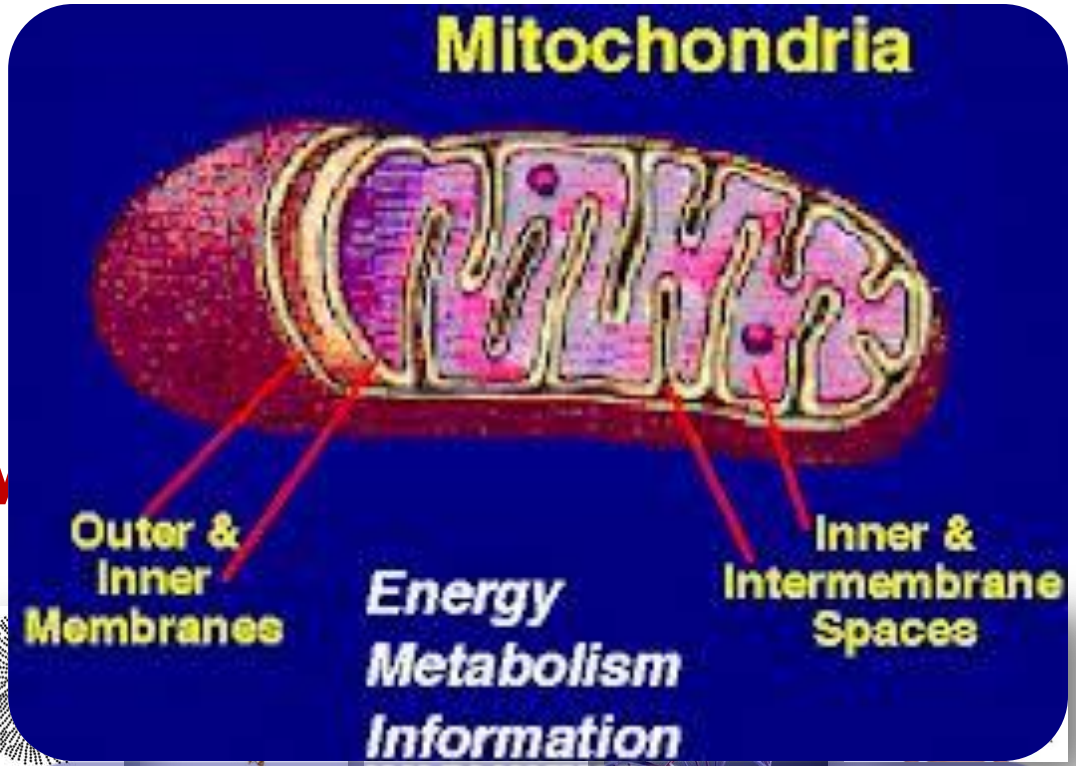


- The beta-oxidation of fatty acids take place inside of the mitochondria of both eukaryotes and prokaryotes for the production of energy
- The activation of fatty acids is necessary for beta-oxidation and it happens in the outer mitochondrial membrane



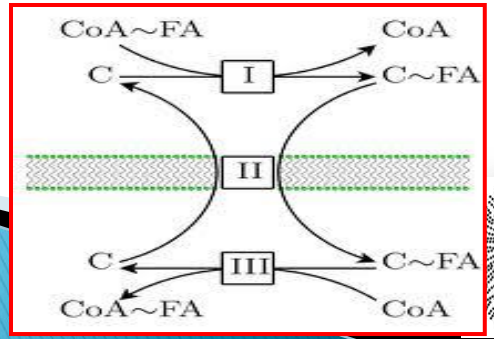
Carnitine in FAs oxidation

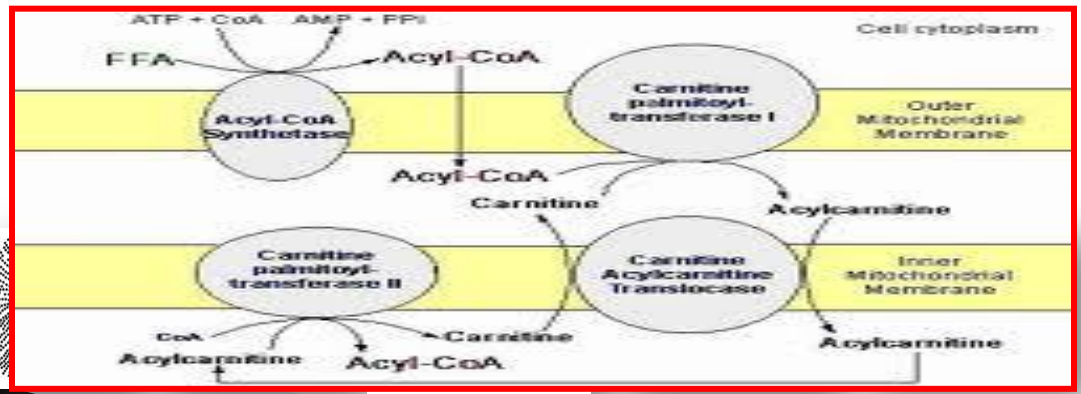
- **Although fatty acid activation as well as fatty acyl-CoA formation is occurred into the outer member membrane of mitochondria but the CoA has no access to the inner membrane of mitochondria**
- **The overcome this difficulty carnitine works as a shuttle to carry as fatty acyl-carnitine via the inner membrane of mitochondria**
- **As soon as fatty-acyl carnitine enters into the mitochondria, the fatty-acyl part joins with mitochondrial CoA and carnitine returns to carry another mole of FA**



Carnitine in FAs oxidation

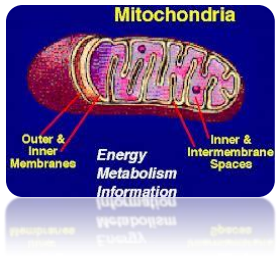
- **Two enzymes are involved with carnitine in this process:**
  - **Carnitine acyl transferase I**
  - **Carnitine acyl transferase II**
- **On the outer surface of the inner mitochondrial membrane, carnitine acyl transferase I catalyzes the transfer of the acyl group from CoA to carnitine**
- **The acyl carnitine then passes through the inner mitochondrial membrane.**
- **On the inner surface of the inner mitochondrial membrane, carnitine acyl transferase II catalyzes the transfer of acyl group to mitochondrial CoA, which is released into the matrix for β-Oxidation.**

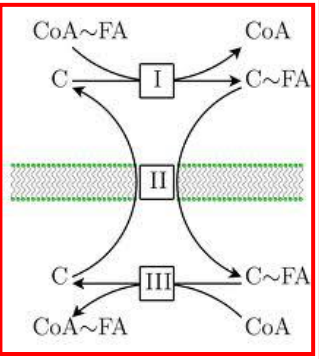


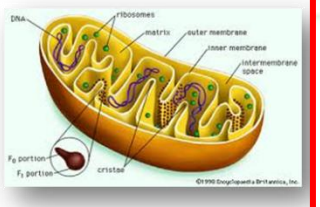


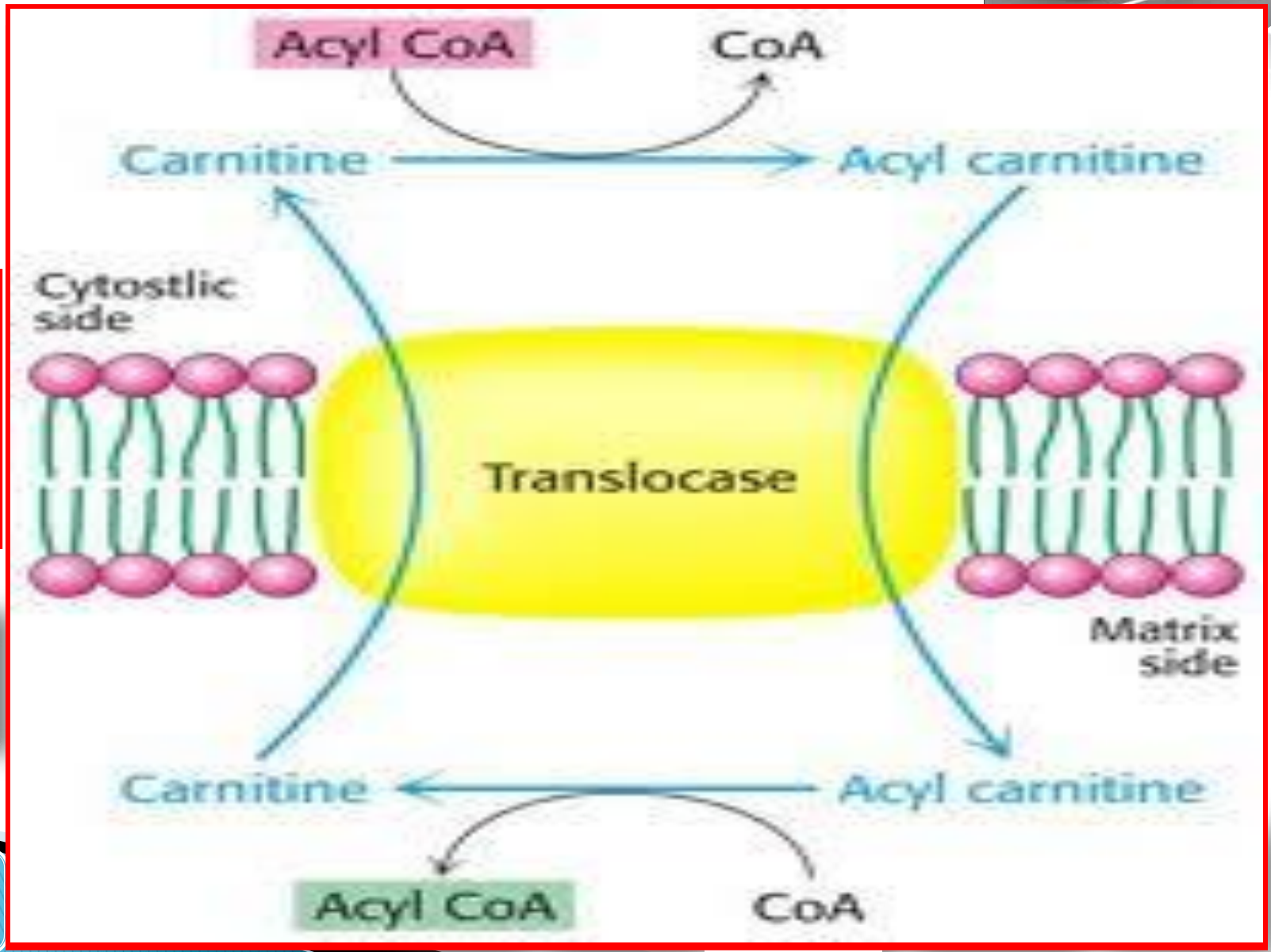
Page 14 in Handouts

Carnitine shuttle system

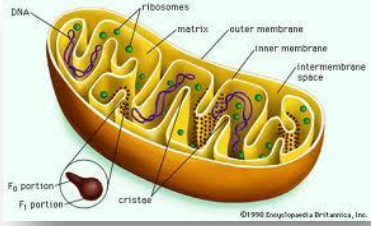




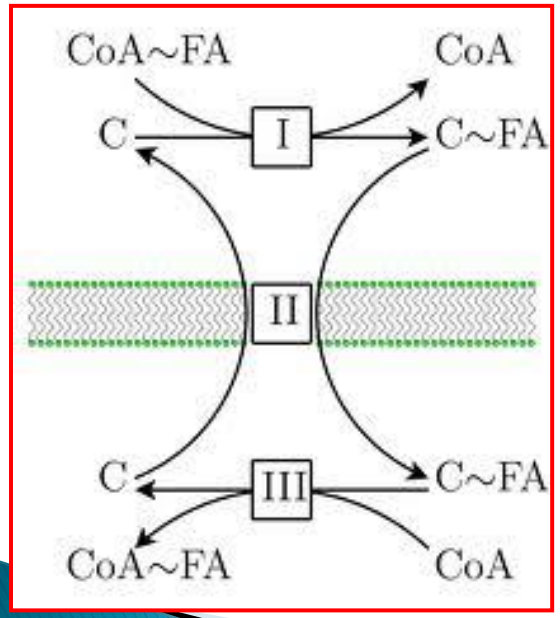


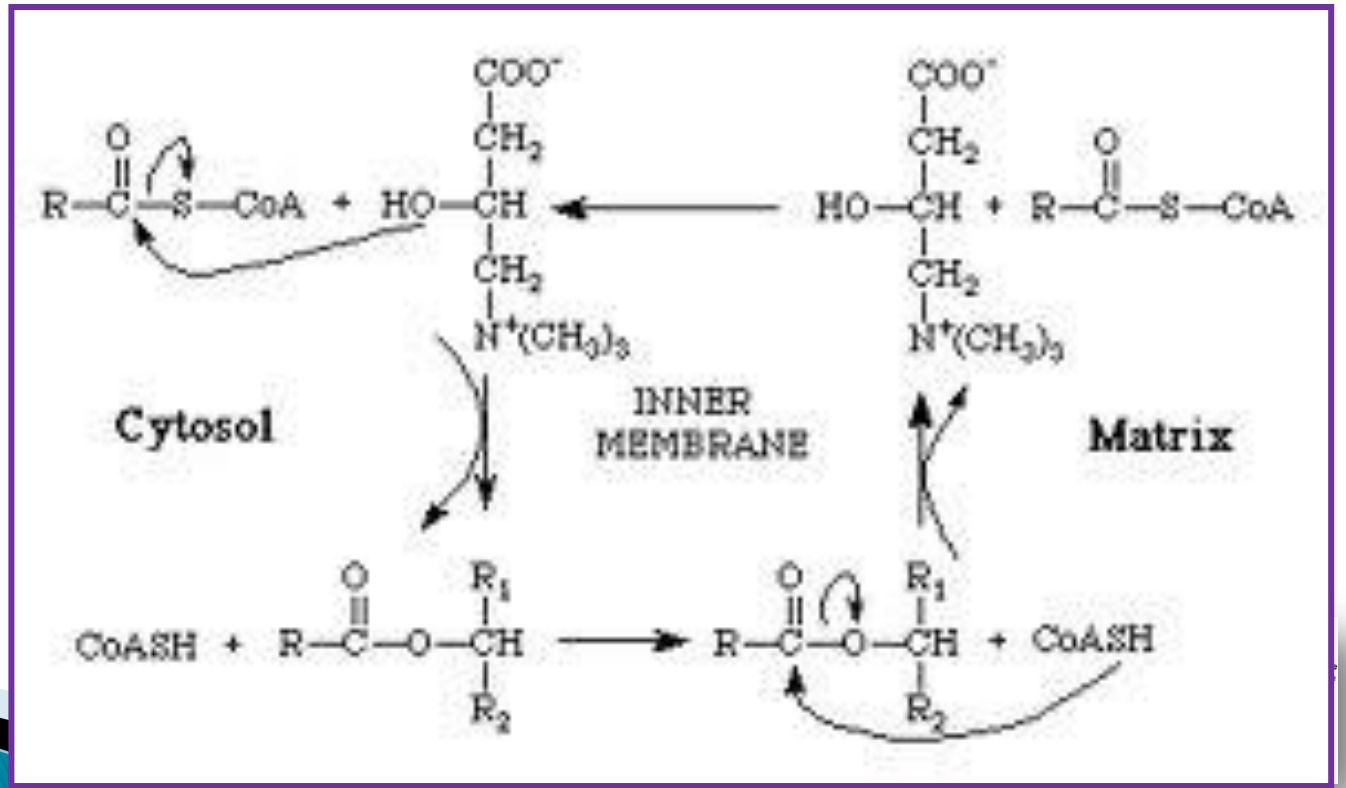


Beta oxidation of FAs

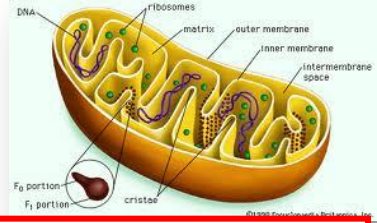


- **Carnitine shuttle system for fatty acid transfer usually occur for C12 – C20 fatty acids**
- **Smaller chain fatty acids (< C12 fatty acids) have access to the inner membrane of mitochondira**
- **So they can cross the mitochondrial membrane and become activated for beta-oxidation**



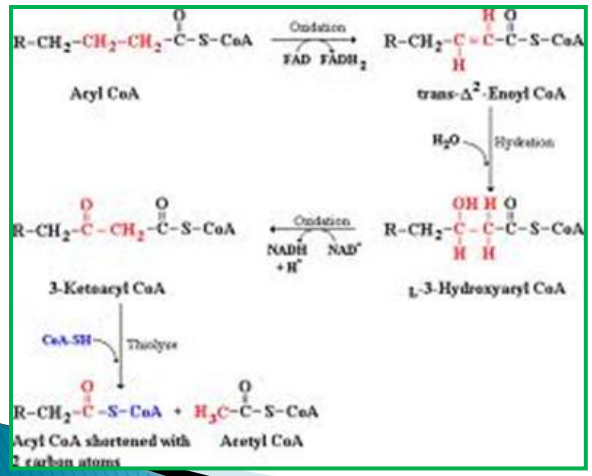


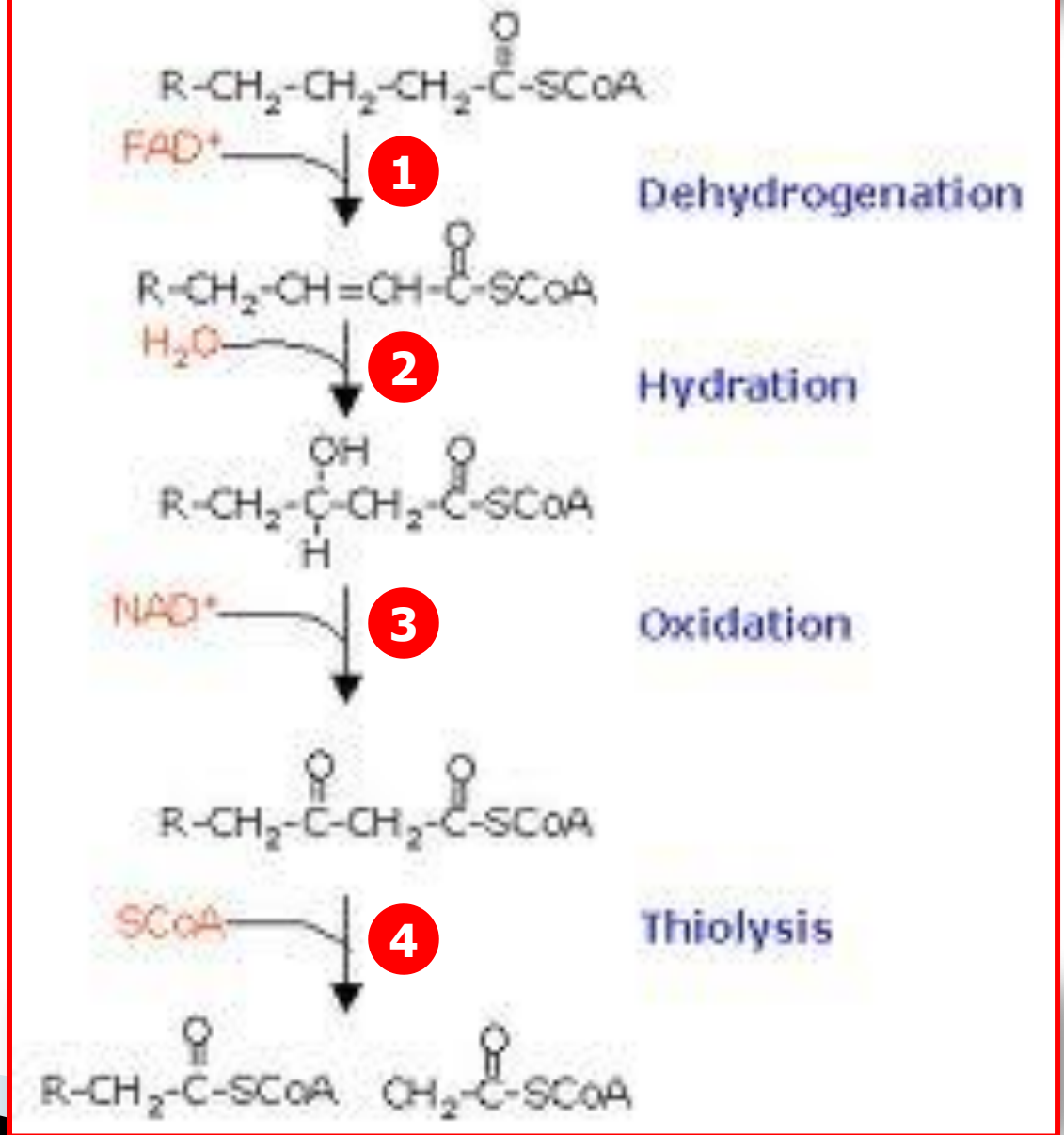
Beta oxidation of FAs



- **Beta-oxidation of fatty acids is a simple 4 step process**

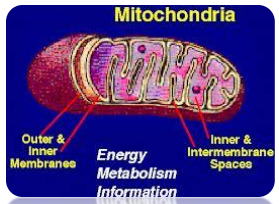
1. Dehydrogenation
2. Hydration
3. Oxidation
4. Thiolysis

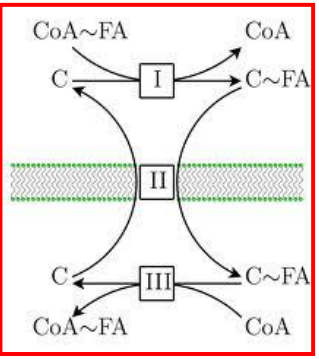


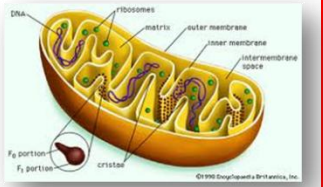


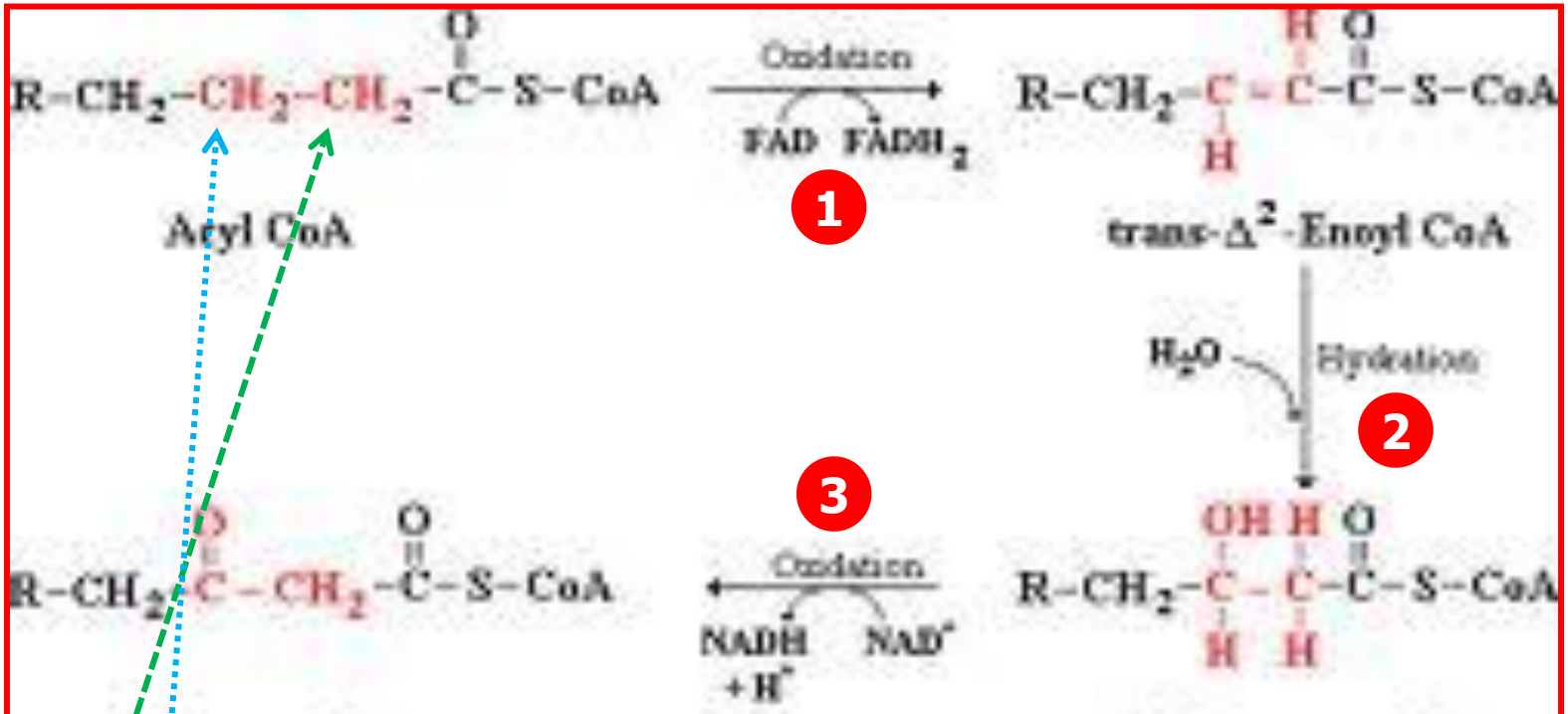
Pg 14-16 in Handouts

Beta oxidation of FAs







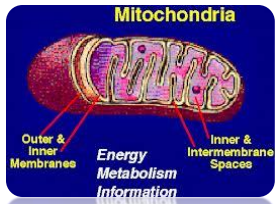


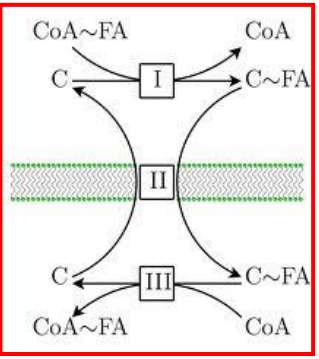
1. αβ-Dehydrogenation of fatty acyl CoA:

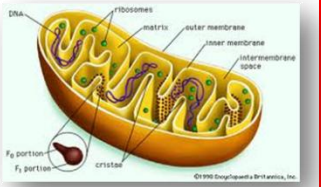
One enzyme called αβ-acyl CoA dehydrogenase is involved in this process, which removes two hydrogen atoms from α(2) and β(3) carbon to form a trans αβ-unsaturated acyl coA.

