DIGESTION AND ABSORPTION OF LIPIDS And Synthesis

Introduction:

The digestion of fats and other lipids poses a special problem because of (a) the insolubility of fats in water, and

(b) because lipolytic enzymes, like other enzymes, are soluble in an aqueous medium.

- The above problem is solved in the gut by emulsification of fats, particularly by bile salts, present in bile.
- The breaking of large fat particles or oil globules, into smaller fine particles by emulsification increases the surface exposed to interaction with Lipases and thus, the rate of digestion is proportionally increased.

Digestion steps

1- Digestion in mouth and stomach: It was believed earlier that little or no fat digestion takes place in the mouth. Recently a lipase has been detected called lingual lipase.

Lingual lipase: The pH of activity is 2.0 to 7.5 (optimal pH value is 4.0 to 4.5). Lingual lipase activity is continued in the stomach also where the pH value is low. Lingual lipase is more active on TG having shorter FA chains. The released short chain fatty acids are relatively more soluble and hydrophilic and can be absorbed directly from the stomach wall and enter the portal vein.

Gastric lipase:

The overall digestion of fats, brought about by gastric lipase is negligible because:

• No emulsification of fats takes place in stomach

• The enzyme secreted in small quantity

• pH of gastric juice is not conducive which is highly acidic, whereas gastric lipase activity is more effective at relatively alkaline pH (average pH 7.8).

Gastric lipase activity requires presence of Ca++.

Role of fat in stomach: Fats do play one important role in the stomach in that they delay the rate of emptying of stomach.

2- Digestion in small intestine: The major site of fat digestion is the small intestine. This is due to the presence of a Pancreatic lipase in the pancreatic juice and presence of bile salts, which acts as an effective emulsifying agent for fats.

Pancreatic lipase is specific for the removal of the primary (or α – positions or 1 and 3 positions fatty acids in a TAG. The resulting β –monoglyceride (or 2 –monoglyceride) first needs isomerization of the fatty acyl chain from β – position to an α – position before being hydrolyzed by the lipase.

This latter process is slow and therefore:

- the 2-monoglycerides (β – monoglycerides) are the major absorbed end products of triglyceride digestion (about 72 %).
- About one fifth (22 %) is completely broken down to fatty acids and glycerol and then absorbed.
- About (6%) is absorbed in the α – monoglyceride form.

Approximately 90% to 95 % of TAGs in the diet are absorbed.

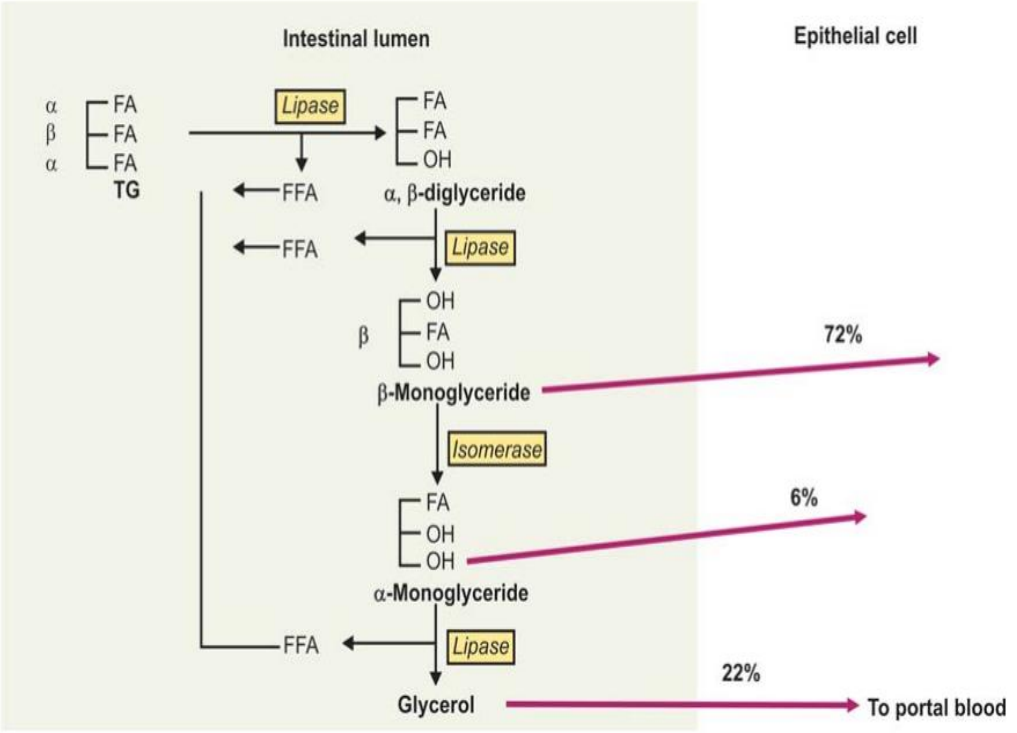


Fig. 24.1: Digestion in intestinal lumen

Digestion and Absorption of Cholesterol

Pancreatic juice contains an enzyme cholesterol esterase, which may either catalyse the esterification of free cholesterol with FA or it may also catalyse the opposite reaction, i.e. hydrolysis of cholesterol esters.