Pg 14-16 in Handouts

Beta oxidation of FAs

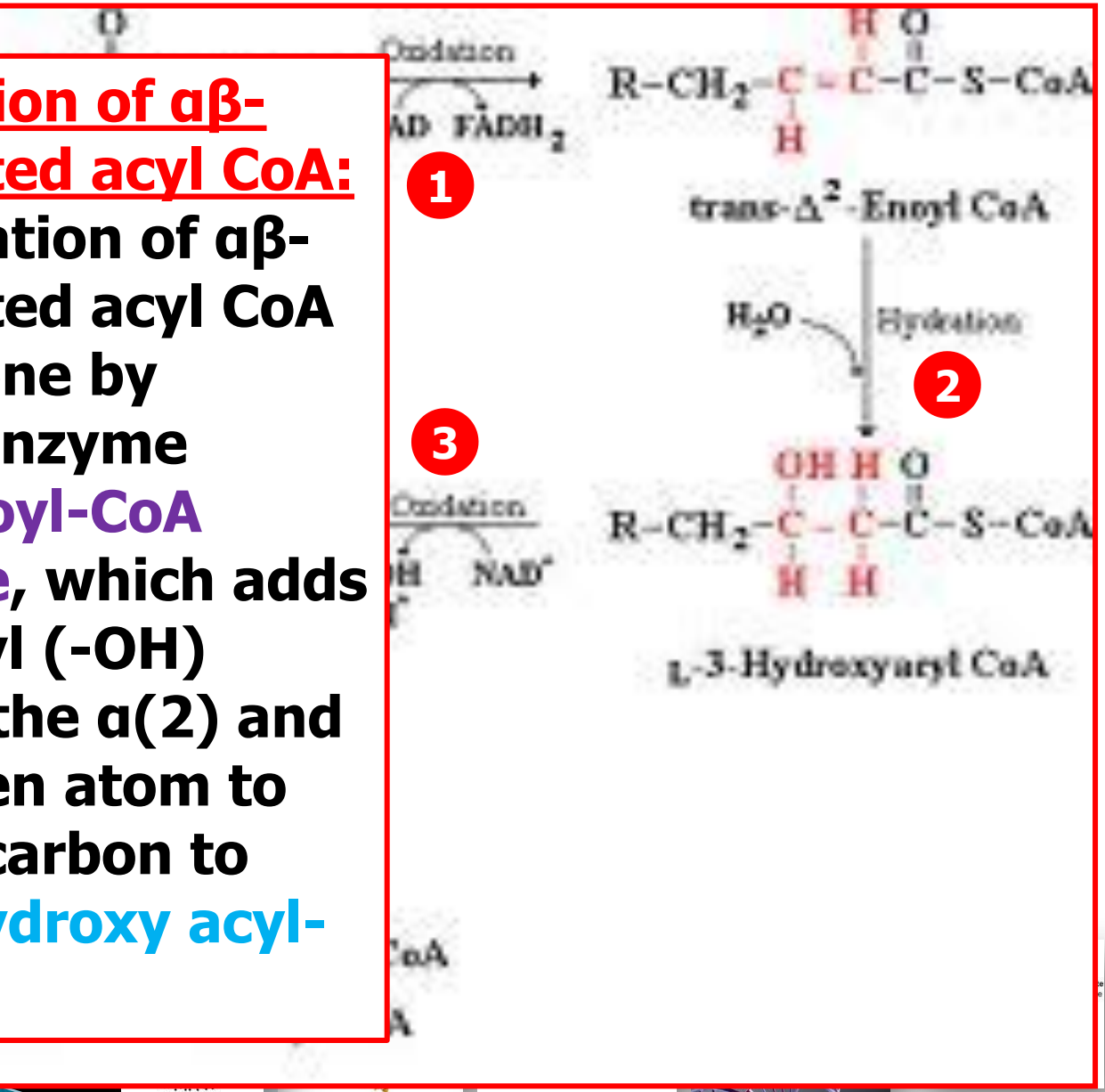






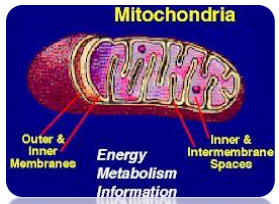
2. Hydration of αβ-unsaturated acyl CoA:

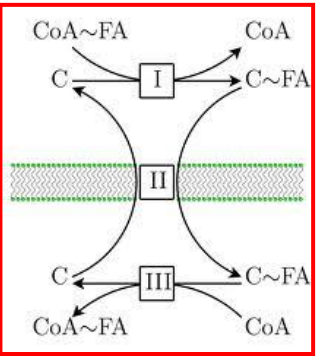
The hydration of αβ-unsaturated acyl CoA will be done by another enzyme called enoyl-CoA hydratase, which adds a hydroxyl (-OH) group to the α(2) and a hydrogen atom to the β(3) carbon to form β-hydroxy acyl-CoA.

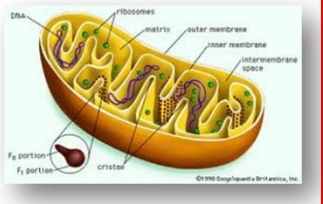


Pg 14-16 in Handouts

Beta oxidation of FAs

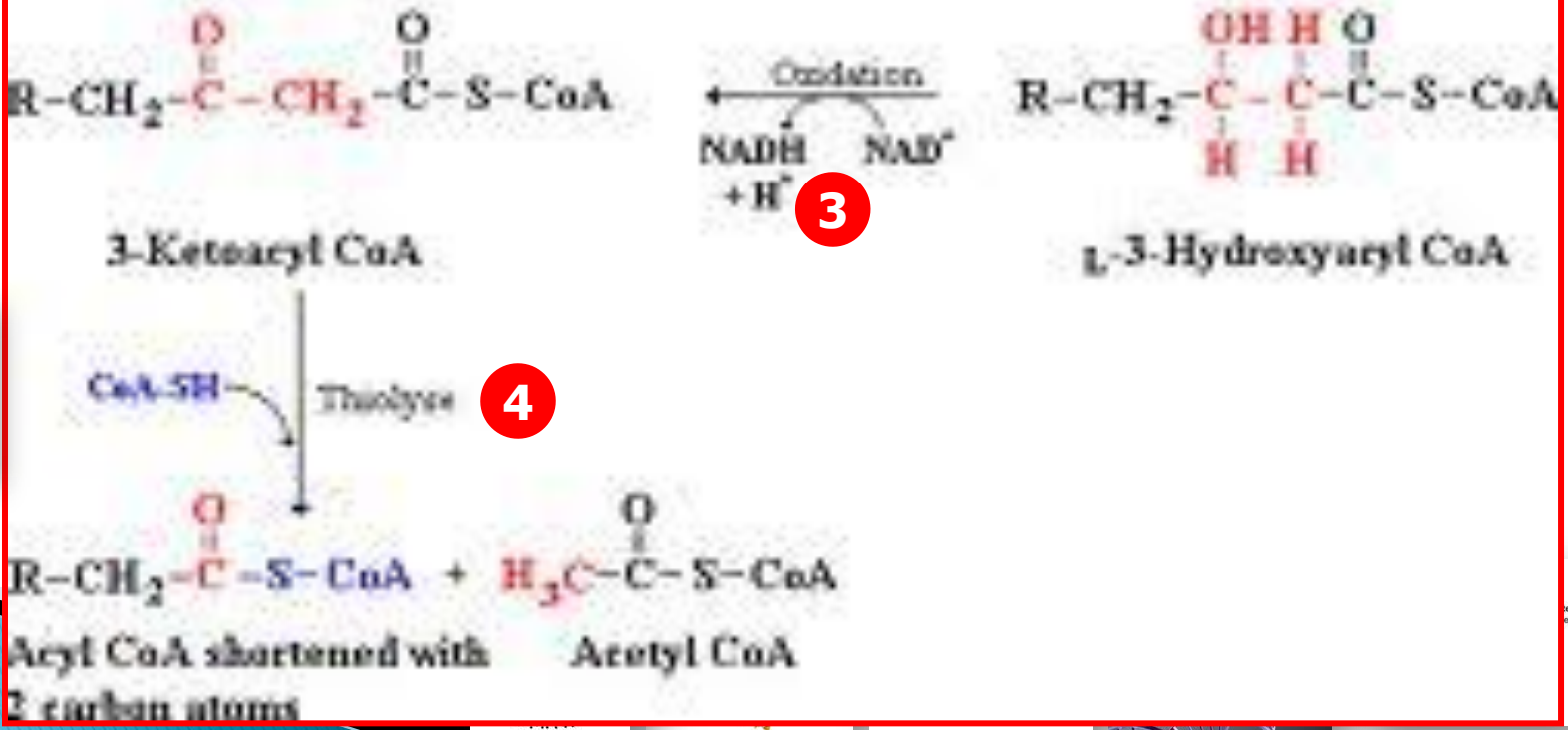






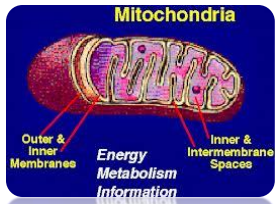
3. Dehydrogenation of β-hydroxy acyl CoA:

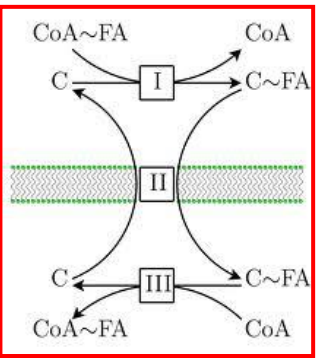
The dehydrogenation of β-hydroxy acyl-CoA is done by the removal of two hydrogen atoms from the β-carbon to form β-keto acyl CoA catalyzed by an enzyme called β-hydroxy acyl-CoA dehydrogenase.

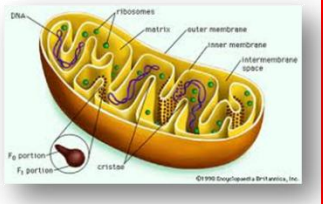


Pg 14-16 in Handouts

Beta oxidation of FAs

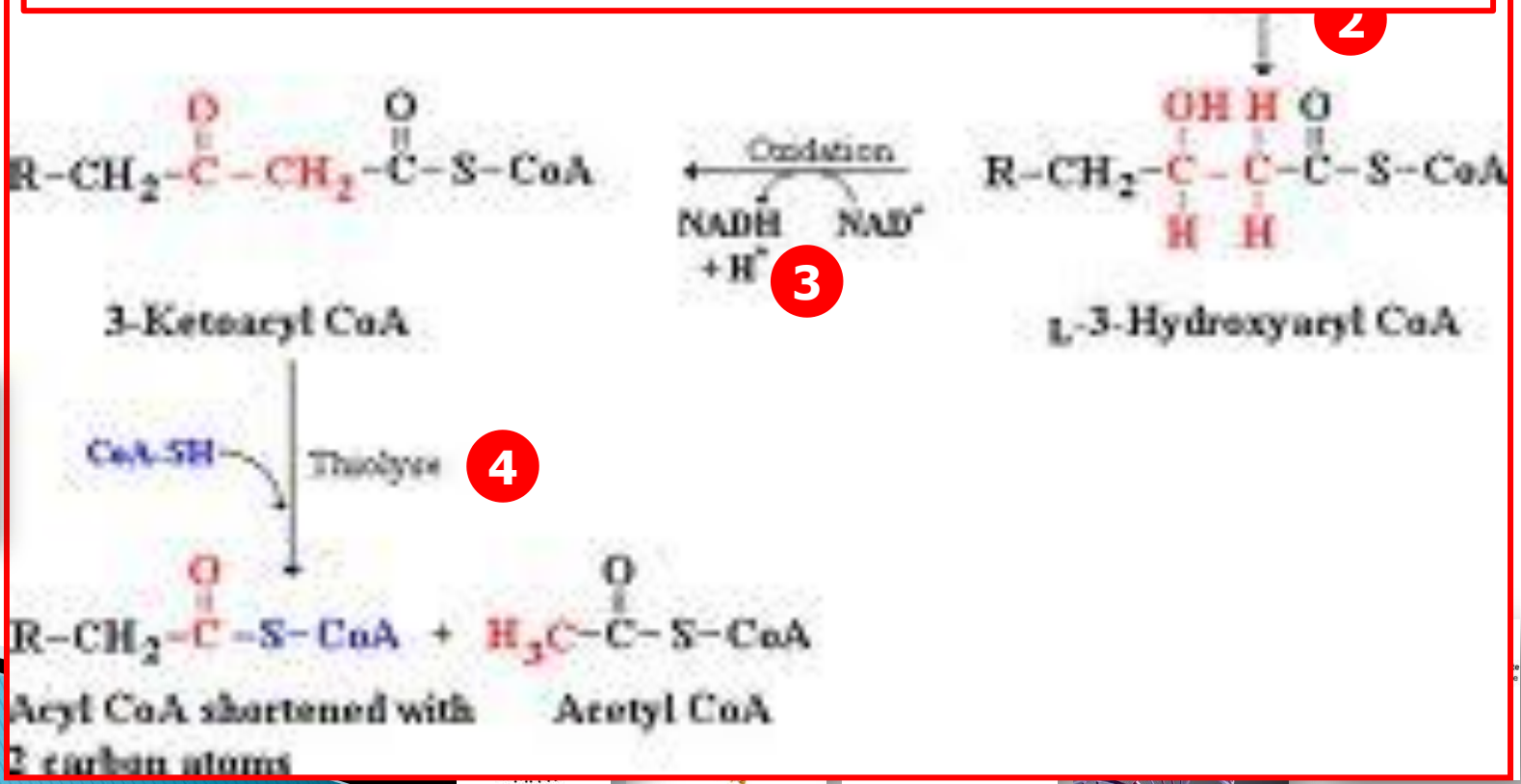






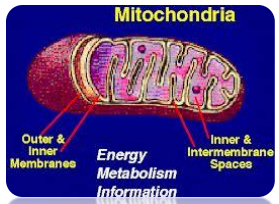
4. Thiolytic cleavage of β-keto acyl CoA:

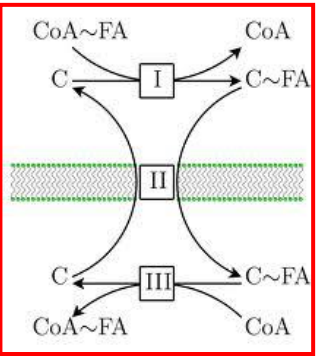
The thiolytic cleavage of β-keto acyl CoA is done by the removal of one mole of Acetyl-CoA and another fatty acyl-CoA catalyzed by an enzyme called thiolase.

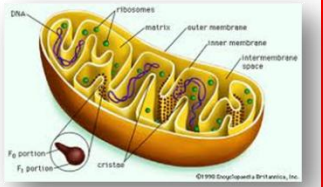


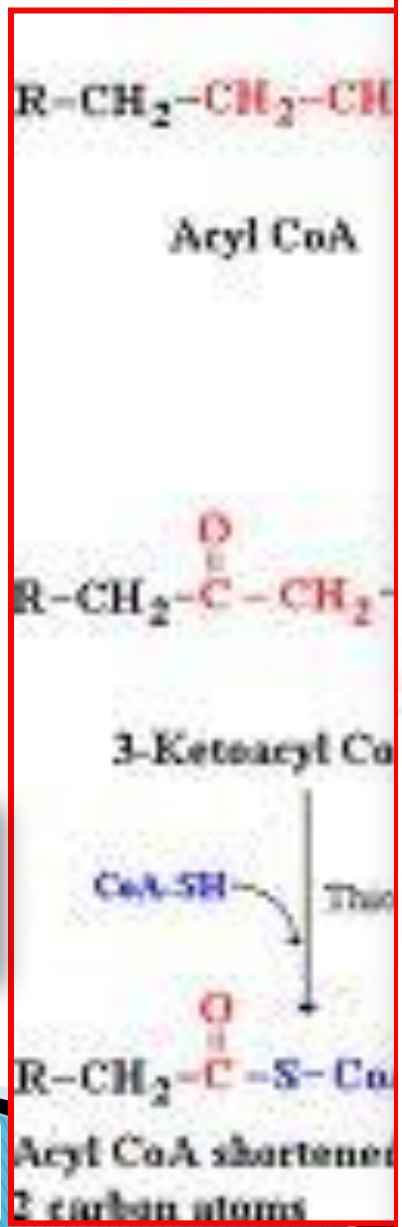
Pg 14-16 in Handouts

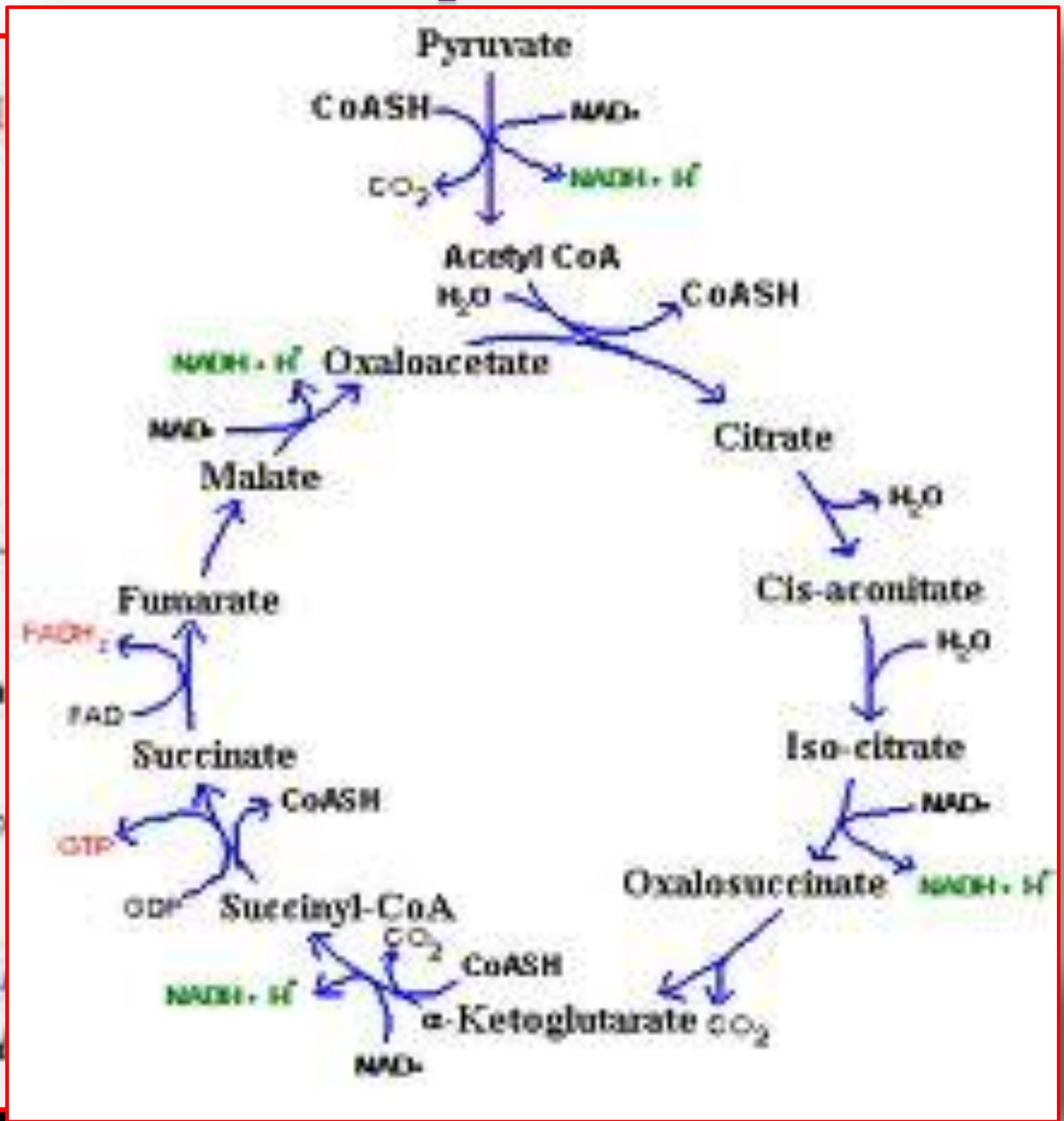
Energy production: β-oxidation











Pg 16 in Handouts

Energy production: β-oxidation

Summary of energy p

Energy production from

1. From step 1
2. From step 3
3. From TCA Cycle

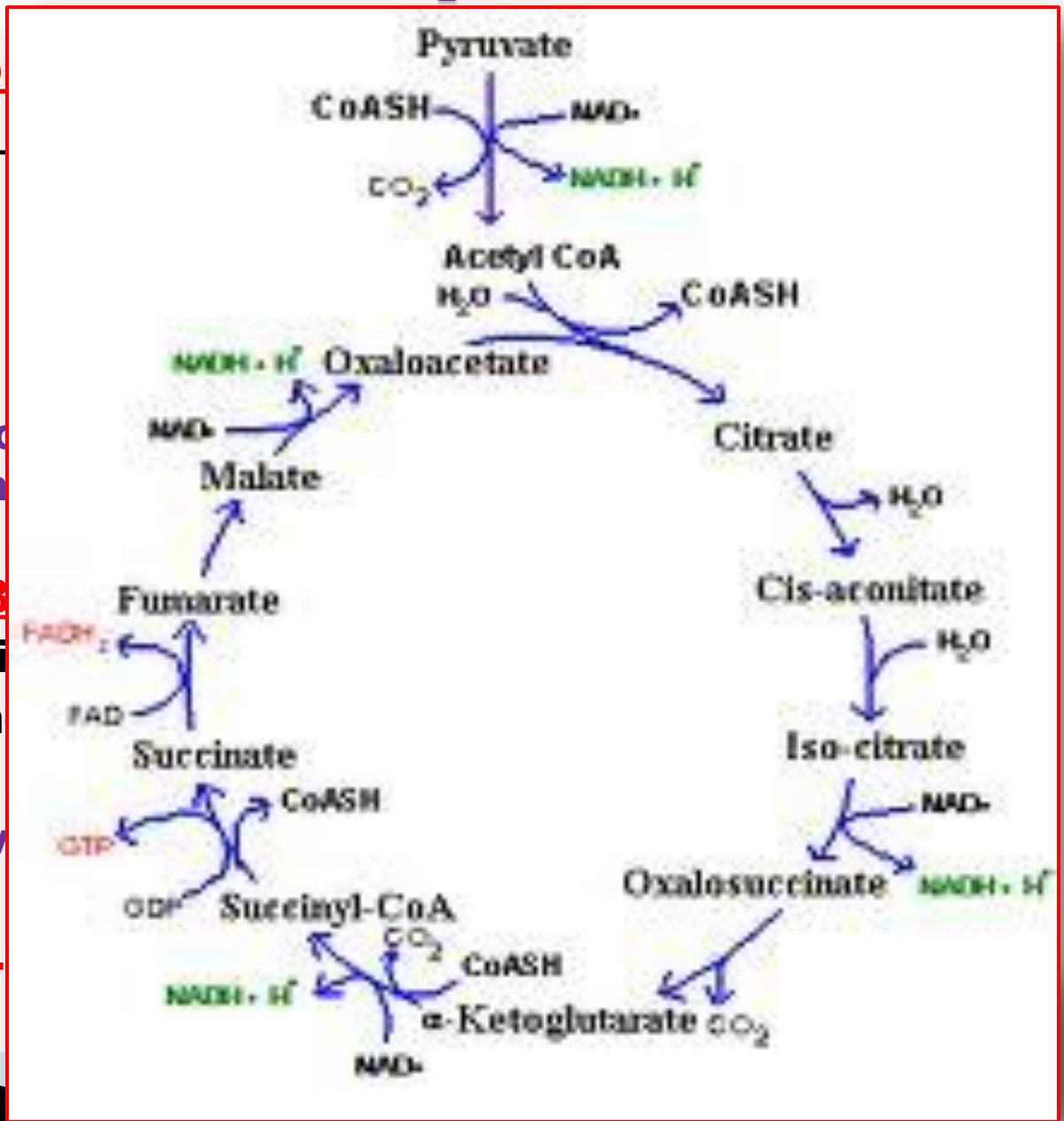
- If a 16 carbon fatty ac
  for β-oxidation then a
  oxidation process:

From these 7 cycles of β

- 1) Production of ATP i
- 2) From remaining on

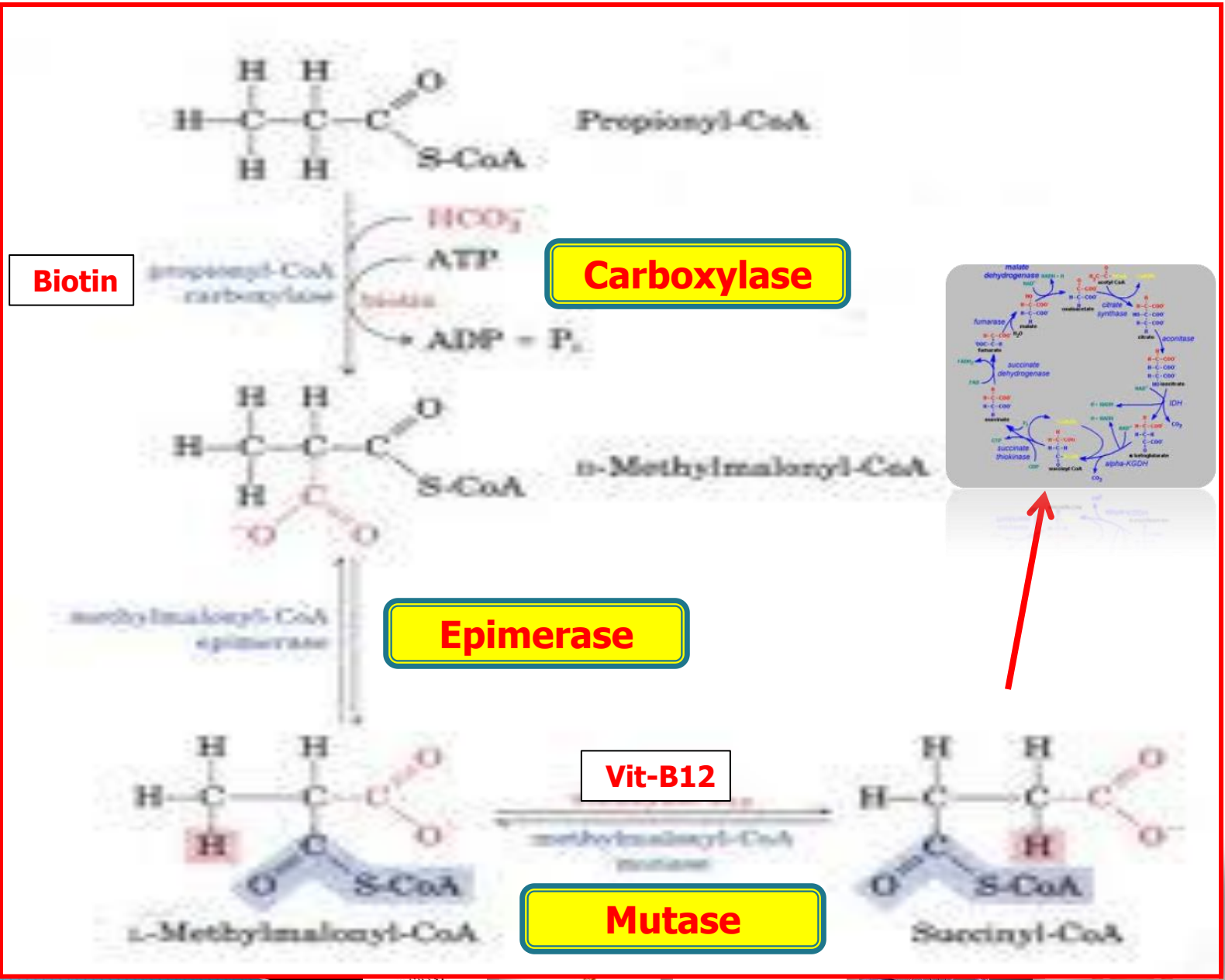
- ATP used for the activ
- Net ATP production /

Note: 1 mole of ATP = 7.



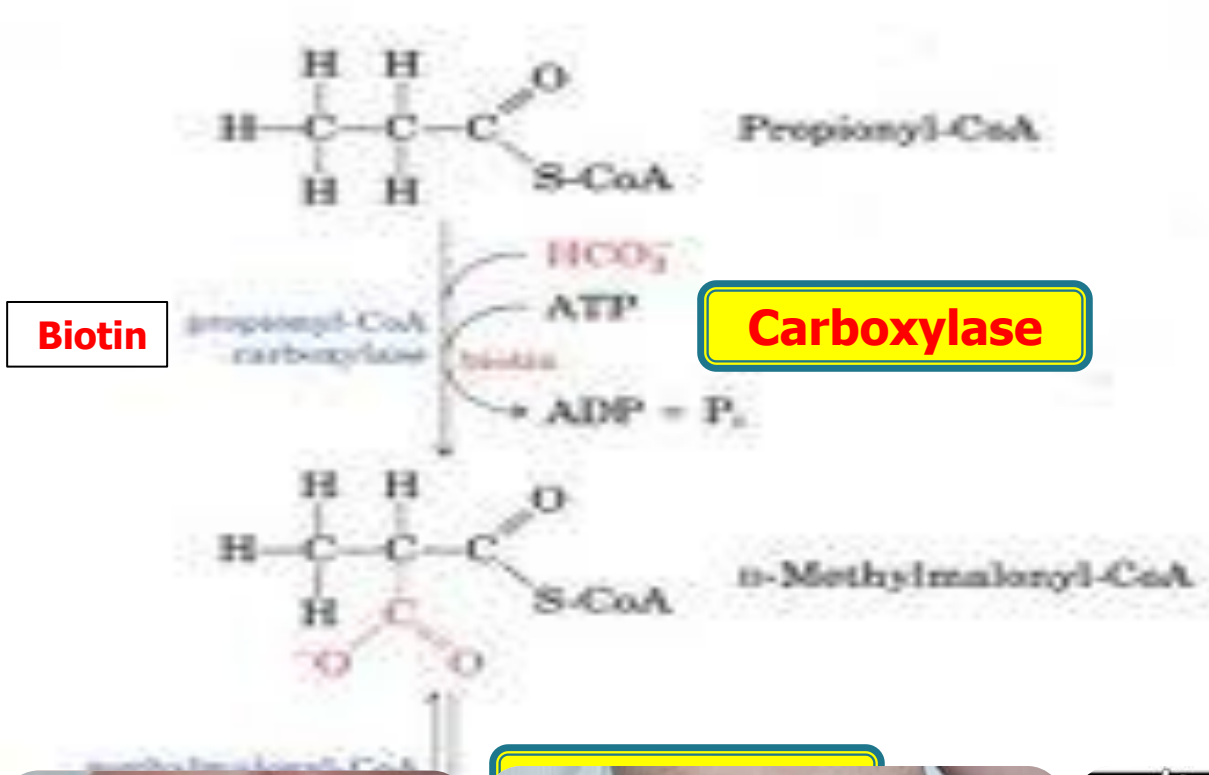
Oxidation of odd carbon FAs

- Most
- Sever
  some
- Long-
  chain
- Howe
  but N
- When
  enzyr
  CoA.
- Acety
  can't
- Propi
  enter



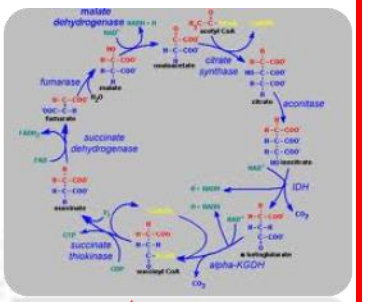
Clinical correlation

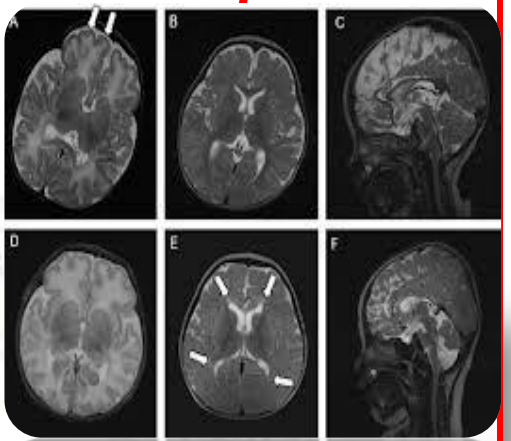
- Inabi
  muta
  cause
- This i
  causi
  the c
- This
  usual
- In ca
  disea
  doses



Biotin

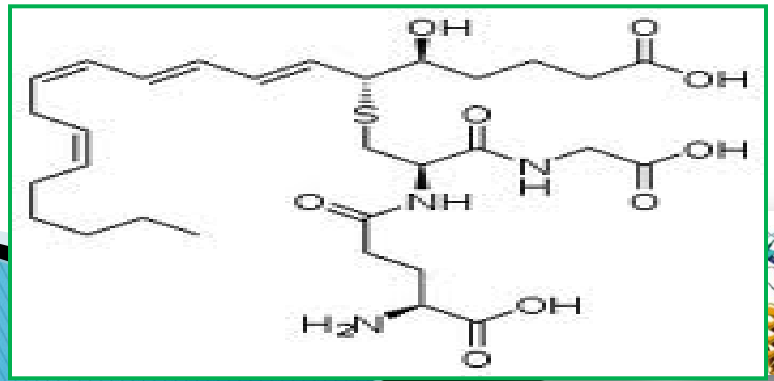
Carboxylase

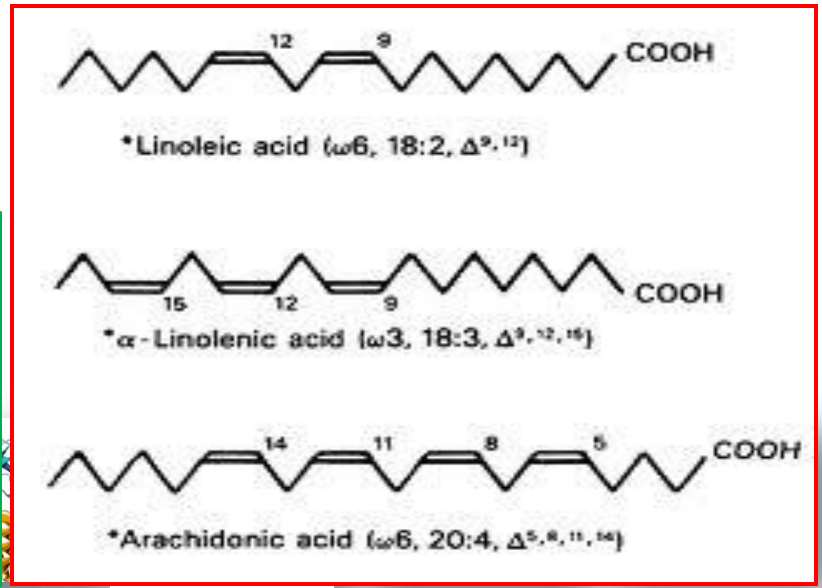




Oxidation of unsaturated FAs

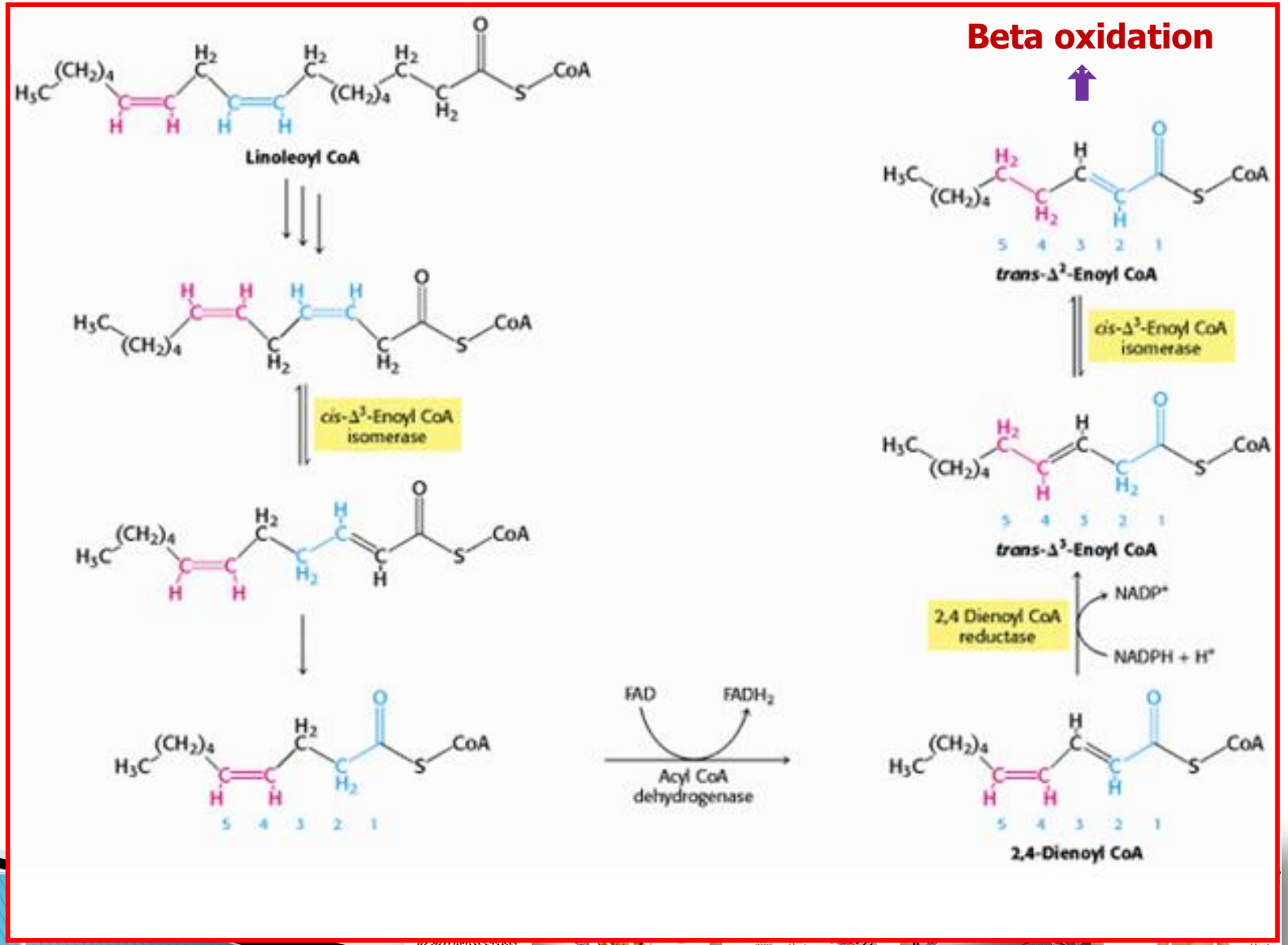
- **Beside saturated fatty acids, many unsaturated fatty acids are used for the production of energy in living systems.**
- **Unsaturated fatty acids have one or more CIS double bonds in a non-conjugated manner.**
- **Hence, these double bonds cannot be used for β-oxidation by the enzyme enoyl-CoA hydratase.**
- **Position of double in the carbon chain is also an issue. (αβ TRANS double bond favours β-oxidation)**
- **Hence, TWO additional enzymes require for the oxidation of unsaturated fatty acids. Such as-**
  - **(1) Enoyl-CoA isomerase and**
  - **(2) 2,4-Dienoyl-CoA reductase**



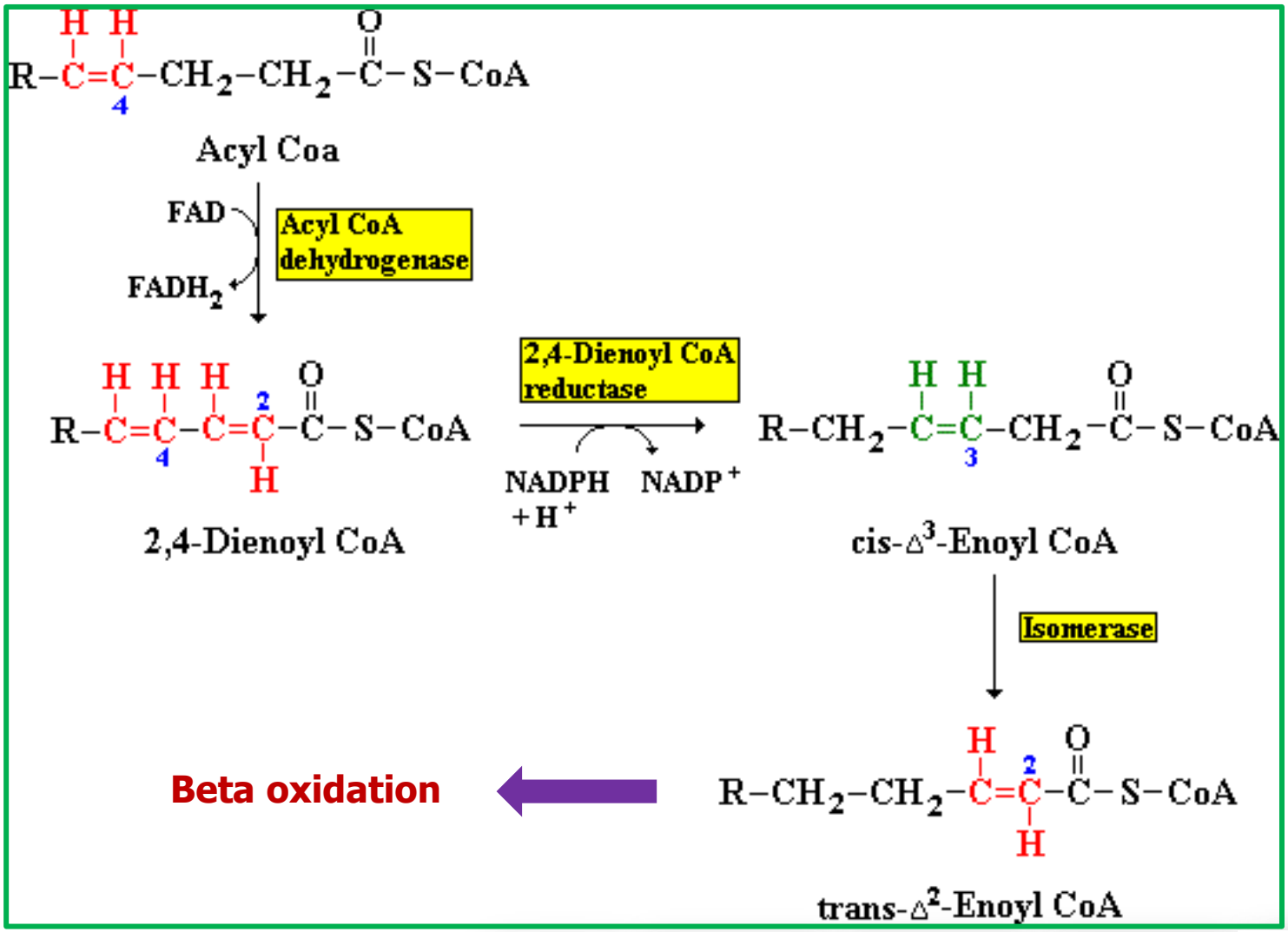


Page 17 in Handouts

Oxidation of unsaturated FAs



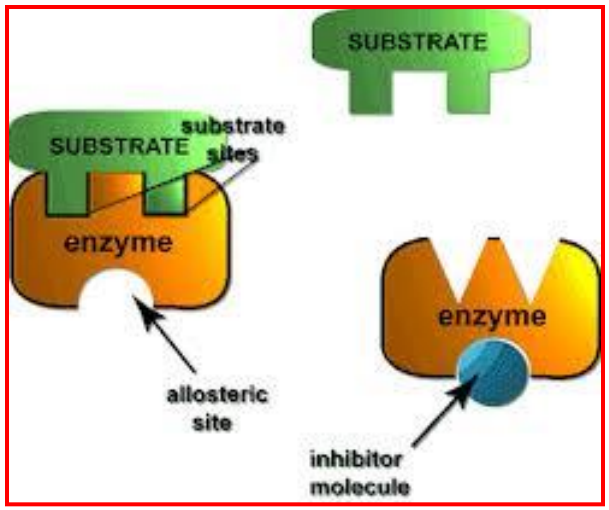
Oxidation of unsaturated FAs



Regulation of energy metabol.

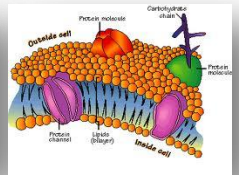
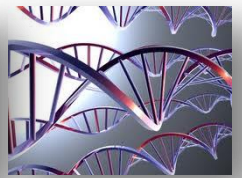
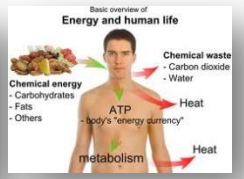
Who regulates the energy metabolism?

- **Several factors involved in the regulation of energy metabolism, such as-**



1. Availability of substrates
2. Concentrations of products
3. Availability of nutrients
4. Availability of enzymes & coenzymes
5. Concentrations of cellular ATPs
6. Concentrations of hormones
7. Physiological conditions
8. Physical activities etc.

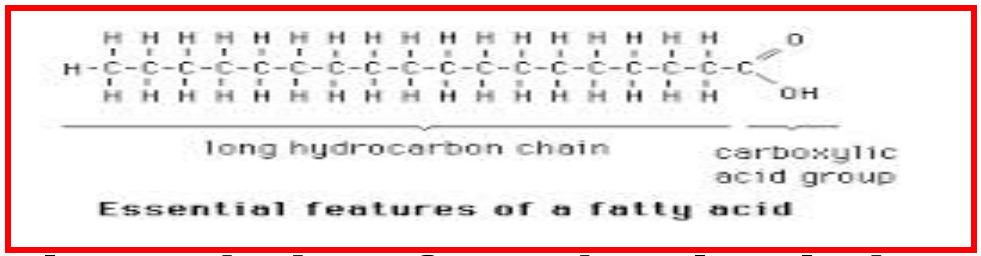


Fatty acids biosynthesis

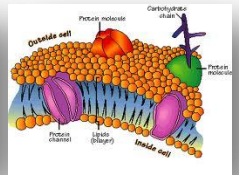
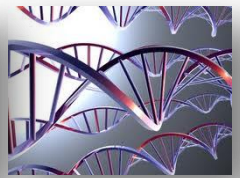
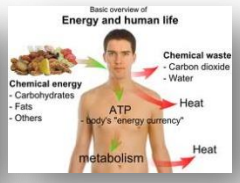
- **Fatty acid biosynthetic pathways are simply opposite of fatty acids beta-oxidation (will discuss later)**
- **Most of the biosynthetic pathways are active in the cytoplasm and most of the degradation pathways are active in the inside of the mitochondia**
- **Fatty acids biosynthetic pathway is active in inside of the cytoplasm of the cells, two components are mainly used as major raw materials of fatty acid biosynthesis, such as-**

(1) Acetyl-CoA and
(2) Malonyl-CoA



- **In feeding condition, acetyl-CoA derives from the glycolytic pathway is used for the biosynthesis Malonyl-CoA as well as fatty acids, however mitochondrial acetyl-CoA can also be used for the biosynthesis of fatty acids (will discuss later)**

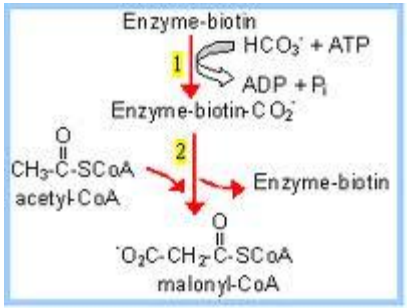


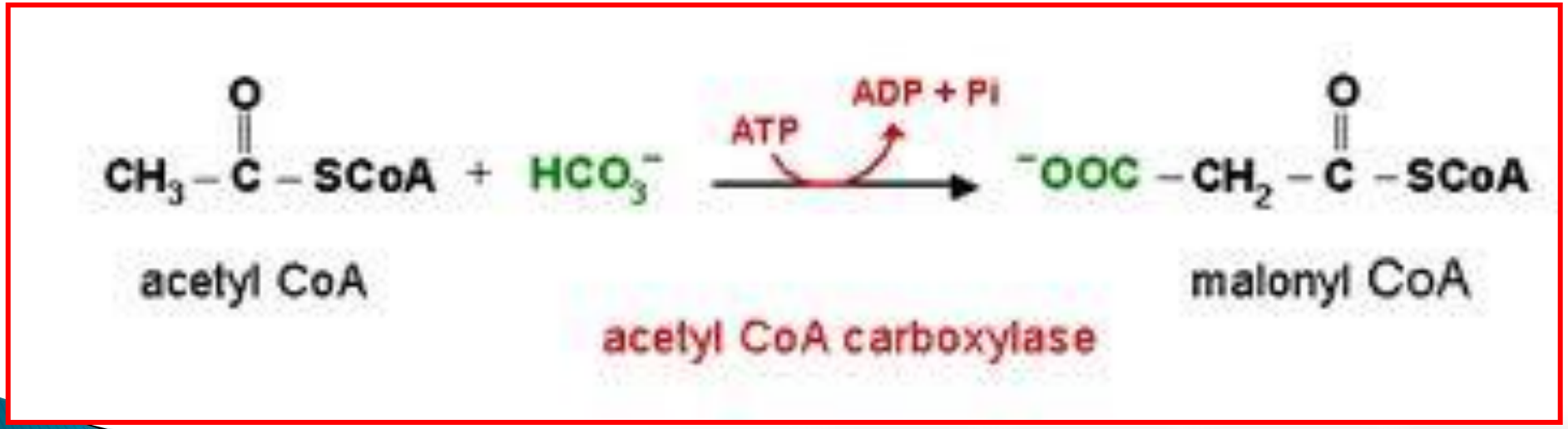




Extramitochondrial FAs synthesis

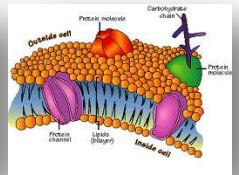
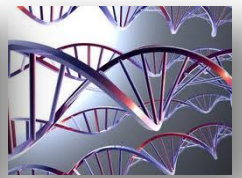
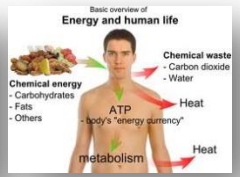
Reaction 1: Synthesis of Malonyl-CoA from Acetyl-CoA

- The first step is formation of malonyl-CoA from acetyl-CoA is catalyzed by enzyme called acetyl-CoA carboxylase
- This reaction is exergonic and irreversible
- The enzyme uses a biotic co-factor which binds to bicarbonate and works as a source of CO2