In the intestinal lumen, depending on the equilibrium, the "cholesterol-esters" are hydrolysed by this enzyme. Only 50 % of cholesterol in the diet is absorbed. If it is present in the form of cholesterol esters, then under the conditions of upper intestine, the cholesterol esters are first hydrolyzed by cholesterol esterase into free cholesterol and fatty acids before being absorbed.

• Absorption of cholesterol has been reported to be facilitated by presence of unsaturated FA and bile salts are necessary for the absorption of cholesterol.

Digestion and Absorption of Phospholipids

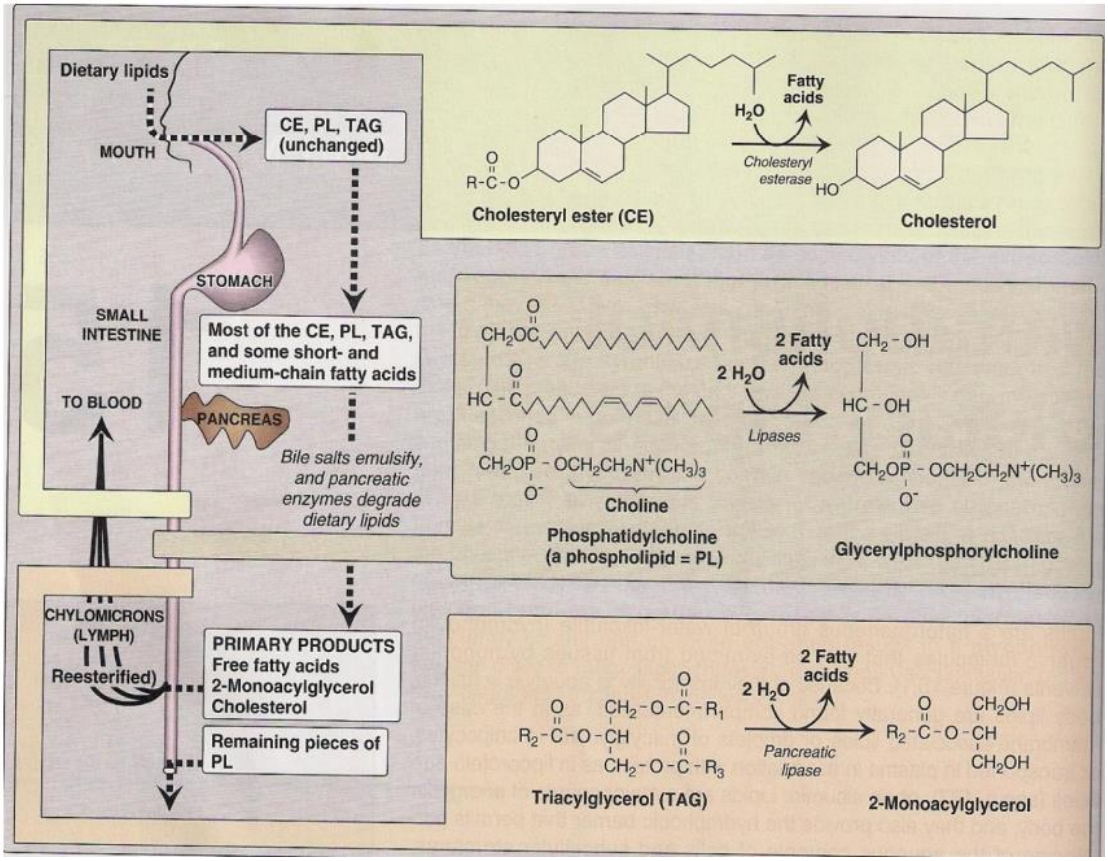
Dietary phospholipids may be absorbed from intestine without any digestion. Due to its polar structure and hydrophilic properties, they are absorbed directly to portal blood and taken to Liver.

• Pancreatic juice contains an enzyme called phospholipase that cleaves the ester bond at C2 site and thus hydrolyze a phospholipid into a lysophospholipid (such as lysolecithin) in addition into an unsaturated FA.

Phospholipase Lysophospholipid

Phospholipid ---------- +

Ca ++ Unsaturated F.A



Fat mobilization from adipose tissues

1- Metabolism of TAG

TG stores in the body is continually undergoing

(a) Esterification (synthesis) and

(b) Lipolysis (breakdown).