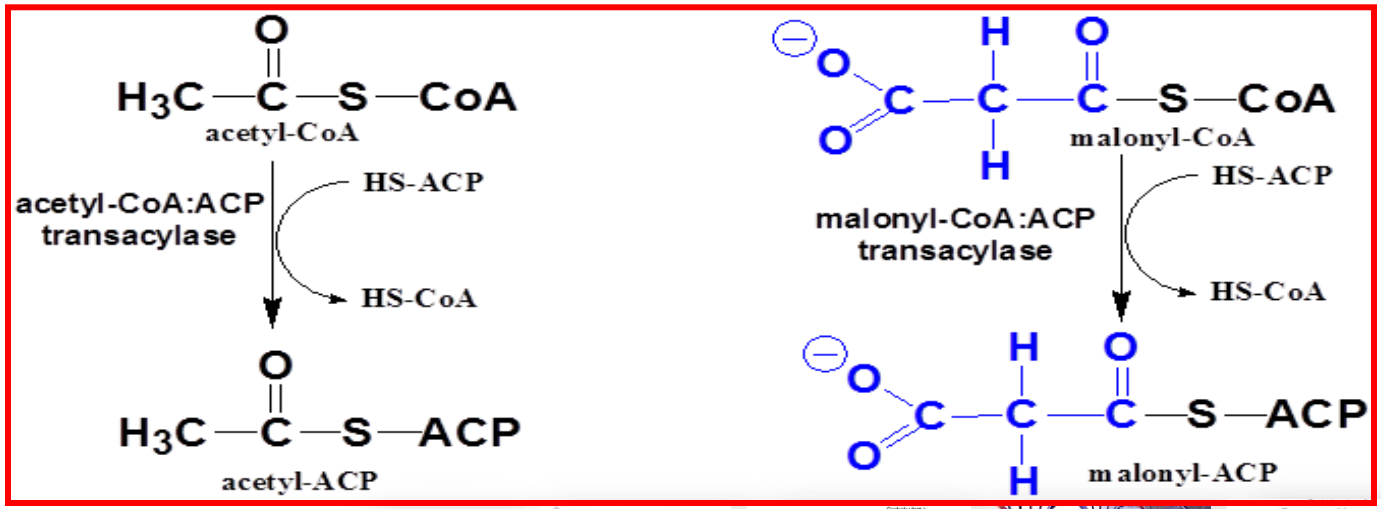


Extramitochondrial FAs synthesis

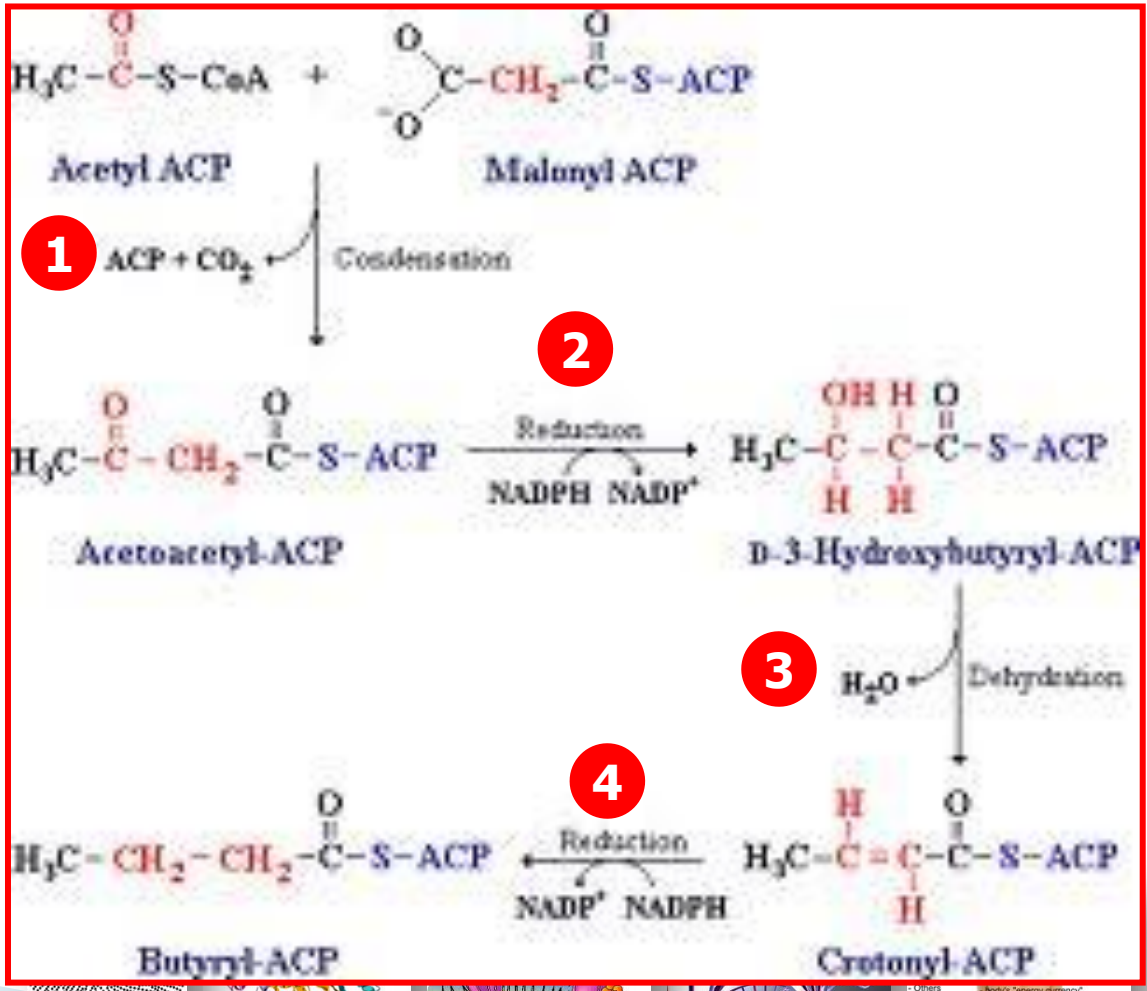
Reaction 2 & 3: Activation of Malonyl-CoA and Acetyl-CoA

- The activation of Malonyl-CoA and Acetyl-CoA is very important for the biosynthesis of fatty acids
- Both of them bind with Acyl Carrier Protein (ACP) and converted to Malony-ACP and Acetyl-ACP as their active forms for fatty acid biosynthesis
- The Malonyl transacylase and Acetyl-CoA ACP transacylase are used as enzymes respectively to catalyse these reactions.



Extramitochondrial FAs synthesis

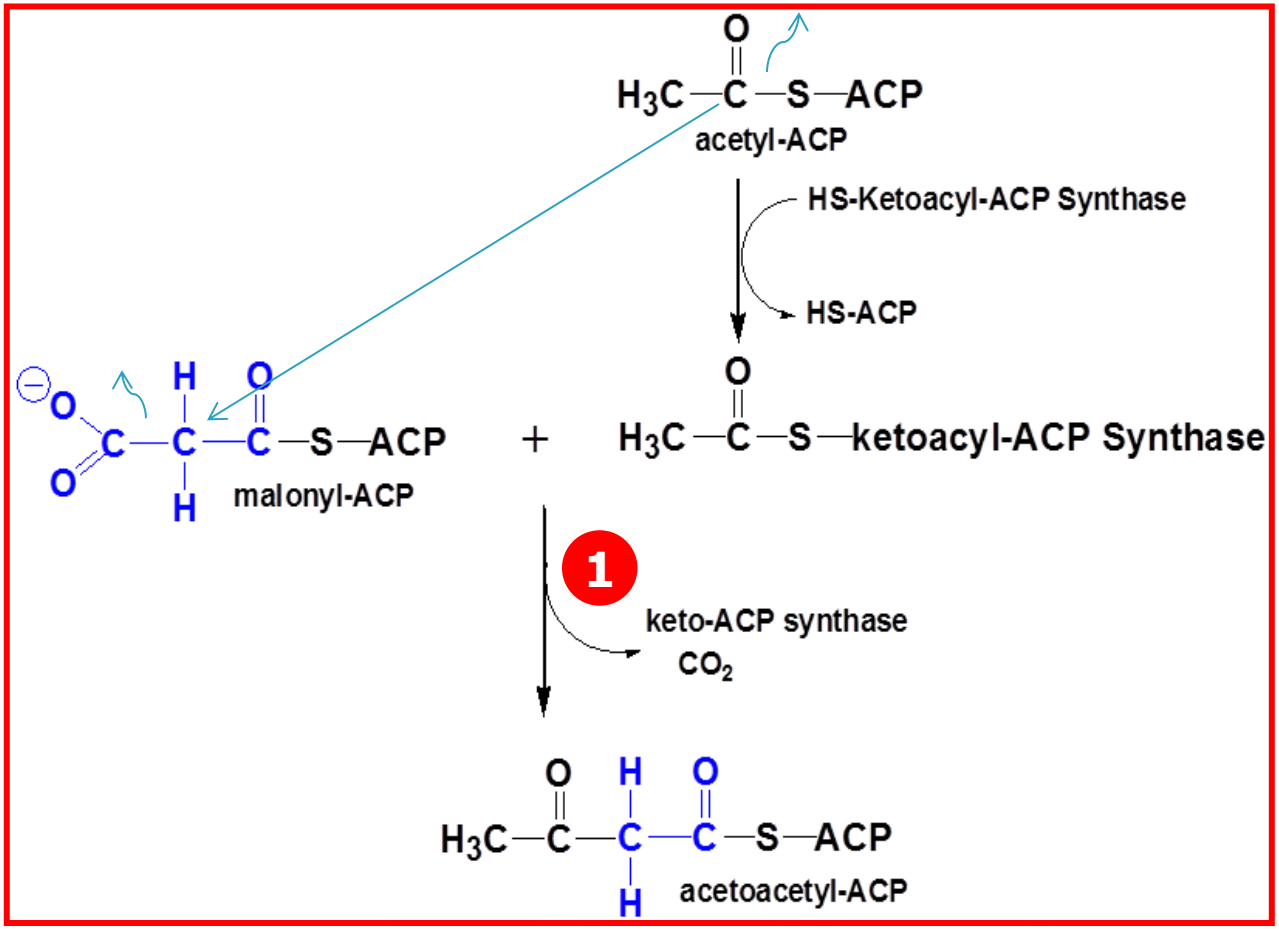
- **After the activation of Malonyl-CoA and Acetyl-CoA fatty acids biosynthesis is completed by following FOUR step reactions:**
  - **(1) Condensation**
  - **(2) Reduction**
  - **(3) Dehydration**
  - **(4) Reduction**



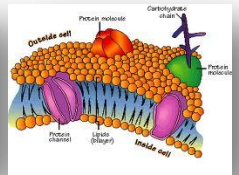
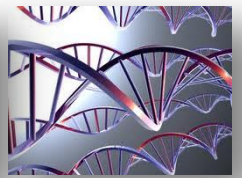
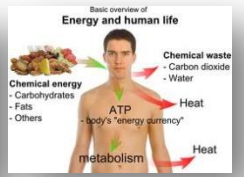
Extramitochondrial FAs synthesis

(1) Condensation reaction:

- **In this reaction Acetyl-ACP and Malonyl-ACP join together via a condensation reaction catalyzed by enzyme called beta-keto acyl-ACP synthase**



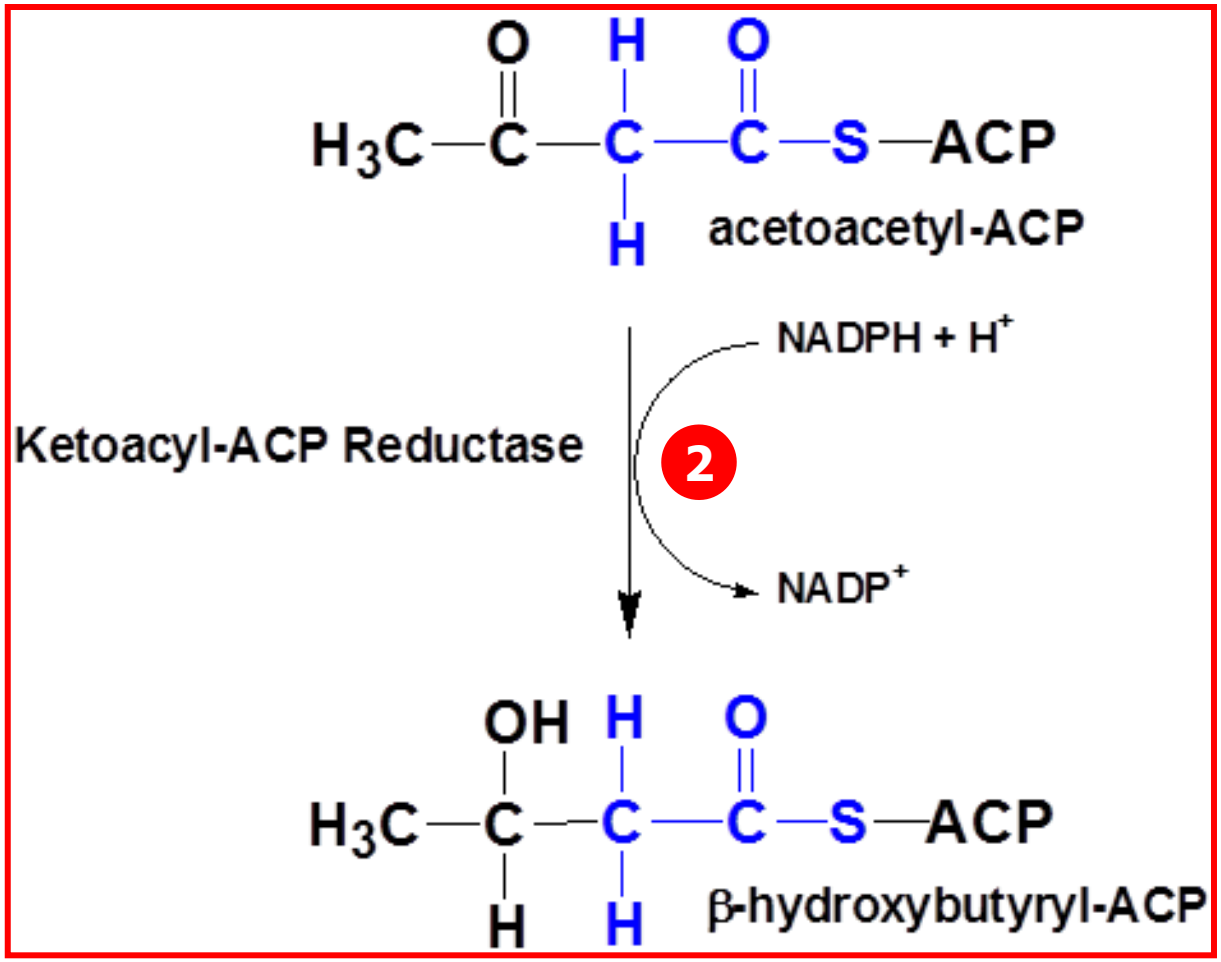


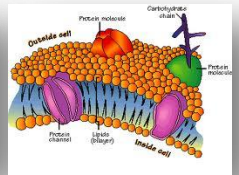
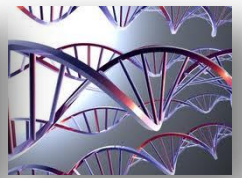
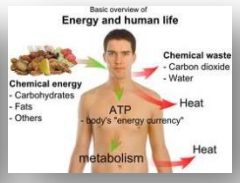
Extramitochondrial FAs synthesis

(2) Reduction:

- In this reaction TWO hydrogen atoms are added to the beta-keto group of Acetoacetyl-ACP catalyzed by enzyme called beta-keto acyl-ACP reductase to for beta-hydroxy butyryl-ACP



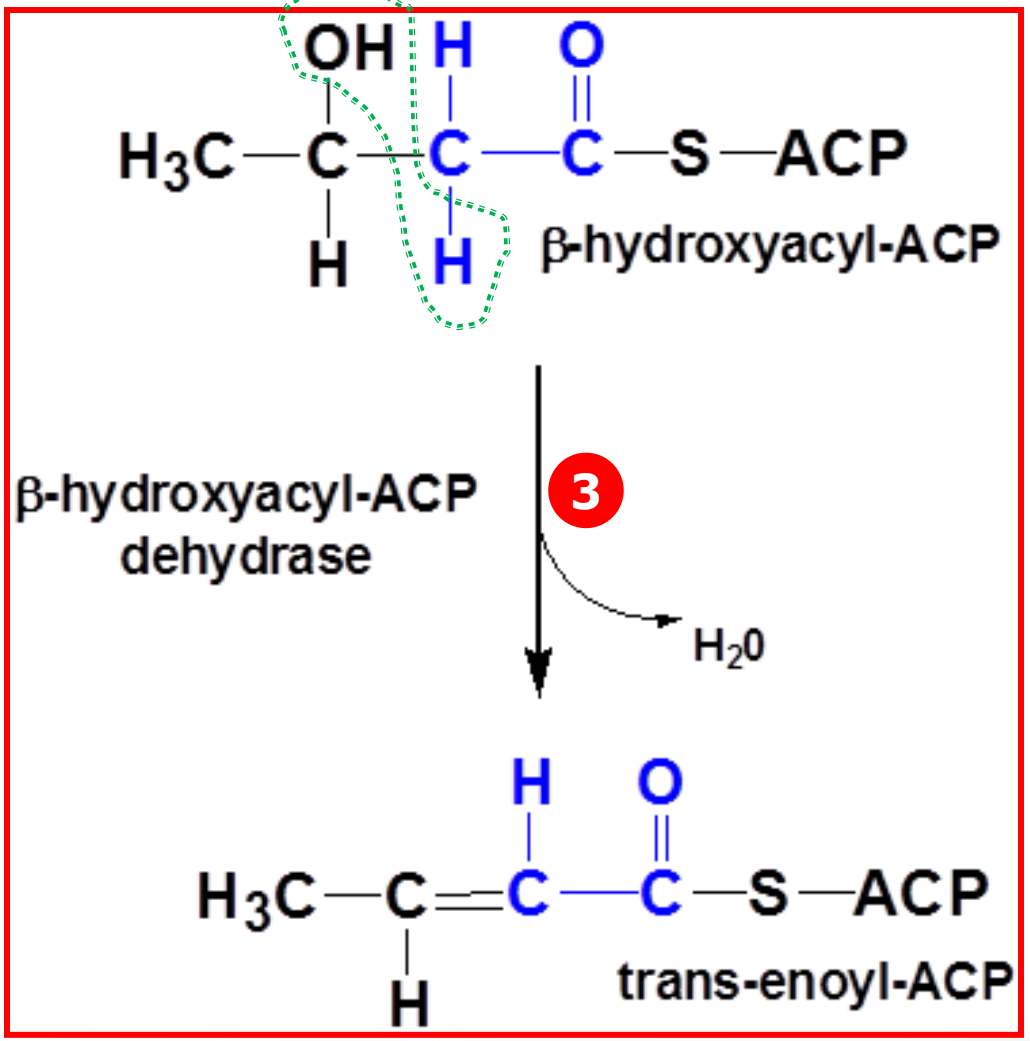


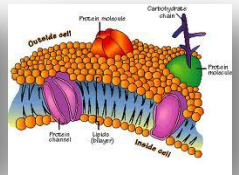
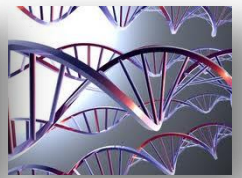
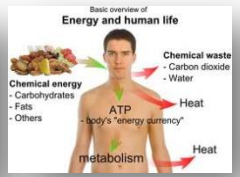
Extramitochondrial FAs synthesis

(3) Dehydration:

- In this reaction a hydroxyl group from the C3 and a hydrogen atom from the C2 released in the form of water by enzyme called beta-hydroxy acyl-ACP dehydrase to for trans-Δ2-enoyl-ACP



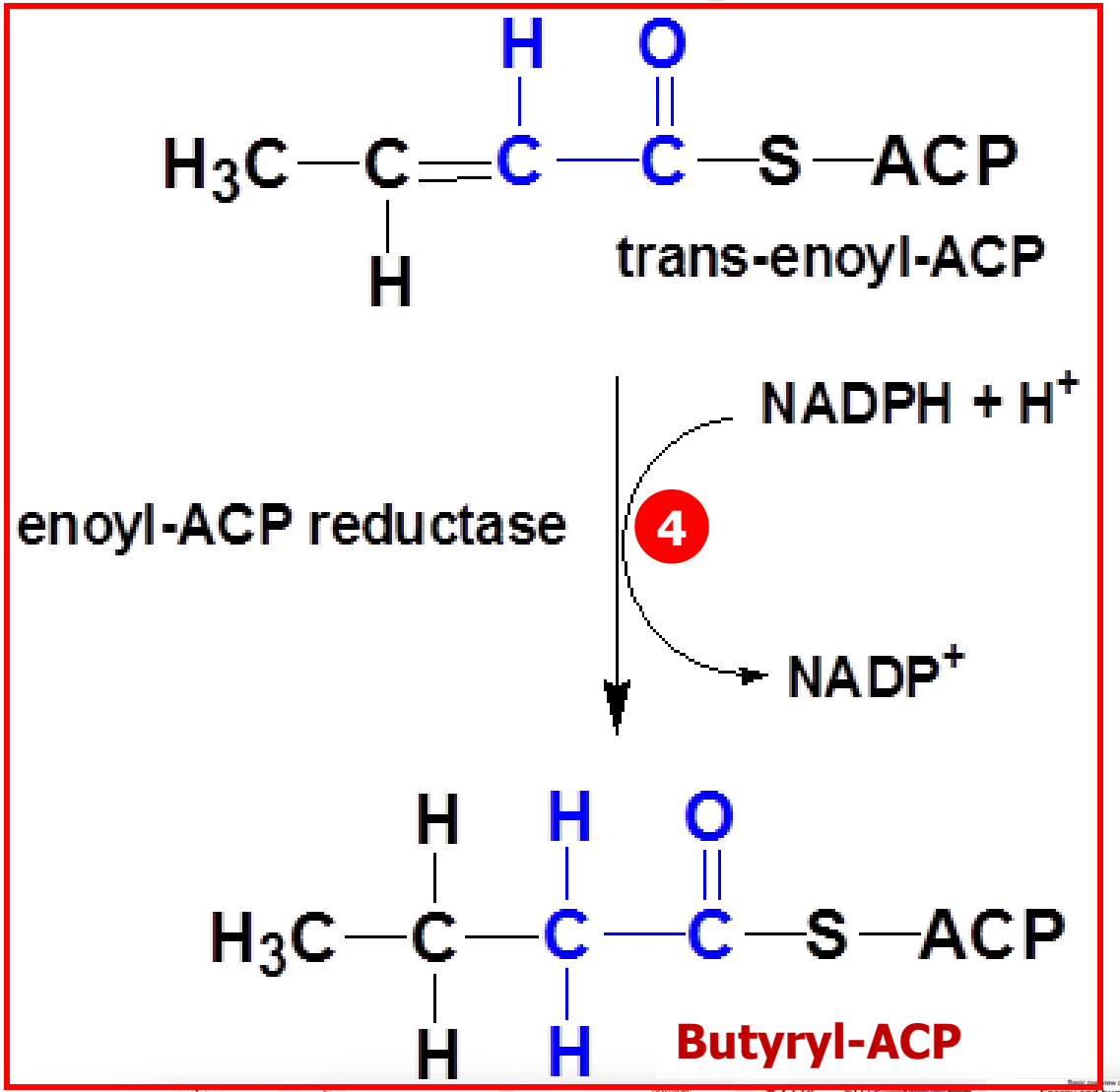


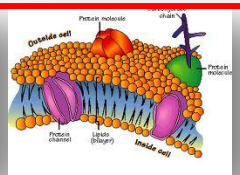
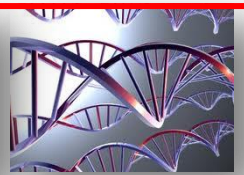
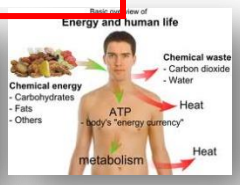
Extramitochondrial FAs synthesis

(4) Reduction:

- **Trans Δ2-enoyl ACP is reduced by NAPDH, H+ to form butyryl-ACP catalyzed by enzyme called enoyl-ACP reductase. Then this butyryl-ACP joins with another mole of Malonyl-ACP to elongate the chain for FA.**





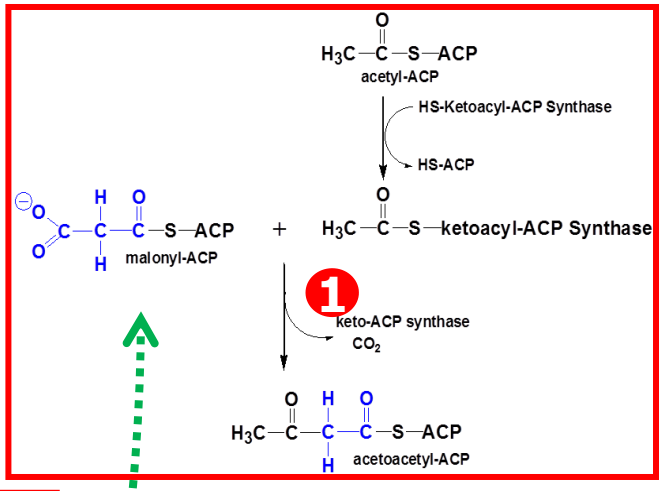




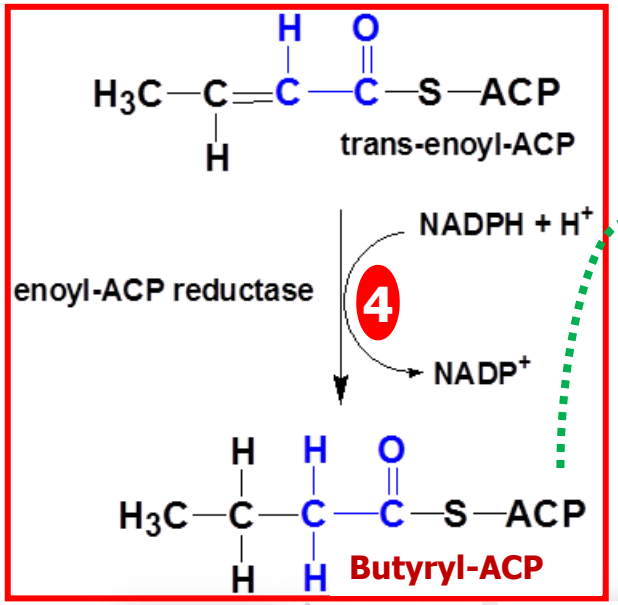
Extramitochondrial FAs synthesis

Continuation:

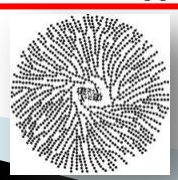
- The final product of the last reaction (step 4) will go back to join with another mole of Malonyl-ACP to synthesize a longer chain fatty acid and this process will continue till the expected FA is synthesized.

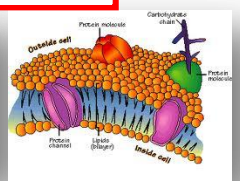
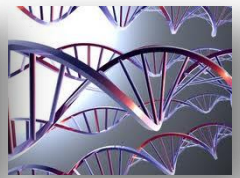
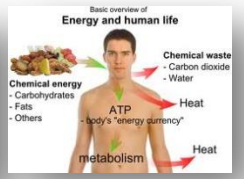
In the last step of reaction, the S-ACP will be released by hydrolysis reaction.





Continue fatty acid biosynthesis till expected chain length is achieved.



Extramitochondrial FAs synthesis

Continuation:

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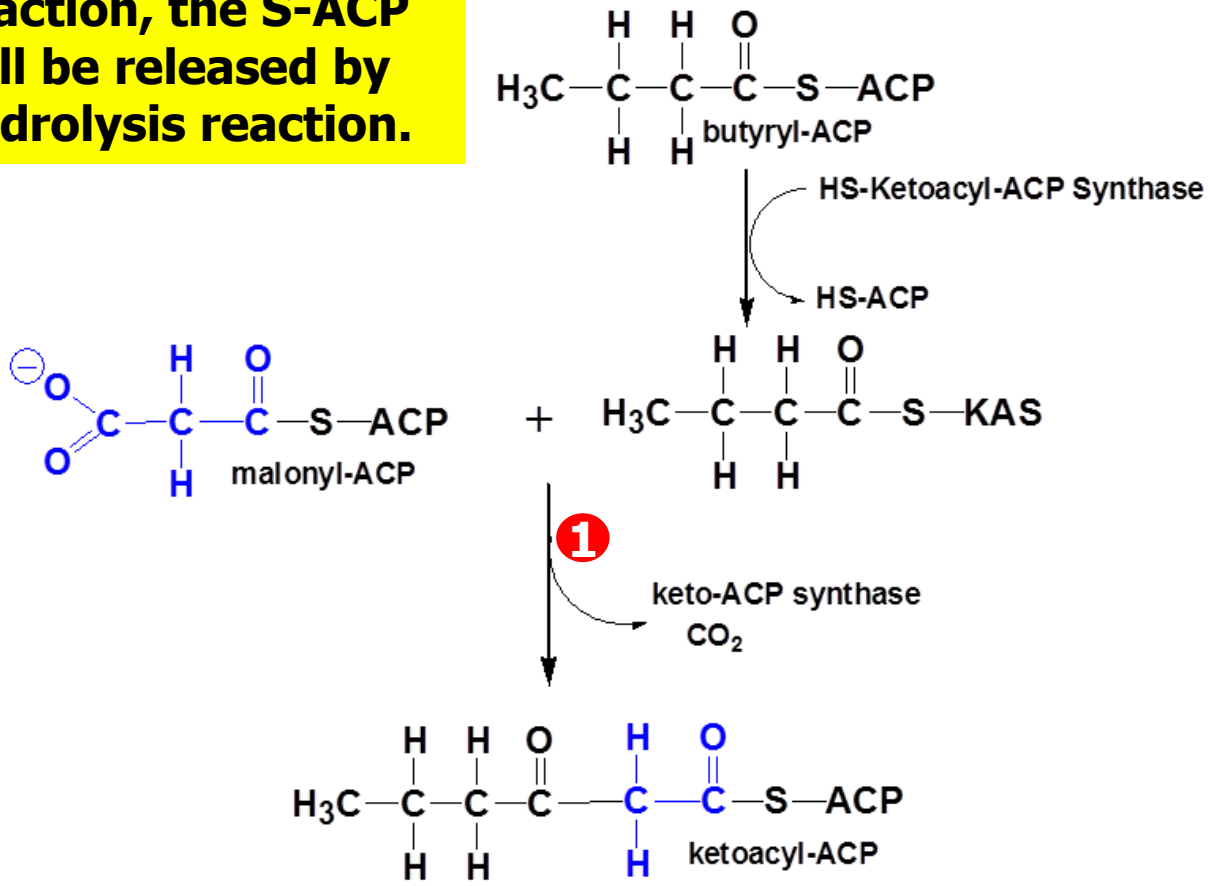
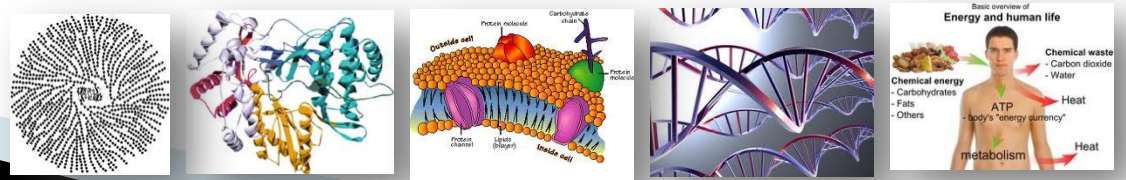
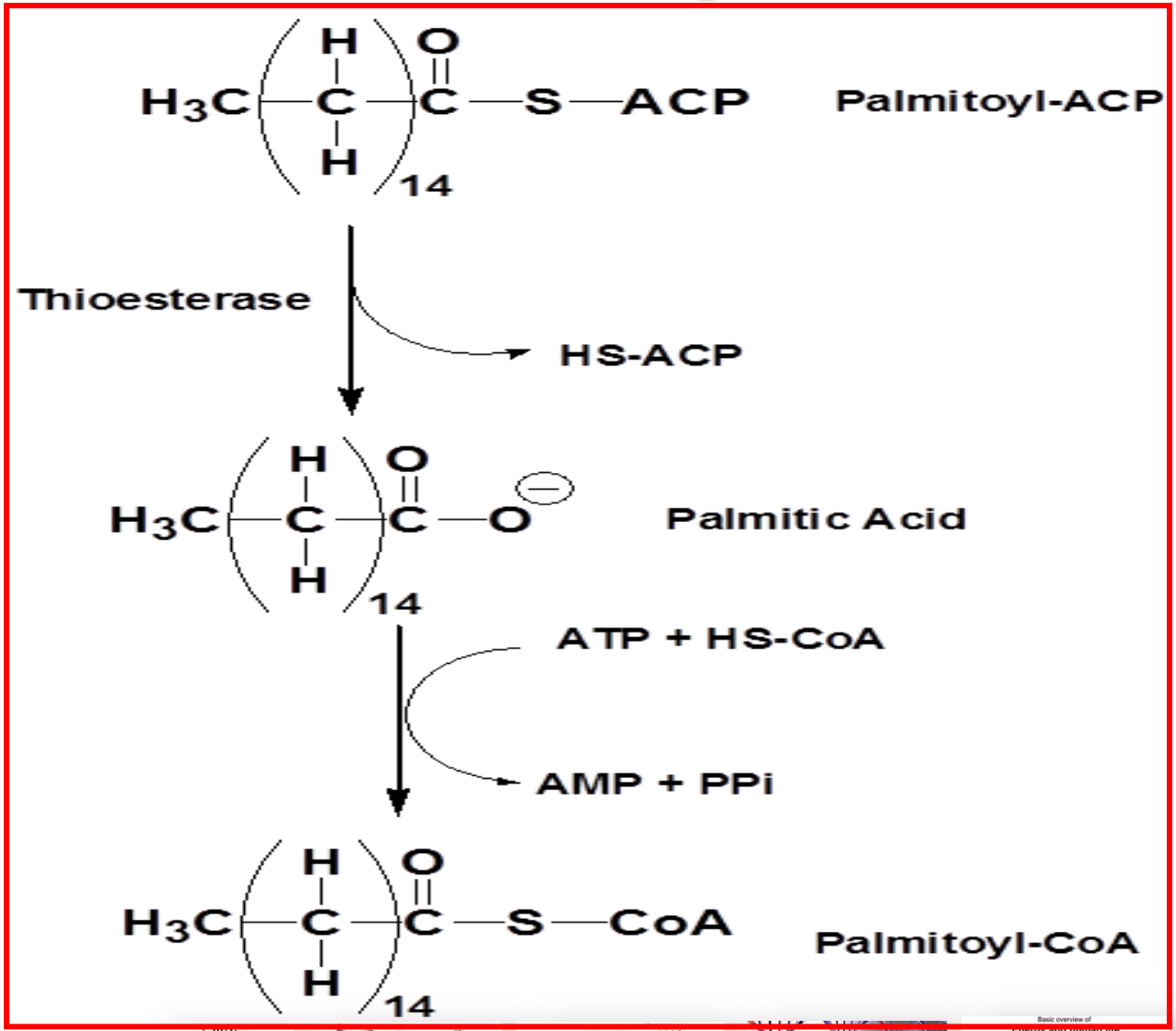


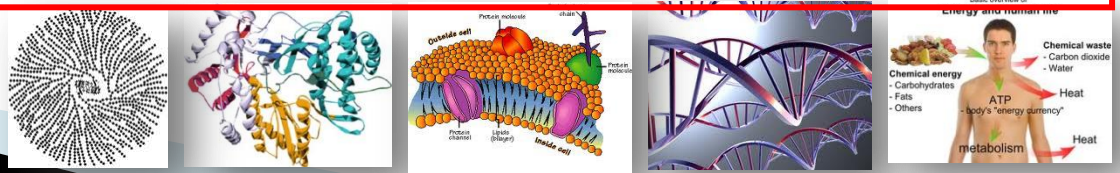


Extramitochondrial FAs synthesis

Termination:

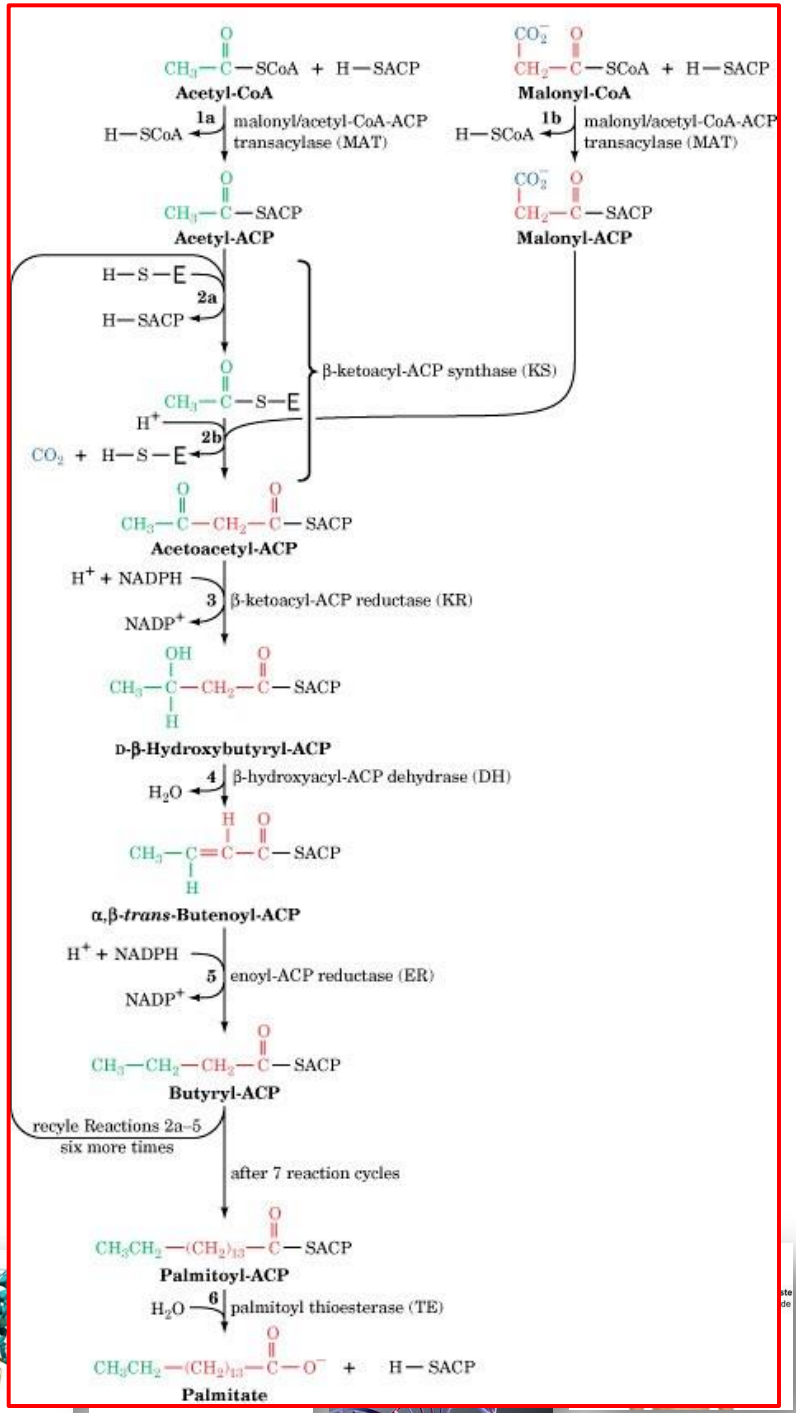
- As soon as the desired chain of fatty acid is achieved the S-ACP group will be removed from the final product by hydrolysis reaction to make a normal fatty acid which can go for beta-oxidation as well.





FAs biosynthesis

1. Acetyl-CoA is converted by MAT to Acetyl ACP
2. Acetyl-ACP is attached to KS (condensation reaction).
3. Malonyl ACP is formed by MAT.
4. Acetyl-group is coupled to beta carbon of malonyl-ACP with release of CO_2 to form acetoacetyl-ACP(2b) by KS.
5. Reduction of acetoacetyl-ACP with NADPH to form D-β-hydroxybutyrl-ACP by DH
6. Dehydration of D-β-hydroxybutyrl-ACP by ER to form α,β-trans-butenoyl-ACP
7. Reduction of the double bond to form butyryl-ACP
8. Repeat until Palmitoyl-ACP (C16) is formed.
9. ACP is cleaved by TE releasing free fatty acid.

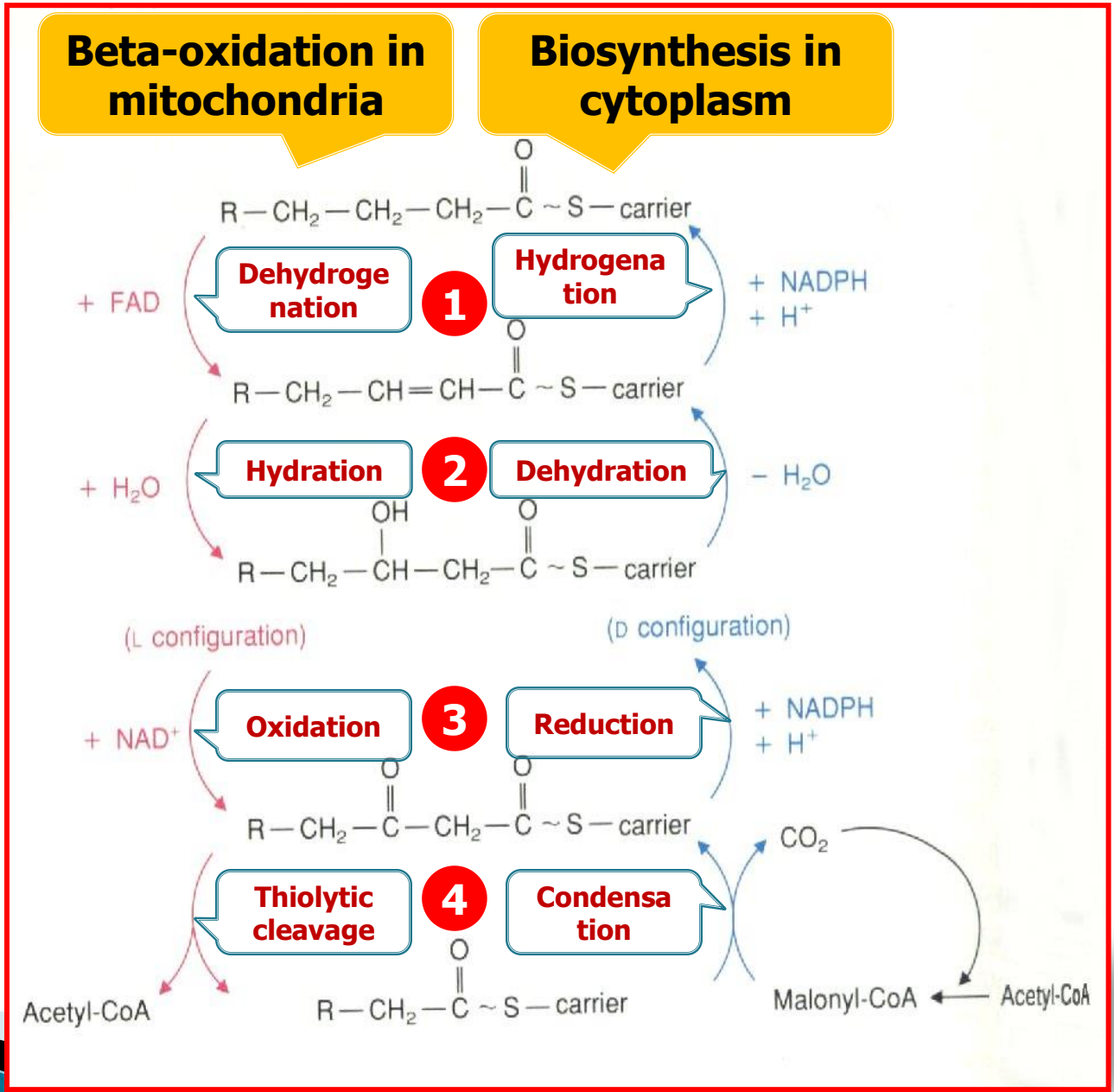


Page 20 in Handouts

FAs synthesis vs oxidation

B-oxidation vs biosynthesis of fatty acids:

- The fatty acid beta-oxidation in the mitochondria and biosynthesis in the cytoplasm are two inverse or opposite pathway.

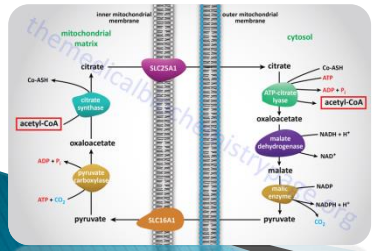


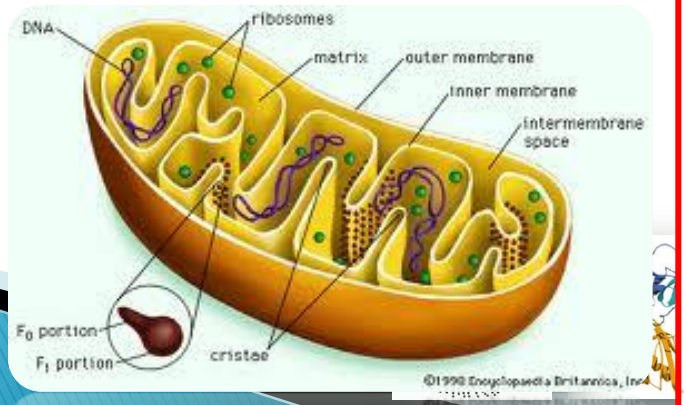
Page 18 in Handouts

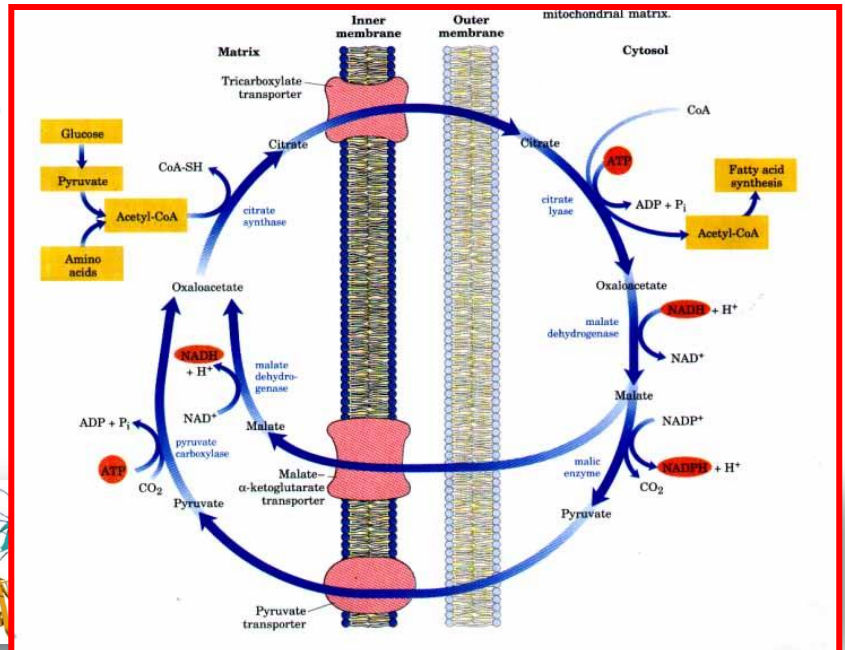
Mitochondrial acetyl-CoA

Malate-citrate and pyruvate-citrate shuttle:

- As soon as fatty acid β-oxidation is stopped after a change in physiological condition from FASTING to FEEDING, the remaining Acetyl-CoA will move to cytoplasm to be used for the fatty acid biosynthesis.
- However, the mitochondrial CoA has no access to the inner membrane of mitochondria
- Hence, they need to use some shuttle systems to move from the mitochondrial matrix to the cytoplasm
- Two shuttle systems are work in this case called Malate-Citrate and Pyruvate-Citrate shuttle

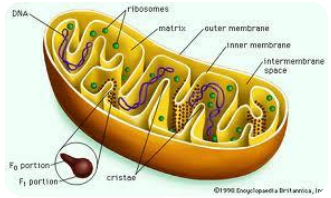




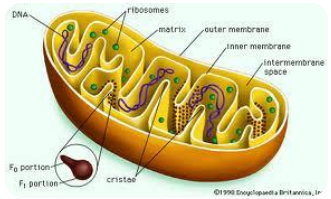


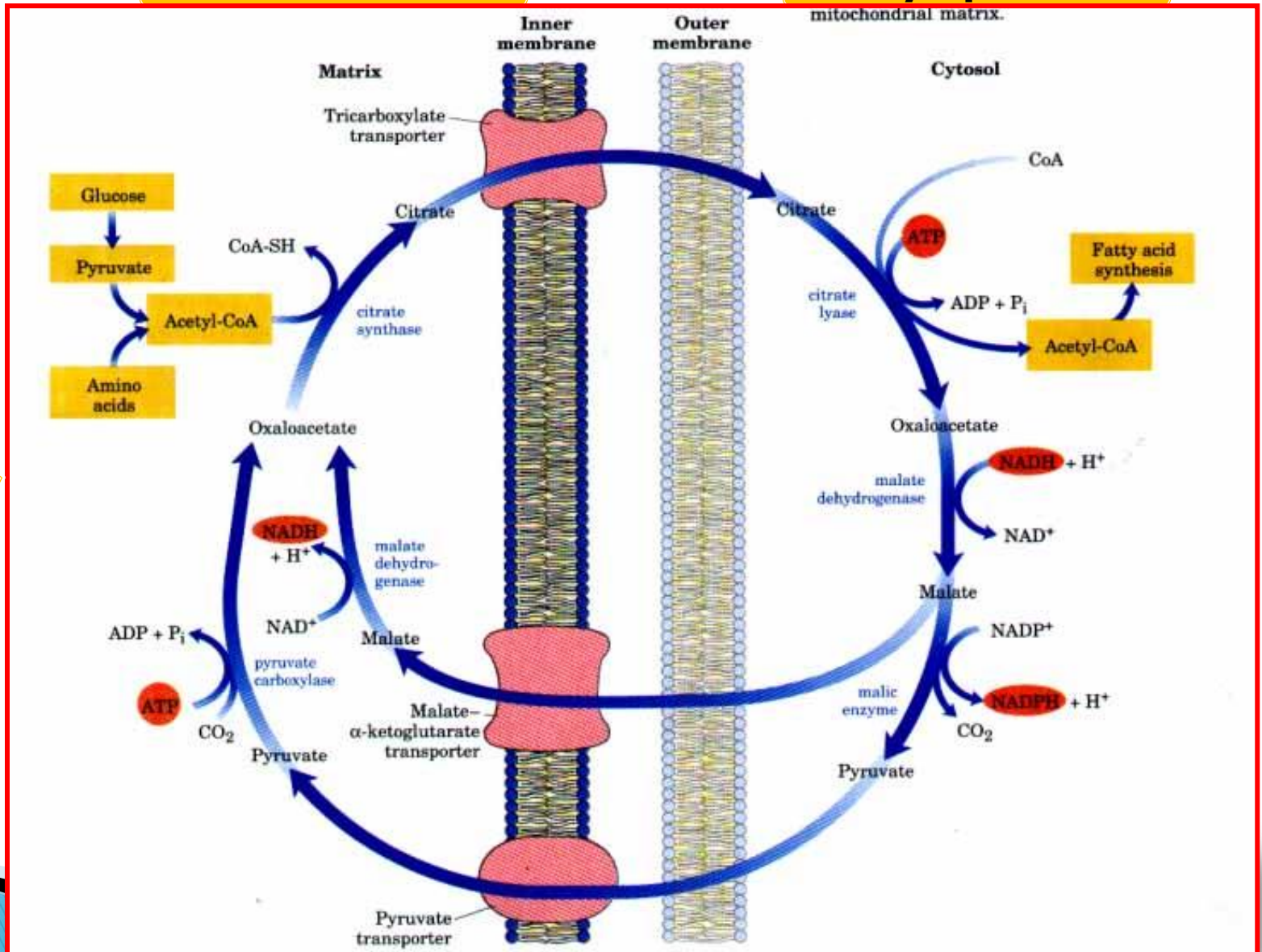
Page 18 in Handouts

Mitochondrial acetyl-CoA



Malate-Citrate & Pyruvate-Citrate Shuttle System



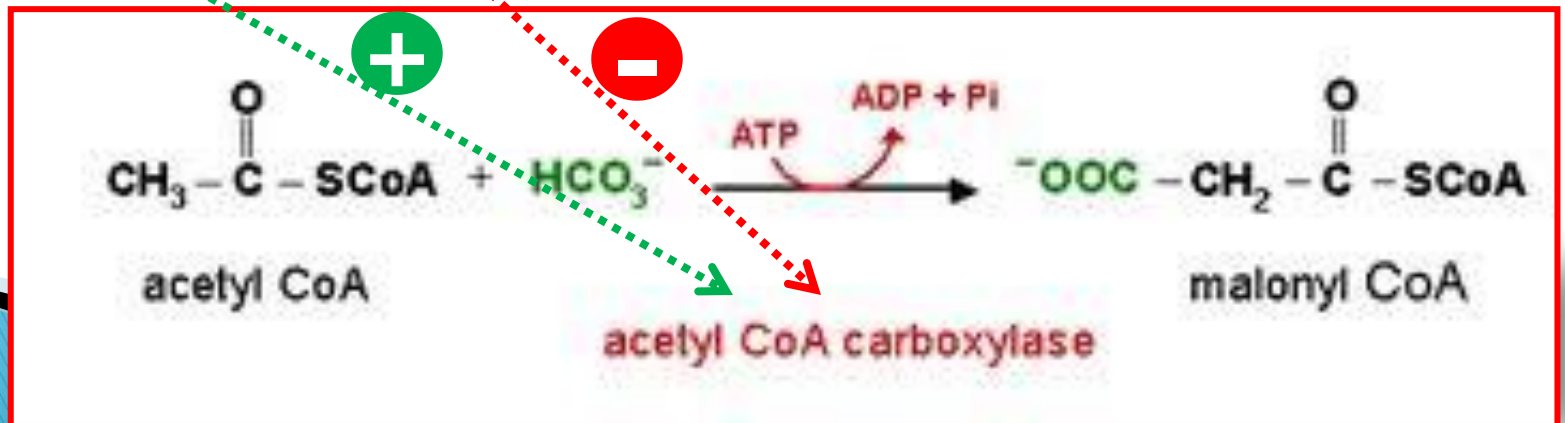


Regulation of FAs biosynthesis

- Several enzymes and substrates regulate the biosynthesis of fatty acids, such as-
  - (1) Acetyl-CoA carboxylase
  - (2) Malonyl-CoA
  - (3) Fatty acid synthase (multienzyme complex)
  - (4) Various hormones (hormonal regulation)