- These two processes are not the forward and reverse processes of the same reaction. They are entirely different pathways involving different reactants and enzymes. Many of the nutritional, metabolic and hormonal factors regulate either of these two mechanisms, i.e. esterification and lipolysis.

- Lipolysis (Breakdown of TG)

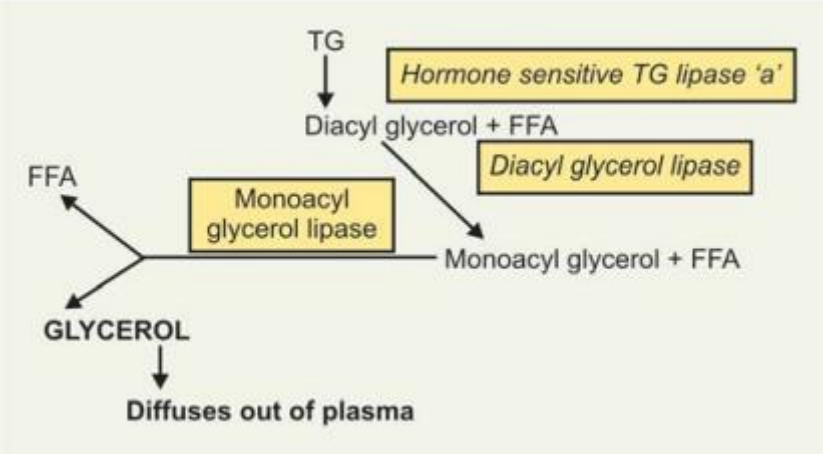
TG in adipose tissue undergoes hydrolysis by a hormone-sensitive TG lipase enzyme to form free fatty acids and glycerol.

Adipolytic lipases are three:

1. Hormone sensitive triacyl glycerol lipase: Key regulating enzyme.
2. Two others are not hormone-sensitive:

• Diacyl glycerol lipase

• Monoacyl glycerol lipase.



Hormone-sensitive lipase can remove a F.A from either carbon 1 or carbon 3 of a TAG. Additional lipases, specific for diacylglycerol (DAG) and monoacylglycerol, remove the remaining F.As.

Lipolyic factors:

1. Fasting,

2. Anxiety, and

3. Many hormones rapidly stimulate F.A release from adipose

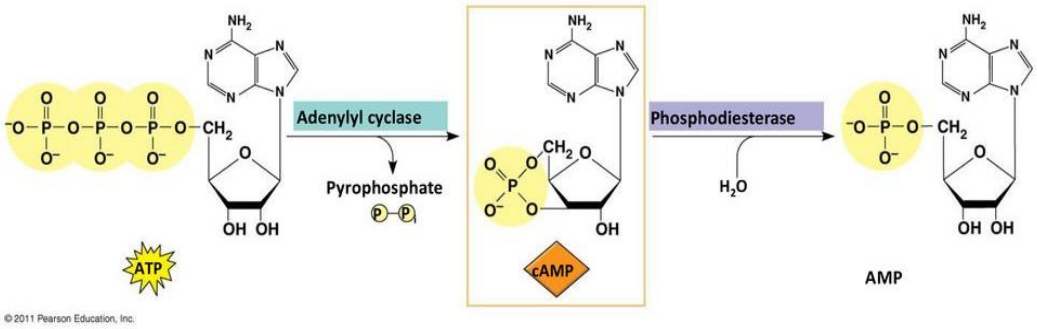
tissues: Epinephrine, norepinephrine, glucagon, and ACTH all activate adenylate cyclase that converts ATP into cAMP.

cAMP will activate the hormone – sensitive lipase that hydrolyze TAGs into diglycerides and F.F.As.

- Growth hormone, thyroxine, and cortisol facilitate the action of the above lipolytic hormones.

3. Methyl xanthine compounds such as caffeine (present in tea and coffee) enhance fatty acid mobilization from adipose tissue because they inhibit the enzyme phosphodiesterase, if phosphodiesterase is inhibited then this will maintain the hormone sensitive lipase in an active form and so there would be more lipolysis.

Phosphodiesterase normally acts to inactivate cAMP and thus the hormone sensitive lipase will return into its inactive form and lipolysis stops. It is significant to note that the drinking of tea or coffee, containing caffeine, causes marked and prolonged elevation of plasma F.F.As in humans.