(1) Acetyl-CoA carboxylase:

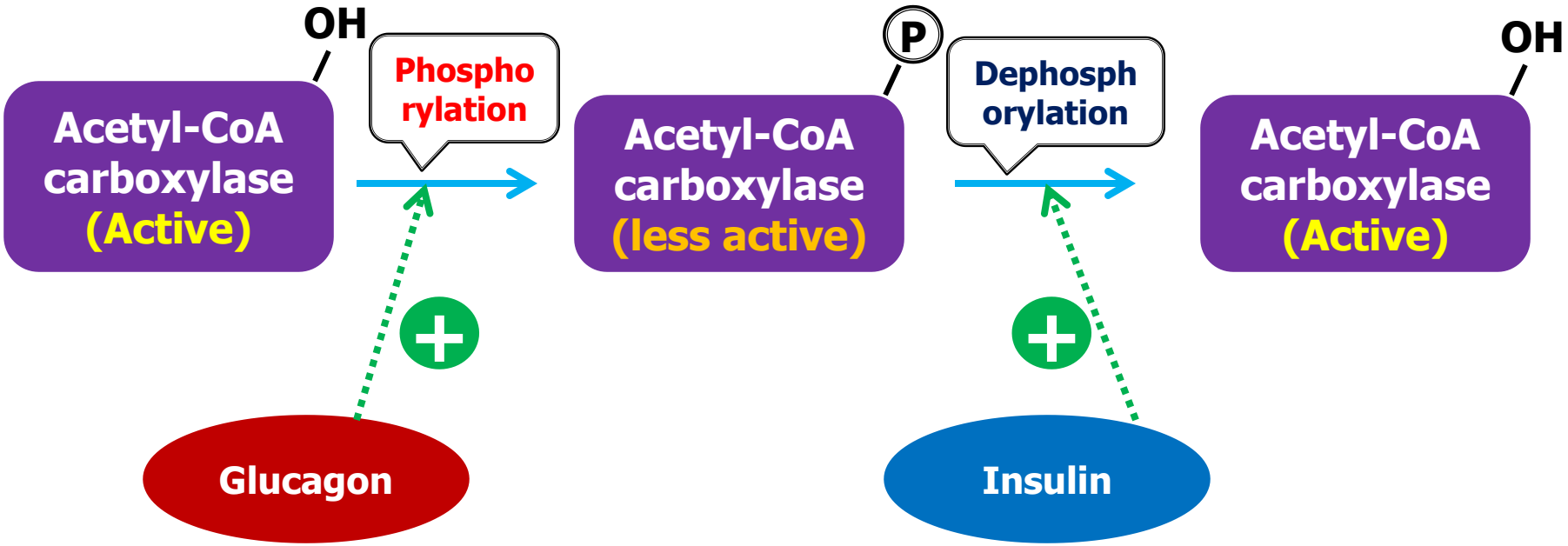
- The long chain fatty acyl-CoA inhibit and on the other hand CITRATE stimulate the activity of Acetyl-CoA carboxylase enzyme which is involved in the conversion of acetyl-CoA to malonyl-CoA

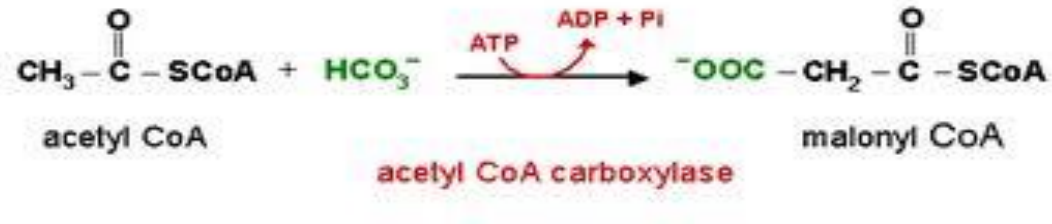


Regulation of FAs biosynthesis

(1) Acetyl-CoA carboxylase: contd…

- The activity of acetyl-CoA carboxylase can be covalently activated by two different hormones e.g. insulin and glucagon

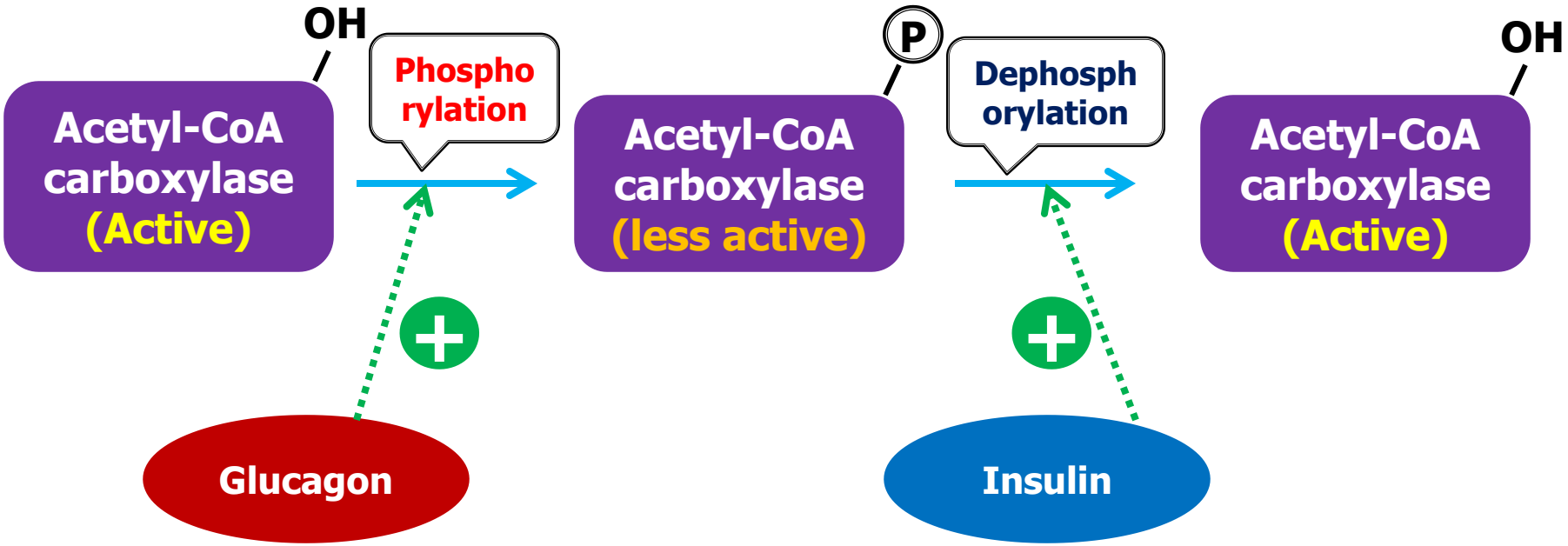




Regulation of FAs biosynthesis

(1) Acetyl-CoA carboxylase: contd…

- **The activity of acetyl-CoA carboxylase can be covalently activated by two different hormones e.g. insulin and glucagon**

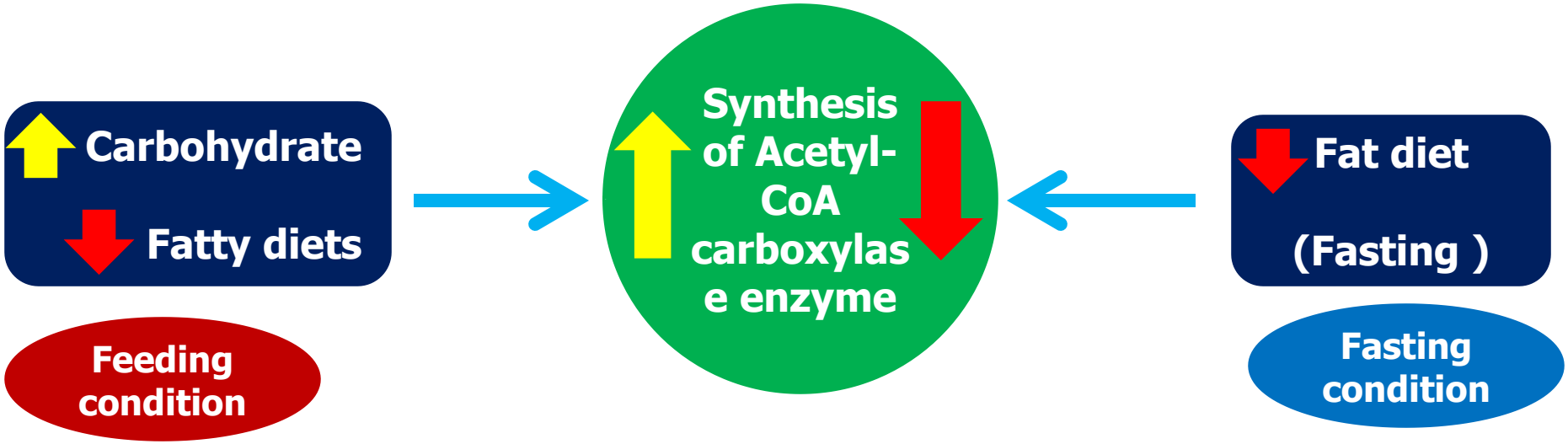


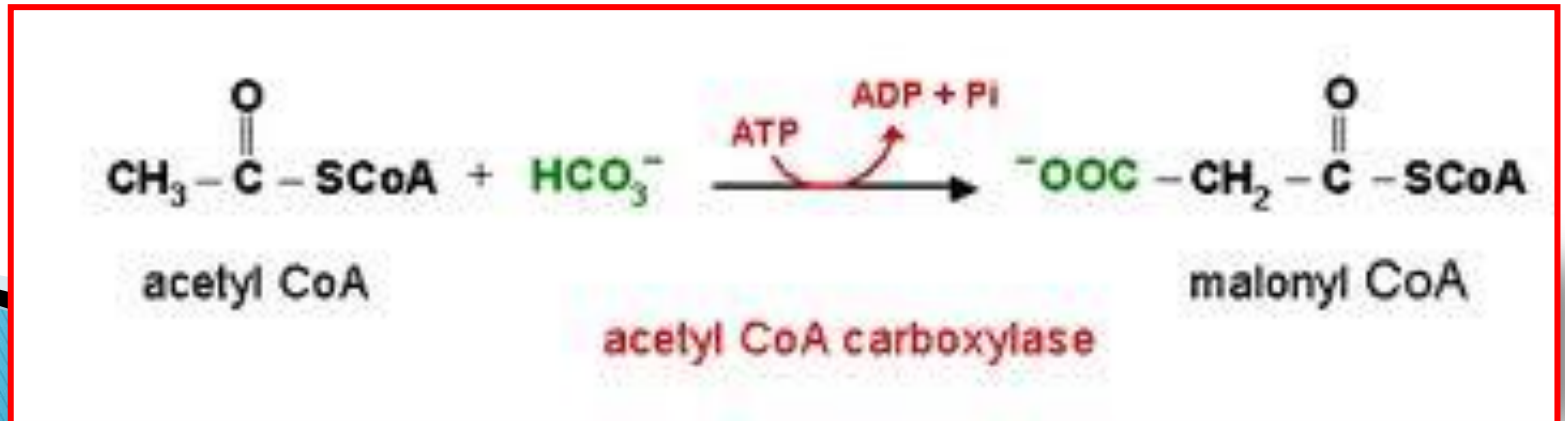
↑ Insulin	↑ Fatty acid biosynthesis
↑ Glucagon	↓ Fatty acid biosynthesis

Regulation of FAs biosynthesis

(1) Acetyl-CoA carboxylase: contd…

- **The activity of acetyl-CoA carboxylase can be adapted based on the dietary pattern and physiological condition as follows.**



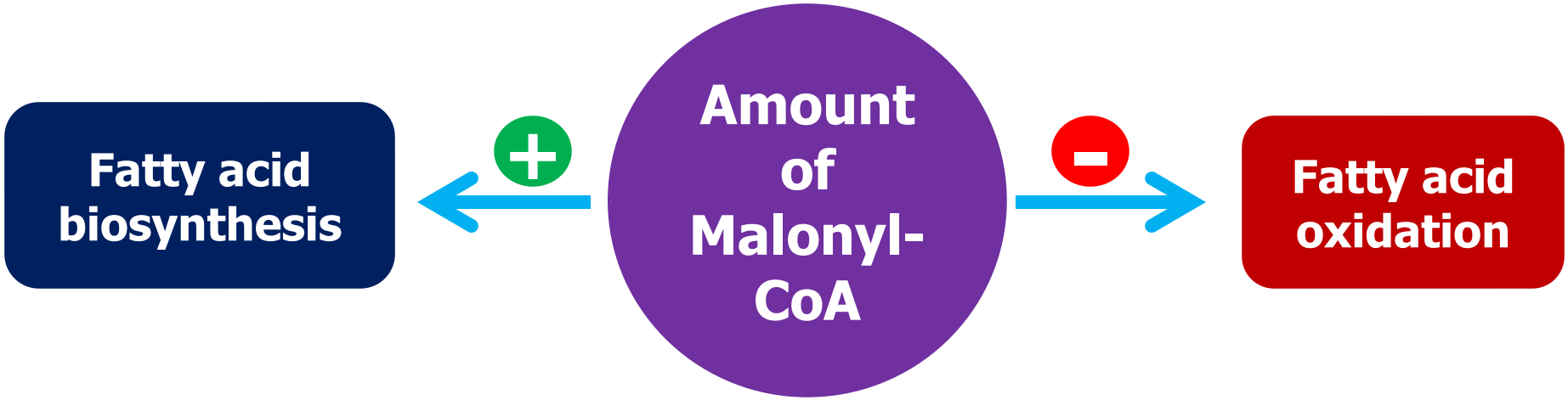


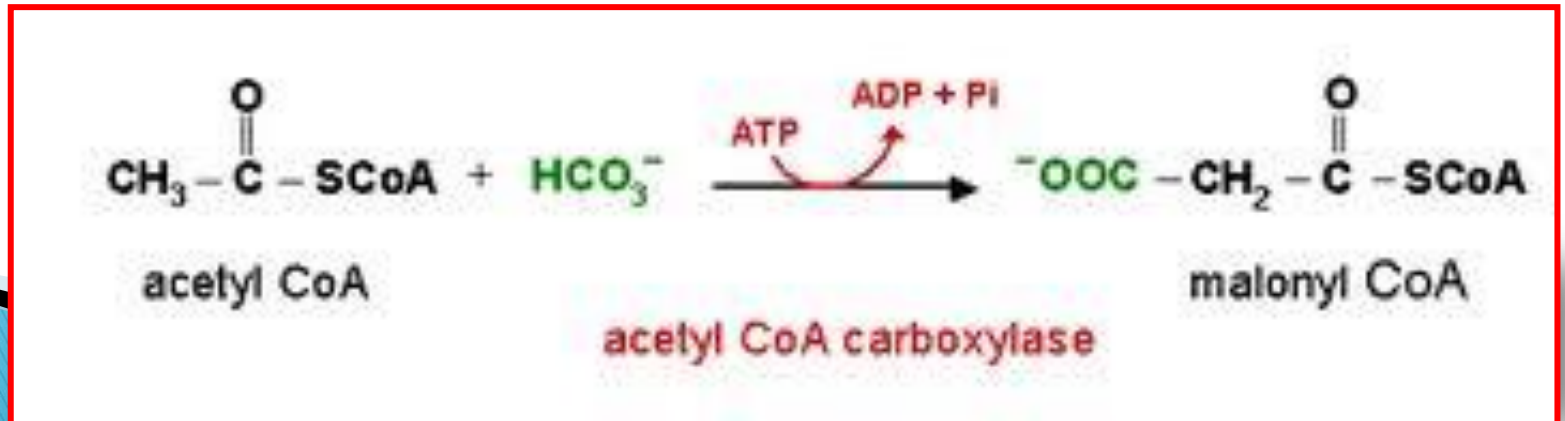
Page 21 in Handouts

Regulation of FAs biosynthesis

(2) Malonyl-CoA:

- **The concentration of Malonyl-CoA stimulate the fatty acid biosynthesis and at the same time inhibit the fatty acid oxidation as follows**



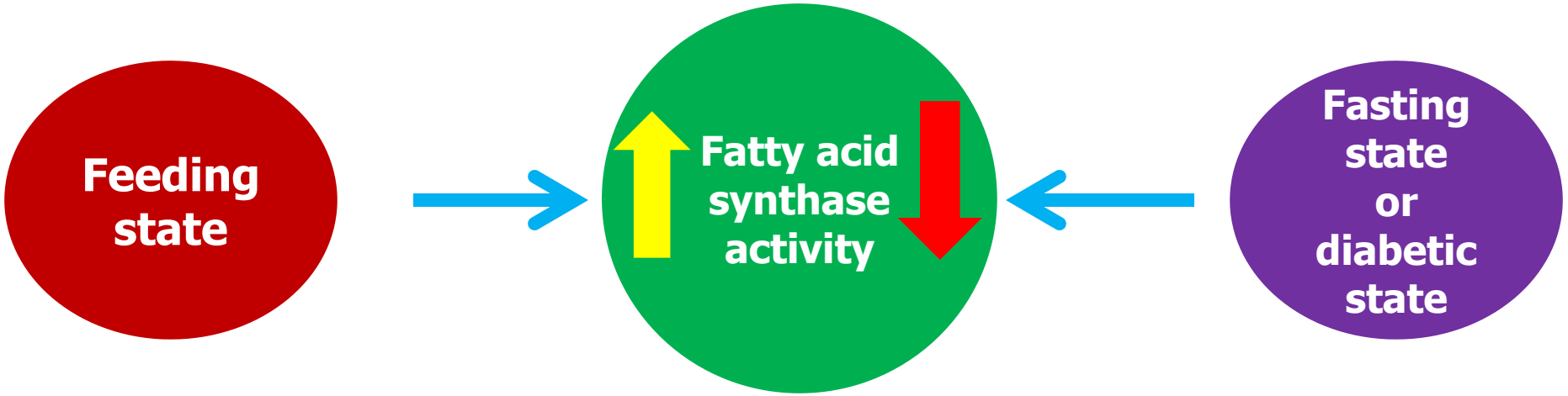


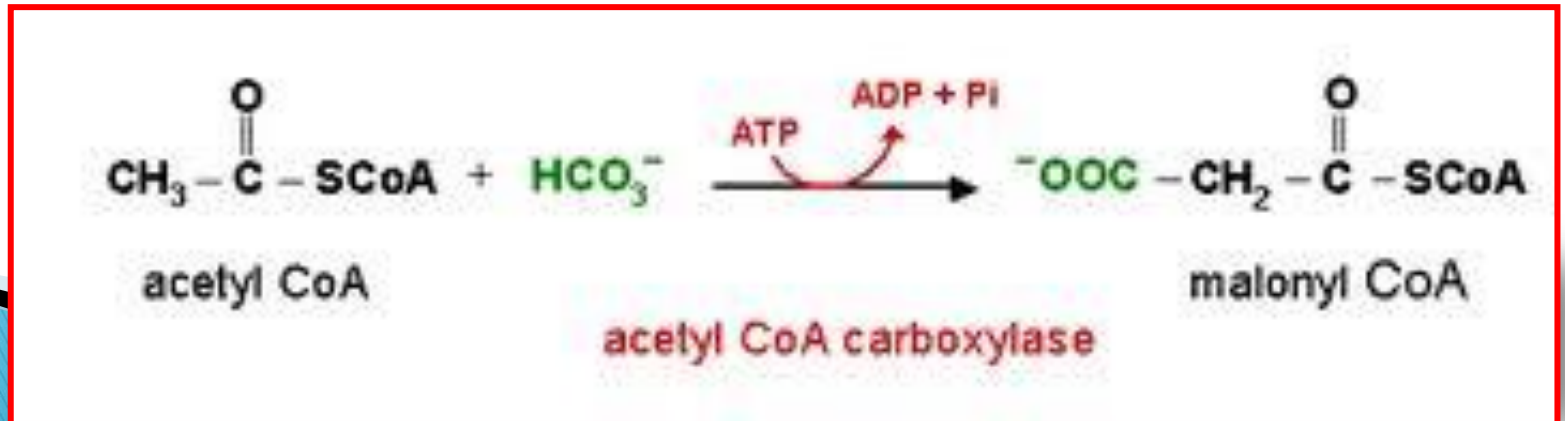
Page 22 in Handouts

Regulation of FAs biosynthesis

(3) Fatty acid synthase: (multienzyme complex)

- **The physiological condition can largely affect the activity of enzyme fatty acid synthase which is mainly involved in the synthesis of fatty acids**





Page 22 in Handouts

Regulation of FAs biosynthesis

(4) Hormonal regulations:

- **The physiological conditions as well as the secretion of different hormones accordingly largely regulate the biosynthesis of fatty acids as follows:**

Feeding condition

INSULIN

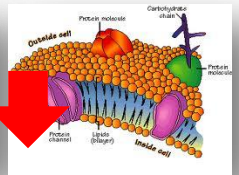
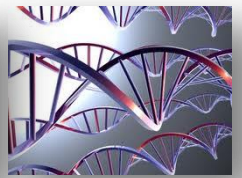
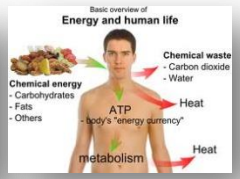
- Stimulate fatty acid biosynthesis
- Inhibits beta-oxidation

Fasting condition

GLUCAGON
EPINEPHRINE

- Inhibits fatty acid biosynthesis
- Stimulations beta-oxidation

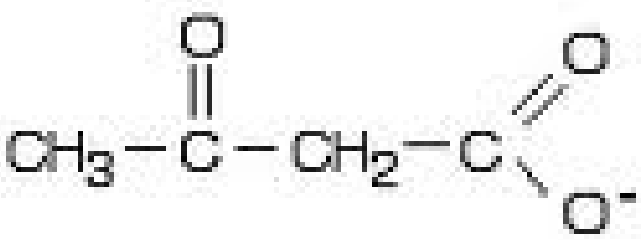


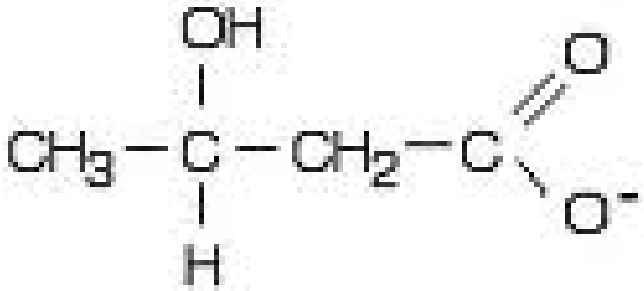
Ketone bodies

Which are ketone bodies?

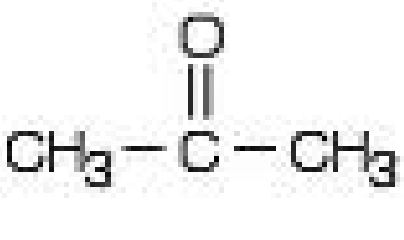
- The following three compounds with keto group (=C=O) group in their structures are called ketone bodies.



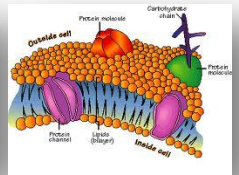
acetoacetate

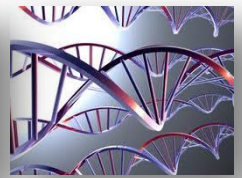


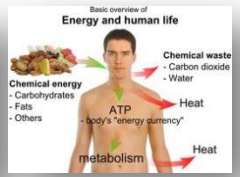
β-hydroxybutyrate



acetone





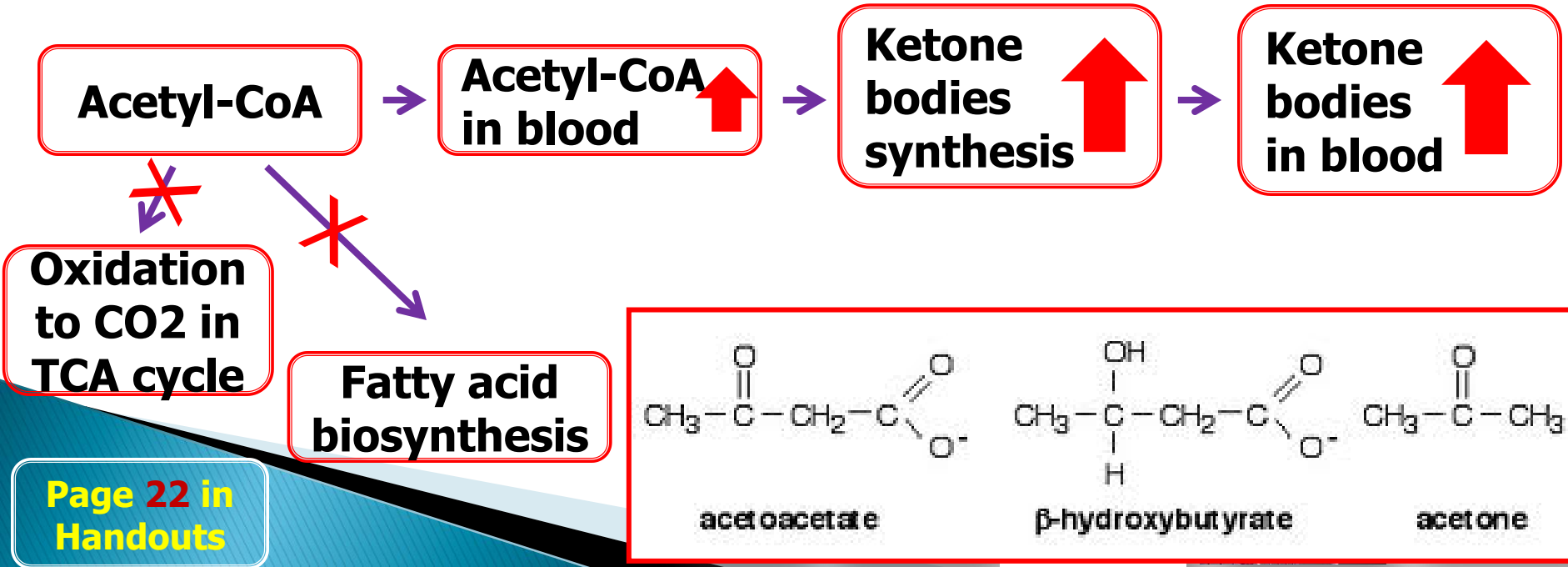


Ketone bodies

Why and how are they synthesized?

- **Acetyl-CoA has more than tow major metabolic fates:**
  - **(1) either oxidation via to CO2 via TCA cycle or**
  - **(2) participate in the biosynthesis of fatty acids**

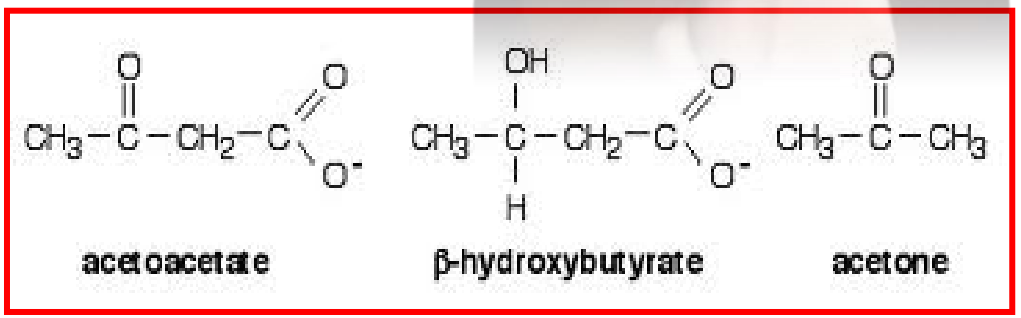
- **When acetyl-CoA accumulates beyond the capacity to be oxidized or used for fatty acid biosynthesis, ketone bodies are synthesized which is also called KETOGENESIS.**



Ketone bodies

What is ketoacidosis or ketosis?

- Ketoacidosis or ketosis is the combination of following three things:
  - (1) Ketonemia
  - (2) Ketonuria
  - (3) Acetone in breath



(1) Ketonemia:

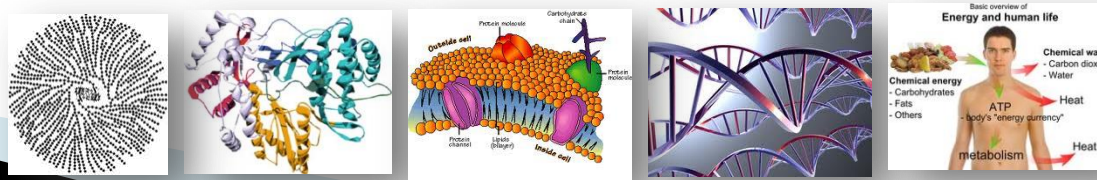
- Dramatic increases of ketone bodies in the blood is called KETONEMIA

(2) Ketonuria:

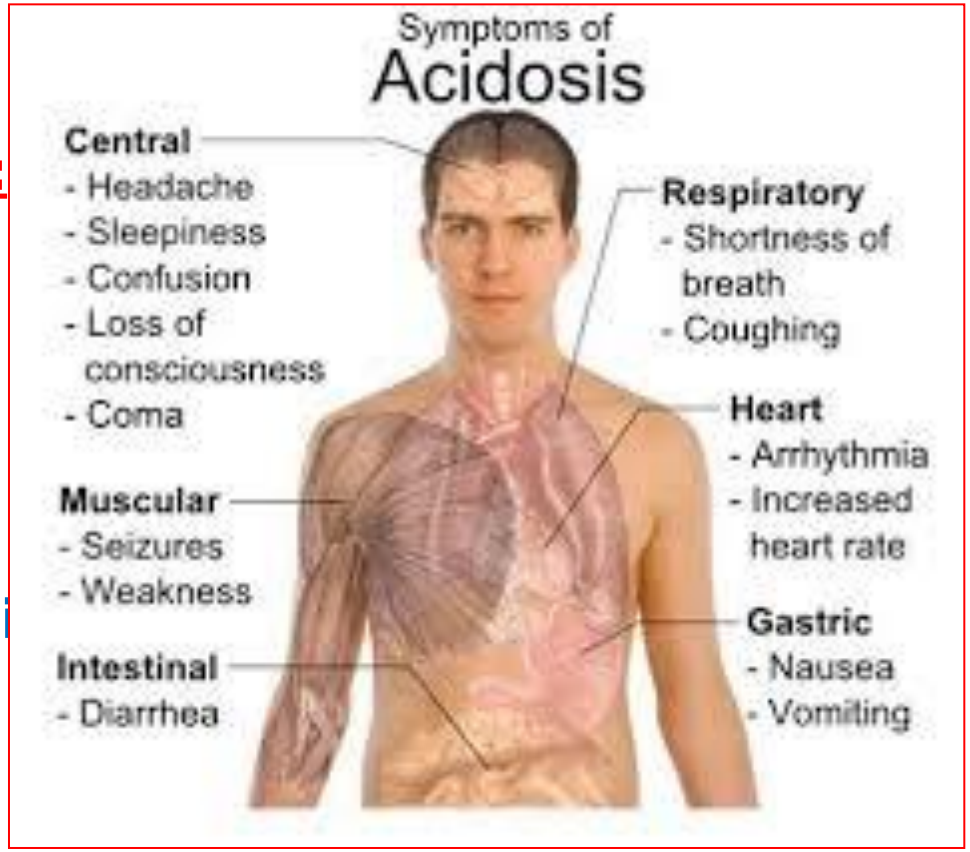
- When ketone bodies are excreted with urine that is called KETONURIA.

(3) Acetone in breath:

- When smell of acetone is detected in the breath



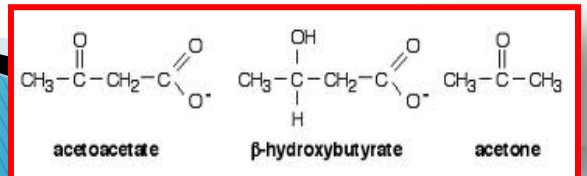
Ketone bodies

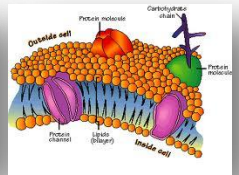


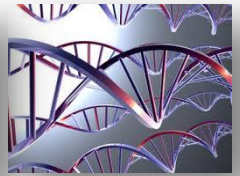
Consequences of ketoacidosis:

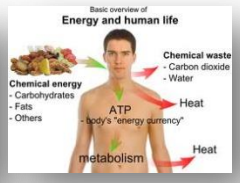
- Two out of three ketone bodies (Acetoacetic acid & β-hydroxy butryric acid) are acidic in nature
- So when the levels of ketone bodies are increased i pH of blood is decreased and severe acidic situation arises
- This decreased blood pH significantly with many other symptoms such as- dehydration, tachycardia (high heart rate), hypotension (due to loss of electrolytes with water)
- This situation is called ketoacidosis or ketosis

Page 22 in Handouts

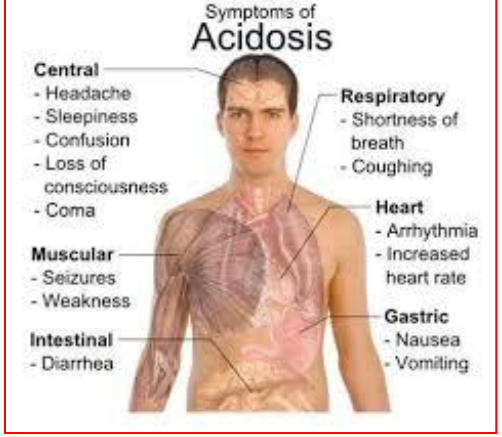






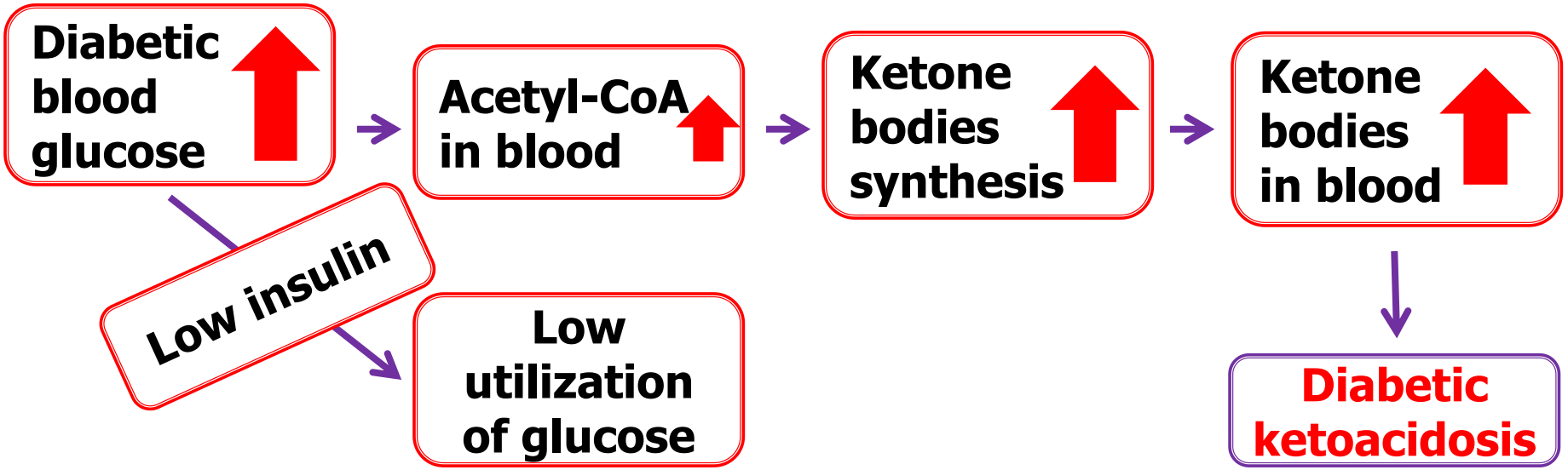


Ketone bodies

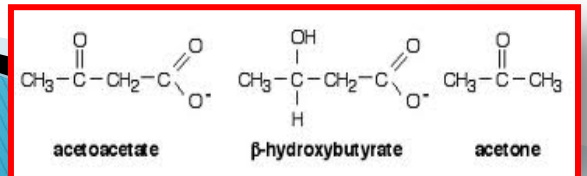


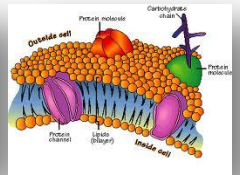
Who are vulnerable to ketoacidosis?

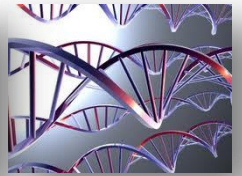
- Diabetic patients are vulnerable to ketosis or Ketoacidosis what is called **DIABETIC KETOACIDOSIS**
- **Due to the low utilization of glucose due to low insulin concentration in diabetic condition, the level of Acetyl-CoA as well as ketone bodies are increased dramatically**

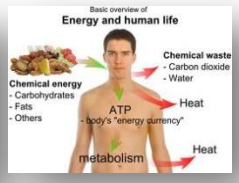


Page 22 in Handouts

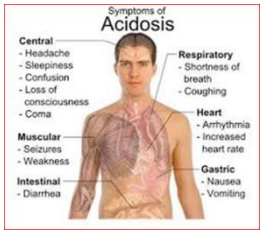








Ketone bodies

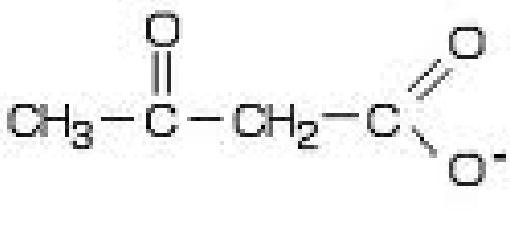


Diagnosis of ketoacidosis:

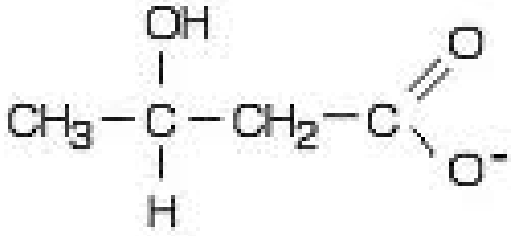
- **The normal concentration of ketone bodies in the blood of a well fed person doesn't normally exceeds 1 mg/100ml.**
- **Loss via the urine is usually less than 1 mg/ 24 hours in man.**
- **If the concentration of ketone bodies in the blood and urine are increased above the normal levels that is called KETOACIDOSIS or KETOSIS.**

Note:

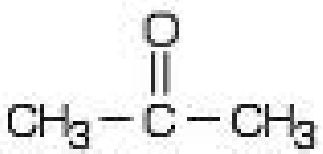
- **Blood ketone bodies can be increased up to 90 mg/ 100 ml.**
- **Urine ketone bodies can be increased up to 500 mg/day.**



acetoacetate



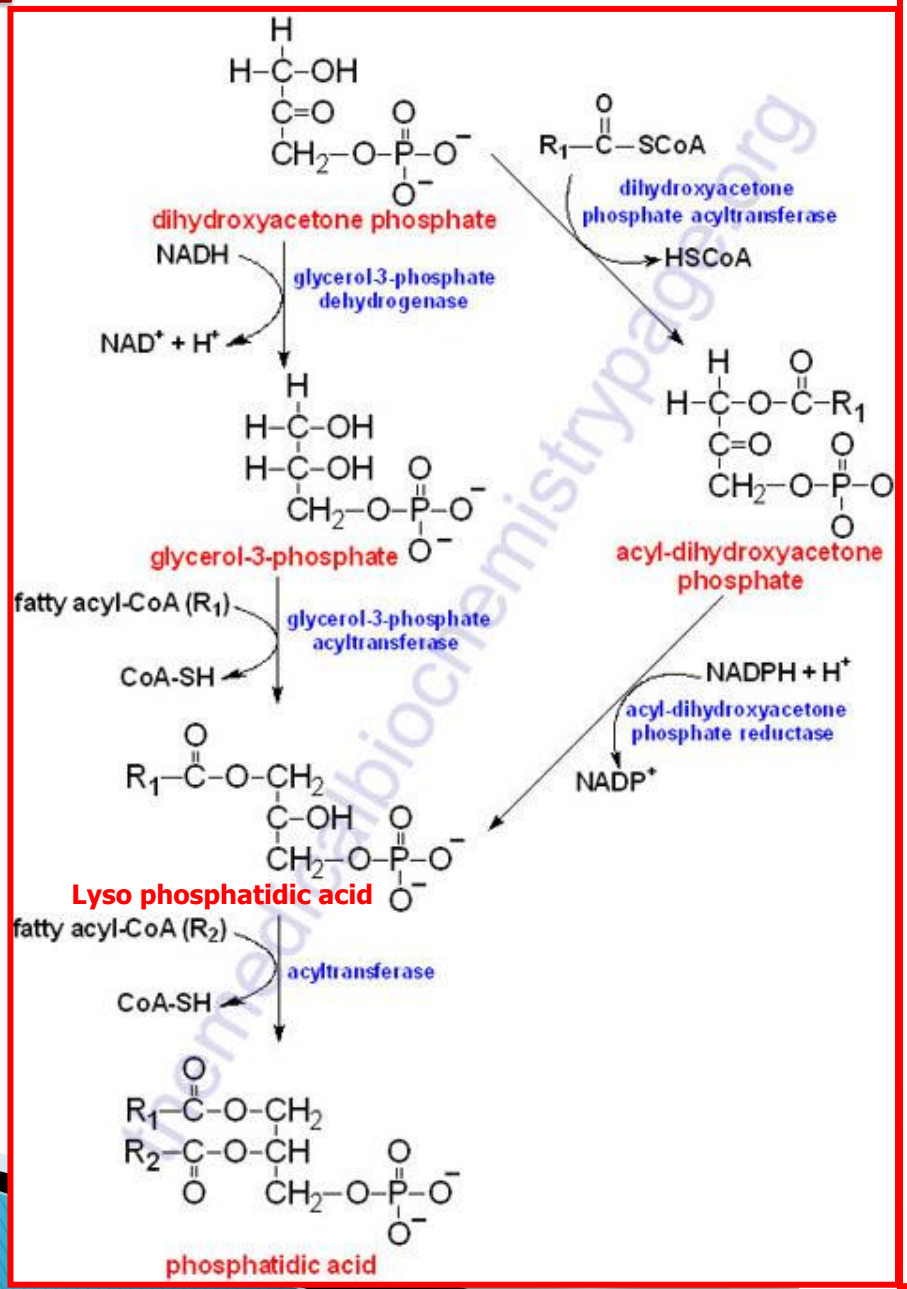
β-hydroxybutyrate

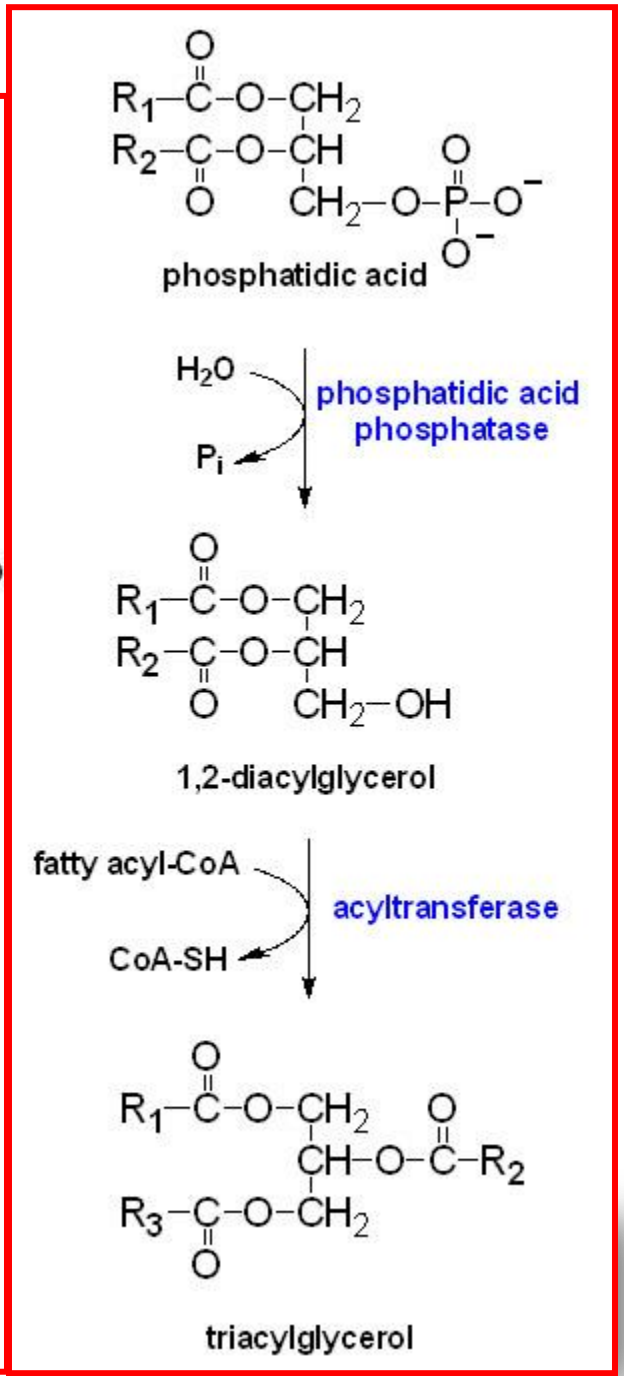


acetone

Biosynthesis of TG

- TG represents major storage form of lipids in humans and animals
- Bears 7 months and human can survive up to 40 days with their deposited TG

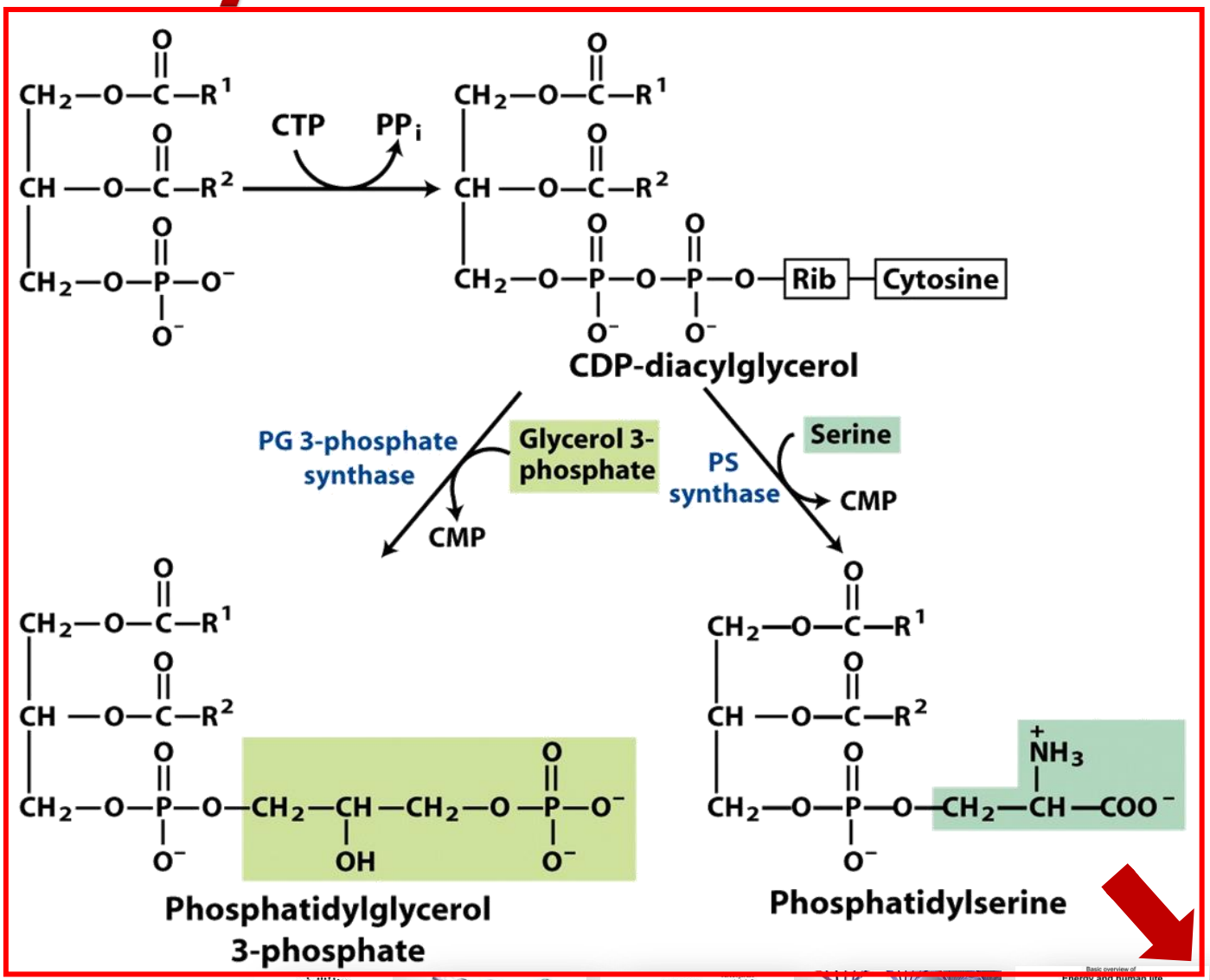




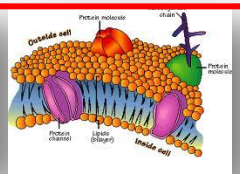
Page 23 in Handouts

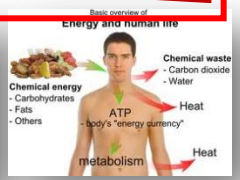
Endogen. synthesis of PLs

- Phospholipids are the most polar ionic lipids, composed of 1,2-diacyl glycerol and phospho-diester bridge linking the glycerol backbone to some polar base, usually nitrogenous bases e.g. choline, serine etc.





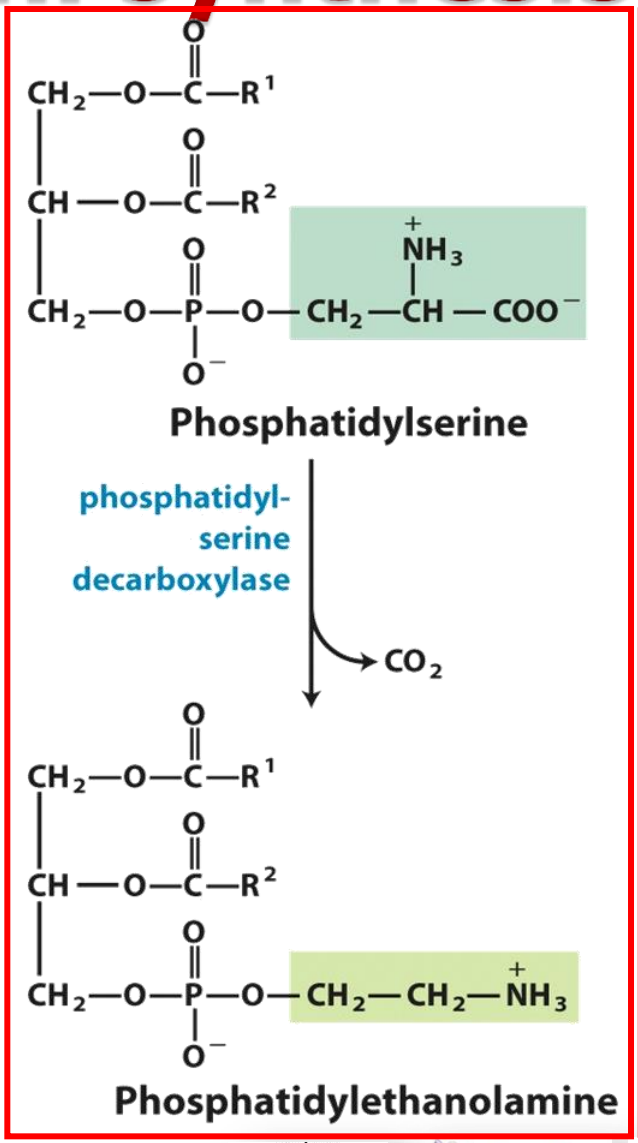


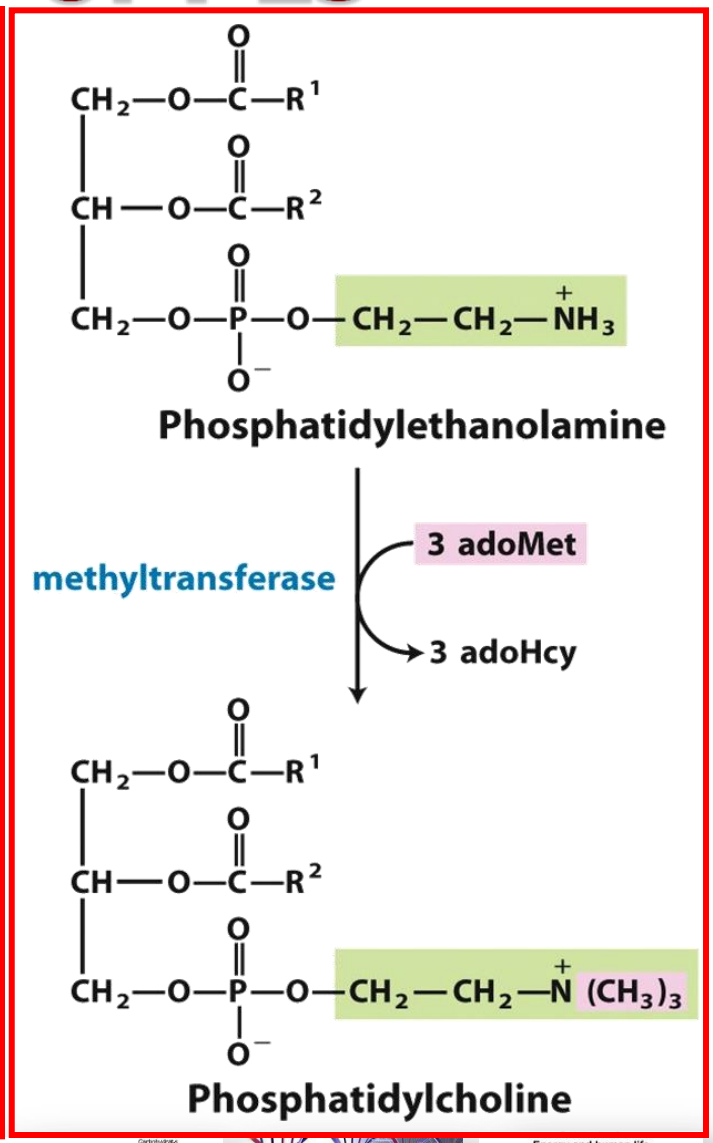


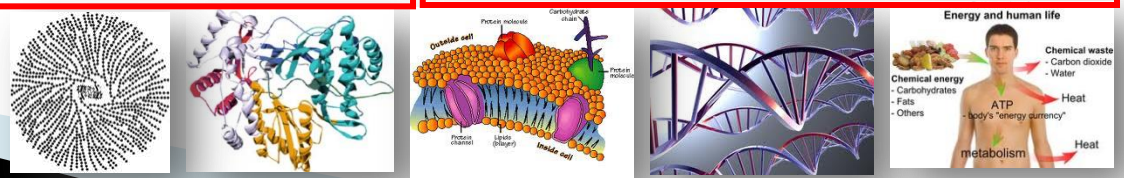
Page 24 in Handouts

Endogen. synthesis of PLs

- These phospholipids are largely absent from body deposit of fat occurring primarily in the fat of glandular organs.
- In biosynthesis, nucleotides activate the phosphate group of phosphatidic acid for the subsequent transfer of polar head group.