- Lipogenic (or anti-lipolytic) factors:
- High levels of insulin and glucose are lipogenic (inhibit lipolysis). Insulin is an activator of the enzyme phosphodiesterase that inactivate cAMP and thus will indirectly inhibit hormone-sensitive lipase and inhibit fat mobilization.
- Insulin is also an inhibitor of the enzyme adenylate cyclase that synthesizes cAMP and thus will indirectly inhibit hormone-sensitive lipase and inhibit fat mobilization.
- Fate of glycerol: The glycerol released cannot be metabolized by adipocytes because they lack glycerol kinase. It will be transported through the blood to the liver, which can activate it into glycerol phosphate. The resulting glycerol – P can be used to form TGs or be converted to dihydroxyacetonephosphate (DHAP) which enters glycolysis or gluconeogenesis.
- Fate of F. F.As: F.F.As, after lipolysis, move through the cell membrane of the adipocytes, bind albumin in plasma and carried to other tissues where they can be oxidized for energy.

Fatty acid synthesis

Excess amounts of carbohydrates and proteins that are obtained from the diet can be converted into fat through fatty acid synthesis.

F.A synthesis occurs primarily:

- in the liver and also

- lactating mammary glands and

- to a lesser extent in adipose tissues, kidney, brain and lung.

- The product of FAS action (fatty acid synthesis) is palmitic acid. (16:0).

The cellular site of the process is mainly the cytosol F.A synthesis requires three precursors:

1- Acetyl CoA

2- Malonyl CoA that is formed from acetyl CoA

3- Reducing equivalents in the form of NADPH+ H+.

A. Extramitochondrial (Cytoplasmic) Synthesis of Fatty Acids:

- The synthesis takes place in cytosol. Starting material is acetyl-CoA and synthesis always ends in formation of palmitic acid.

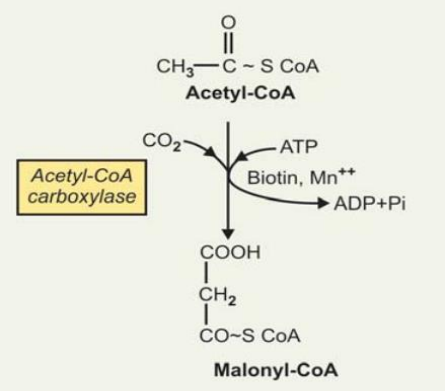
Materials required

• Enzymes
– Fatty acid synthase
– Acetyl-CoA carboxylase
• Coenzymes and cofactors:
Biotin, NADPH, Mn++
• CO2: Source of CO2 is bicarbonate and
• ATP: For energy

Steps of FA Synthesis

• The starting material for the synthesis is acetyl-CoA. Acetyl-CoA is formed in mitochondrion but synthesis occurs in cytosol.

1. Formation of malonyl CoA from acetyl-CoA: In presence of the enzyme "acetyl-CoA carboxylase", the acetyl-CoA is converted to malonylCoA by "CO2-fixation reaction". Mn++ is required as a cofactor and ATP provides the energy



B. Chain Elongation System

1. Microsomal system: A system presents in microsomes which can lengthen existing fatty acid chains. The palmitic acid formed in cytosol is lengthened to stearic acid and arachidonic acids.

2. Mitochondrial system: This system is mostly restricted to lengthening of an existing fatty acid of moderate chain-length.

The overall reaction for palmitate synthesis:

8 Acetyl CoA + 14 NADPH + 14 H+ + 7 ATP + 7 CO2 ---------- Palmitic acid + 8 CoA + l4 $NADP^+$ + 7 ADP + 7 Pi + 6 H2O

• Three hormonal signals determine the state of FA metabolism.

Glucagon and epinephrine inhibit FA synthesis and favor oxidation,

whereas insulin is anti-lipolytic and stimulates FA biosynthesis.

Factors regulating acetyl Co A carboxylase:

1. Short term regulation of acetyl CoA carboxylase by above factors (see equation)

2. Long term regulation of acetyl CoA carboxylase

a. Positive effect:

1. Prolonged consumption of high carbohydrate diet

2. Low fat diet

b. Negative effect:

1. High fat diet

2. Fasting

Fate of Palmitic acid:

1- Esterification: Palmitate may undergo esterification with glycerol

or cholesterol.

2. Chain elongation:

Palmitate may be elongated to form F.As longer than C16.

3. Desaturation:

Stearic acid, derived by elongation of palmitate may undergo desaturation at C9 – C10 to form oleic acid (unsaturated fatty acid).

4. Sphingosine formation:

Sphingosine is formed from palmitoyl CoA and the amino acid

serine.

Energy utilized for the synthesis of palmitic acid:

1. One ATP is utilized in the synthesis of each malonyl CoA so 7 ATPs are utilized.

2. Two NADPH + H^+ are utilized in the two reduction reactions of each cycle with a total utilization of 14 NADPH, each represents about 3 ATPs , for a total of about 42 ATPs.

3. The net ATP consumed for palmitic acid synthesis is about 49 ATPs.