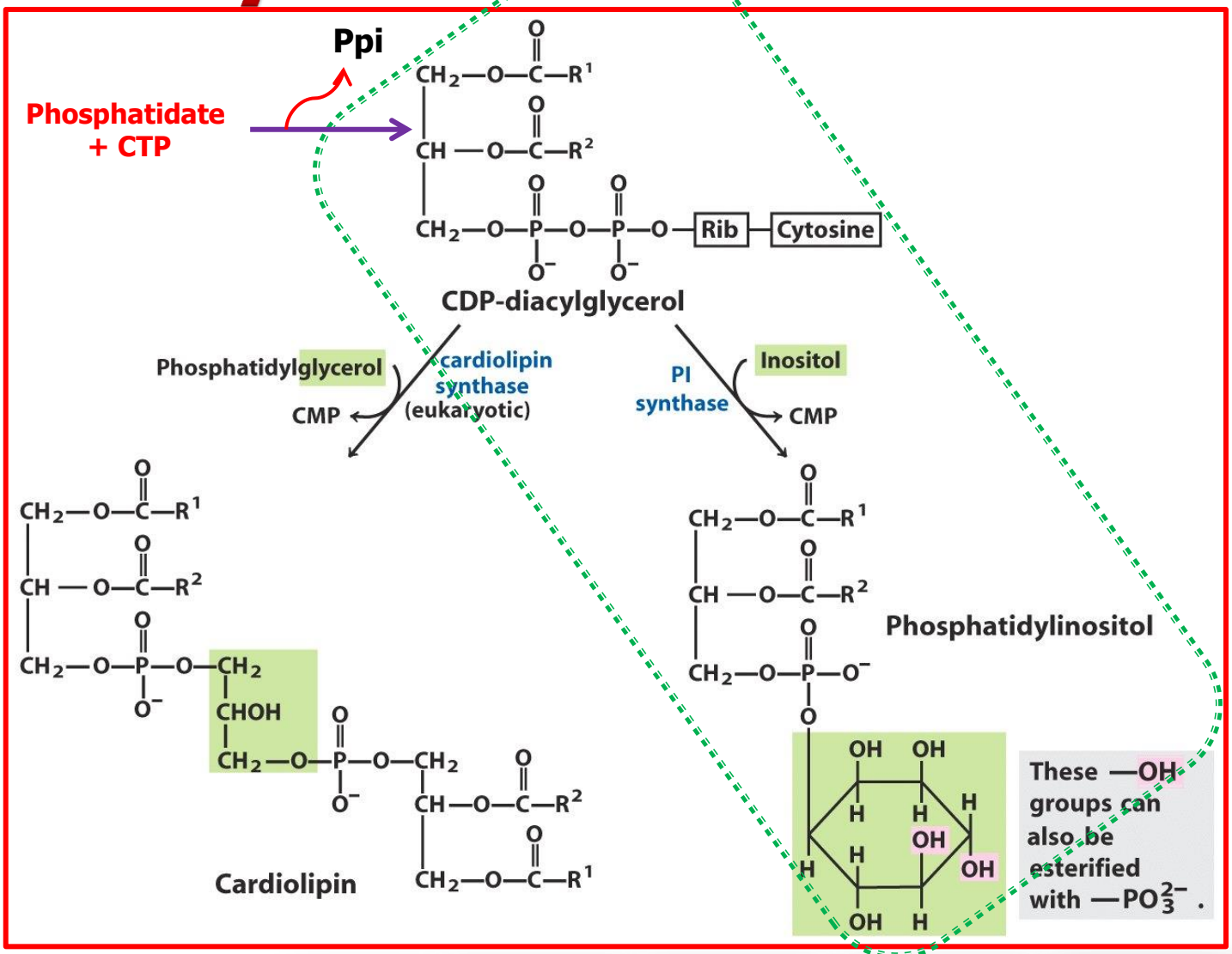






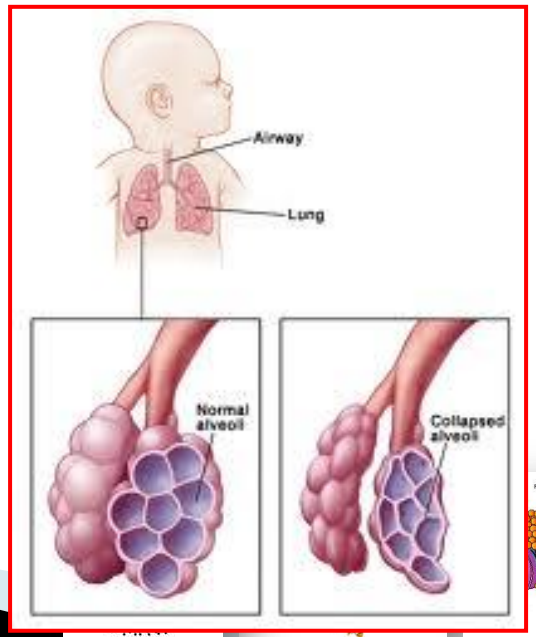
Endogen. synthesis of PLs

- When phosphatidate joins with a mole of CTP then it releases a Ppi and converted to a CDP-diacylglycerol
- Finally, an inositol join with phosphate group and CMP releases to produce a phospholipid called phosphatidyl-inositol



Clinical correlation - PLs

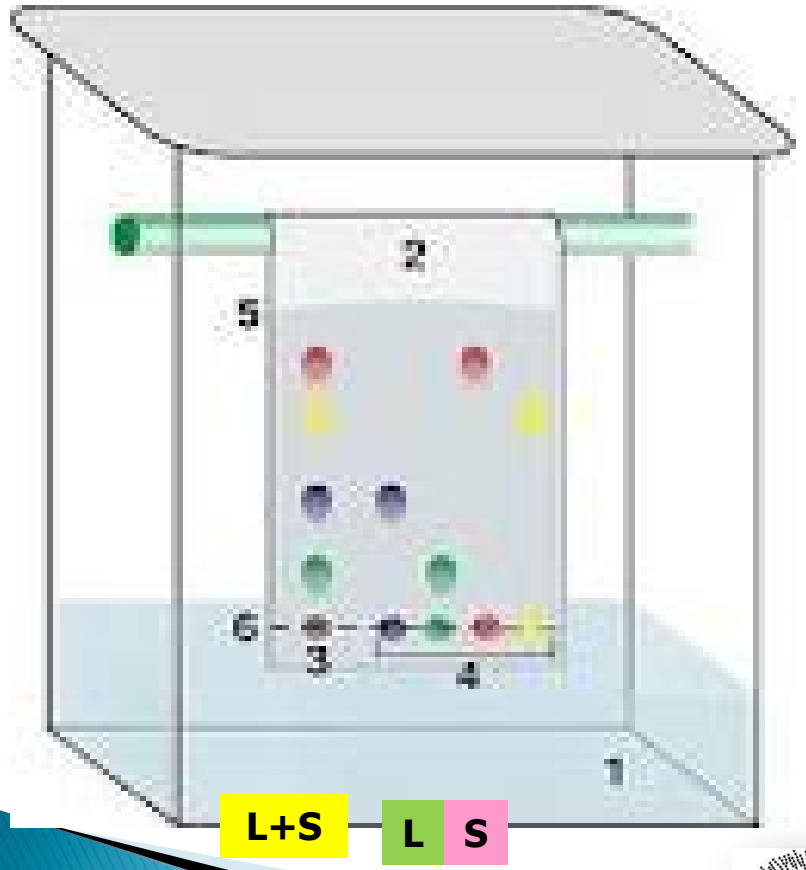
- **The development of respiratory distress syndrome (RDS or hyaline membrane disease) is common in immature neonates**
- **If a baby born early then the alveoli of the lung will not expand normally at birth and infant may suffer from RDS and then respiratory support of ventilation may be needed**
- **Hence, it is very important to confirm the pulmonary (lung) maturity before the delivery of the baby**



Page 24 in Handouts

Clinical correlation - PLs

- The lecithin sphingomyelin area ratio or LSAR can be determined by measuring the area of relevant spots of lecithin and sphingomyelin



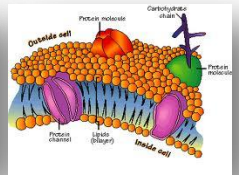
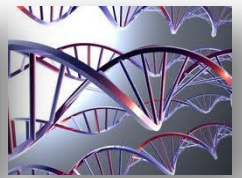
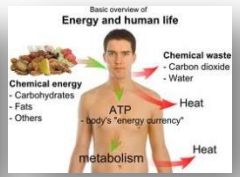
LSAR = [area of lecithin spot (hxw)/ area of sphingomyelin spot (hxw)]

LSAR <1.5:
Immature pattern or surfactant inadequate

LSAR 1.5:
Transition pattern

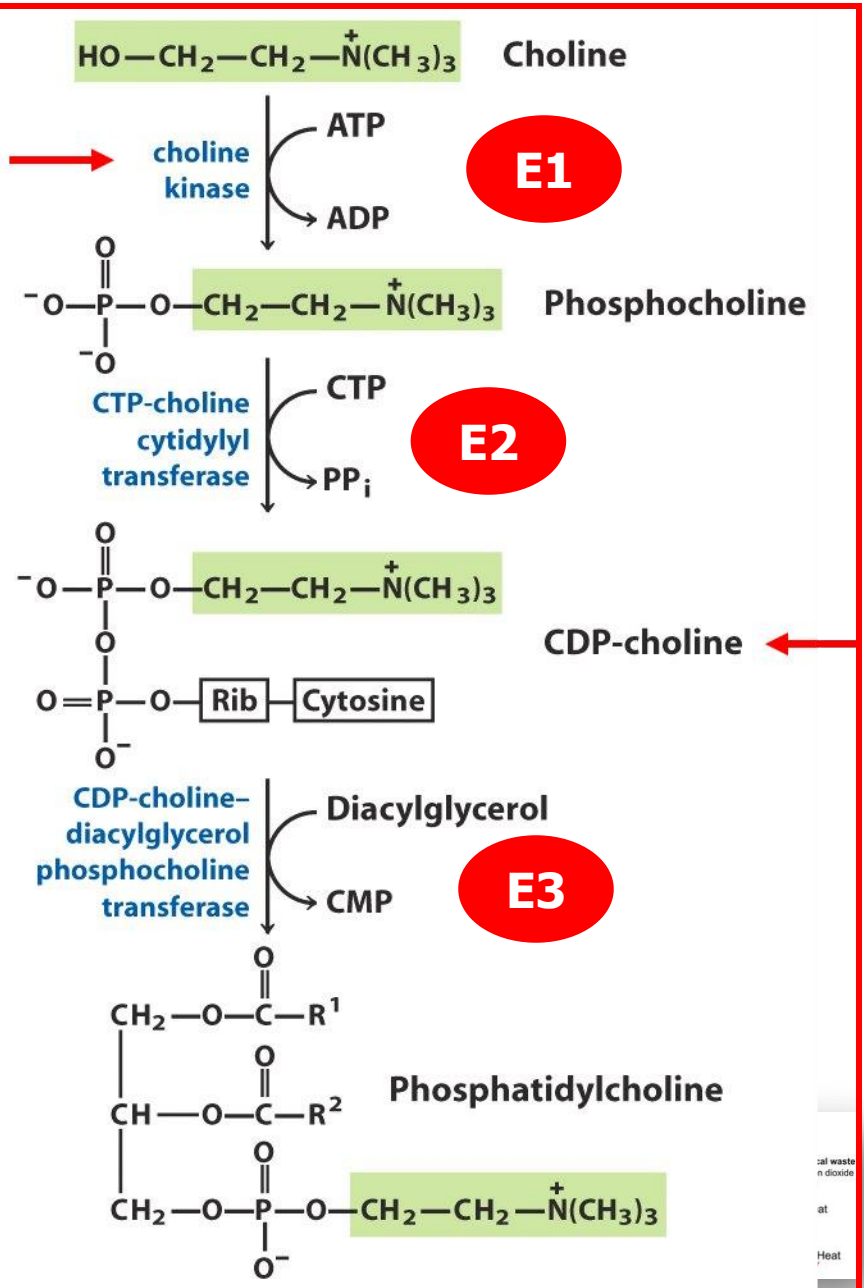
LSAR >1.5:
Mature pattern or surfactant adequate



Salvage synthesis of PLs

- **The most abundant phospholipids in most eukaryotic cells are phosphatidylcholine and phosphatidylethanolamine.**
- **Since choline and ethanolamine arise largely through the turnover of pre-existing phospholipids, the latter pathways can be considered routes for reutilization of these breakdown products.**
- **The significance of reutilization of choline lies in the fact that the three methyl groups of choline are derived from the amino acid methionine, an amino acid which is limiting in many animal diets**



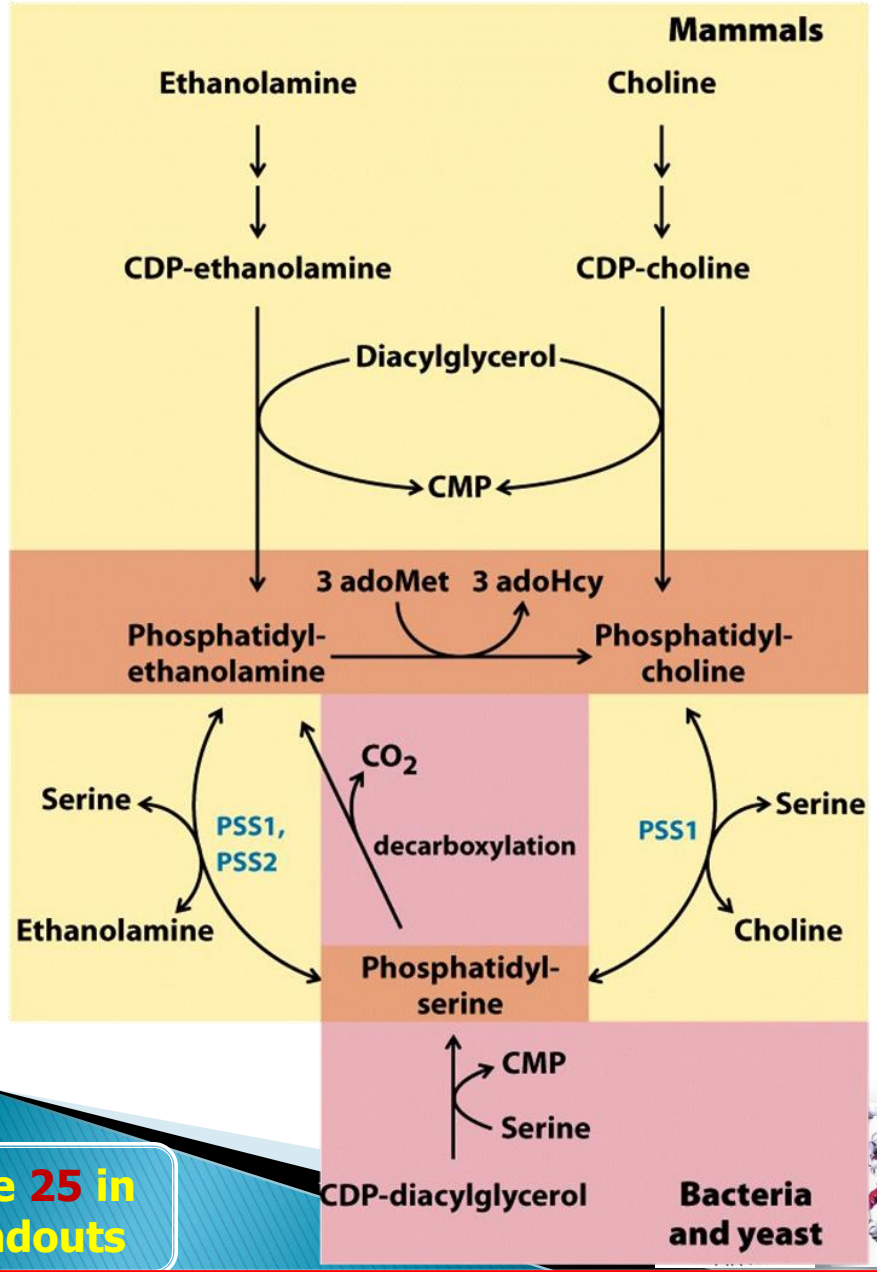
E1 Choline kinase

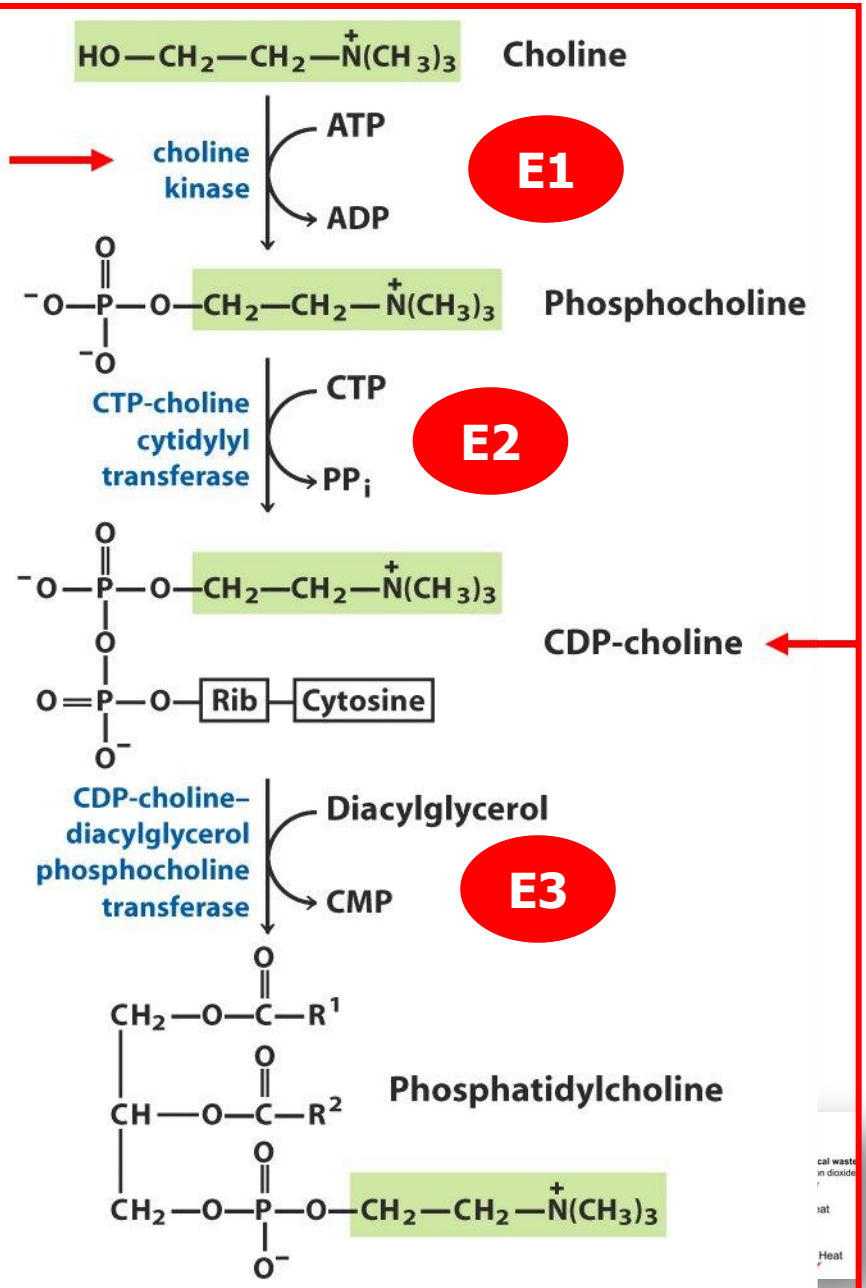
E2 CTP: phosphocholine cytidyl transferase

E3 CDP: chokine : 1-2-diacylglycerol choline phosphotransferase

Pg 24-25 in Handouts

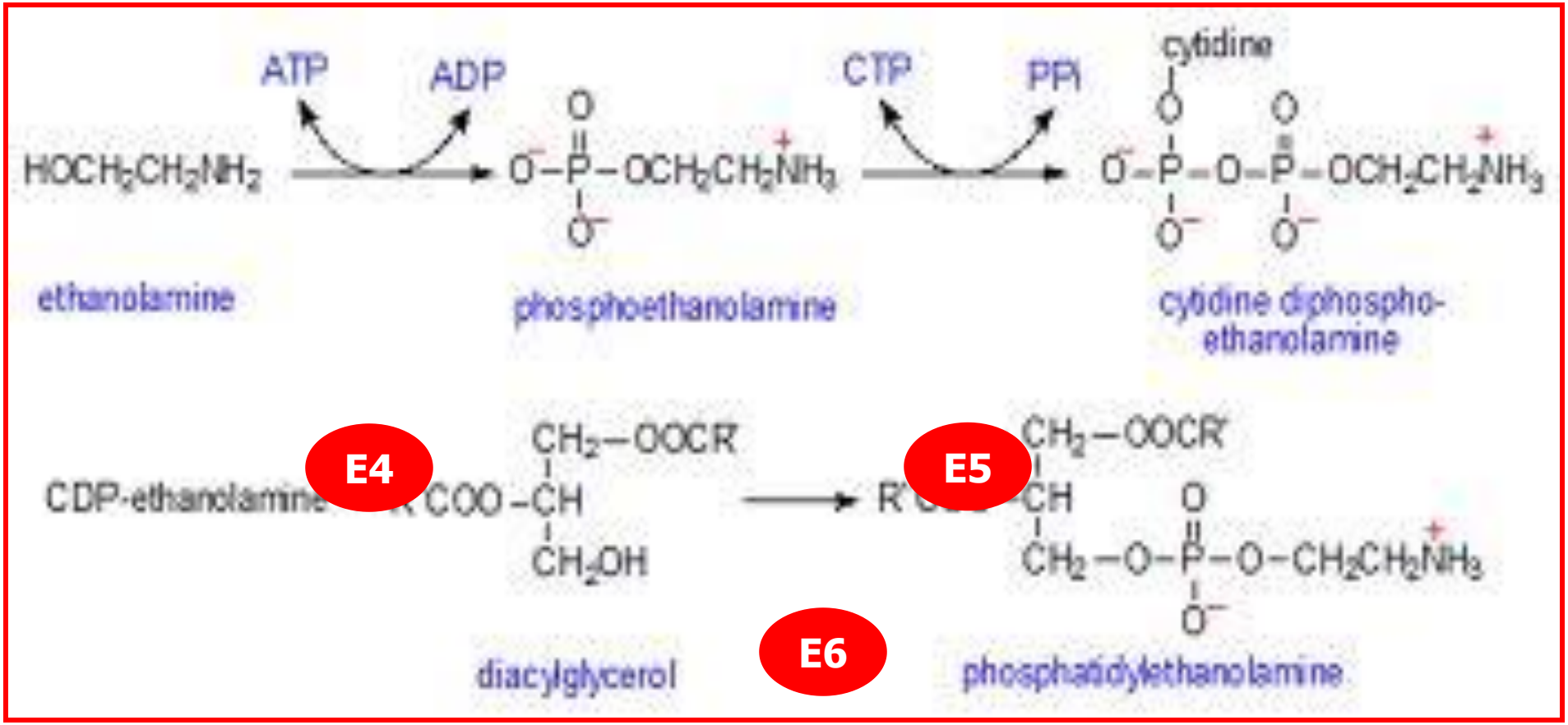
Salvage synthesis of PLs





Page 25 in Handouts

Salvage synthesis of PLs



E4 Ethanolamine kinase

E5 CTP: Phosphoethnolamine cytidyltransferase

E6 CDP: Ethanolamine: 1-2-diacylglycerol ethanolamine phophotransferase