Chapter 16

Lipids: Digestion and Absorption

Triacylglycerol (TAG) is the major dietary lipid constituting about 90% of total lipid intake. Rest of the lipids are cholesterol, cholesteryl ester, phospholipids and free fatty acids.

Digestion of TAG begins in stomach where *lingual lipase* (coming from back of the tongue) and *gastric lipase* enzymes act on dietary TAG at optimum pH of 4 to 6. The TAG which contains short and medium chain fatty acids (e.g. milk fat) is mainly hydrolyzed in this fashion. Gastric digestion of TAG constitutes only 30% of total TAG hydrolysis, remaining TAG hydrolysis occurs in duodenum with the help of pancreatic lipase.

Lipid emulsification is an important process for lipid digestion as this increases the surface area of hydrophobic lipid compounds and enhances the action of digestive enzymes on it.

Emulsification of lipid requires peristalsis and bile salts. Gastric chyme which is released into the duodenum, mostly contains emulsion droplets of <2 mm in diameter. They are further stabilized by bile salts in the duodenum and prevent their coalescence.

Bile salts are amphipathic in nature and they tend to stabilize small droplets of lipids resulting from peristalsis.

Pancreatic lipase is the major enzyme responsible for TAG hydrolysis which acts on 'α' carbon glycerol releasing long chain fatty acids from C–1 and C–3 position of glycerol and MAG (monoacylglycerol).Pancreatic juice also contain a 12kDa colipase which tends to bind the lipase and micelle and prevents inhibitory action of bile acid on lipase.

Olestra: Fatty acids are esterified with sucrose instead of glycerol.

Orlistat: It is nonhydrolyzable analog of TAG and is an inhibitor of pancreatic liapse.

In addition to pancreatic lipase enzyme, the pancreatic juice also contains many other enzymes like unspecified lipid esterases, phospholipases, etc.

Lipid esterases act on cholesteryl esters, monoacylglycerol, vitamin A esters with carboxylic acid to release free cholesterol, glycerol and vitamin A, respectively.

It is pertinent to mention here that dietary cholesterol is mostly in the form of free (unesterified) cholesterol. It is only 10–15% of total cholesterol consumed in diet is in esterified form which needs action of cholesteryl ester hydrolase (cholesterol esterase) to convert it to free cholesterol and fatty acid.

The main phospholipase present in pancreatic juice is phospholipase A2 which acts on C-2 of phospholipids releasing lysophospholipids. Lysophospholipase may act on lysophospholipid to release fatty acid from C-1 position leaving behind glycerophosphoryl base, which is either absorbed or excreted in the faces (Fig. 16.1).

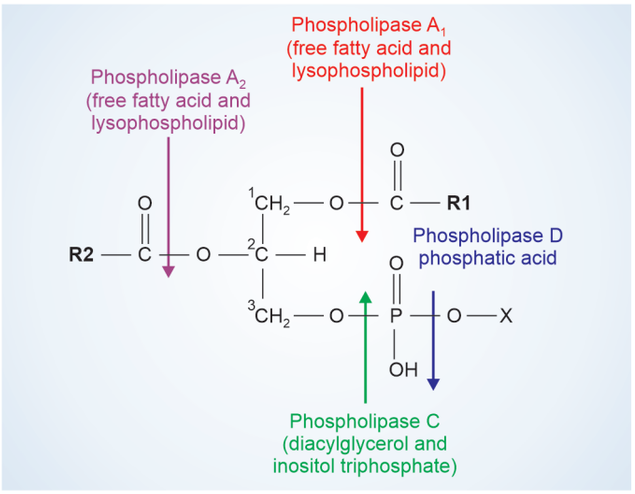

Fig. 16.1: Action of various phospholipases and corresponding product produced

Absorption of Digested Lipid by Enterocytes (Fig. 16.2)

Lipids are taken up by enterocytes by simple diffusion through plasma membrane.

Main products of lipid digestion in the jejunum are free fatty acids, free cholesterol, 2-monoacyl glycerol. These compounds along with bile salts, fat-soluble vitamins (A, D, E, K) form mixed micelles which are disc-shaped arrangements with hydrophobic groups on the inside and hydrophilic groups on outer surface. This makes it soluble in the intestinal aqueous environment.

These mixed micelles traverse the water layer and present to microvilli of apical membrane (brush border of enterocytes) from where the lipids are absorbed into the enterocyte (Fig. 16.3).

Bile salts are absorbed in the terminal ileum.

Cholesterol is poorly absorbed in the small intestine and drugs like ezetimibe further reduce the absorption of cholesterol from intestine.

Short-chain fatty acid (SCFA) and medium-chain fatty acid (MCFA) are soluble in water, hence they do not require mixed micelle for their absorption, rather they are directly absorbed in the GIT mucosa, and from there enter the portal circulation directly. These SCFA and MCFA are then carried to liver with the help of albumin. The other lipids like free cholesterol, LCFA enter the smooth endoplasmic reticulum (SER) of enterocyte where first of all LCFA is converted to their acyl-CoA form by enzyme thiokinase (acyl coenzyme A synthetase).

Now, all these long-chain acyl-CoA are utilized to convert MAG to DAG then TAG, cholesterol to cholesterol ester, lysophospholipid to phospholipids. This is known as re-esterification.

The TAG, CE are nonpolar lipids, hence they need to be surrounded by amphipathic layer of phospholipid and free cholesterol to produce a droplet which has hydrophilic surrounding and hydrophobic core. ApoB-48 is additionally embedded in it and this structure is known as chylomicron.

Microsomal triglyceride transfer proteins (MTTPs) are important in assembly of such TAG rich ApoB containing particles.

These chylomicrons enter in secretory vesicles via Golgi apparatus and are then exocytosed to lymphatic system. The lymphatic system finally empties into the systematic circulation via thoracic duct which enters into the subclavian vein.

Further maturation and metabolization of chylomicron is described in Chapter 21.

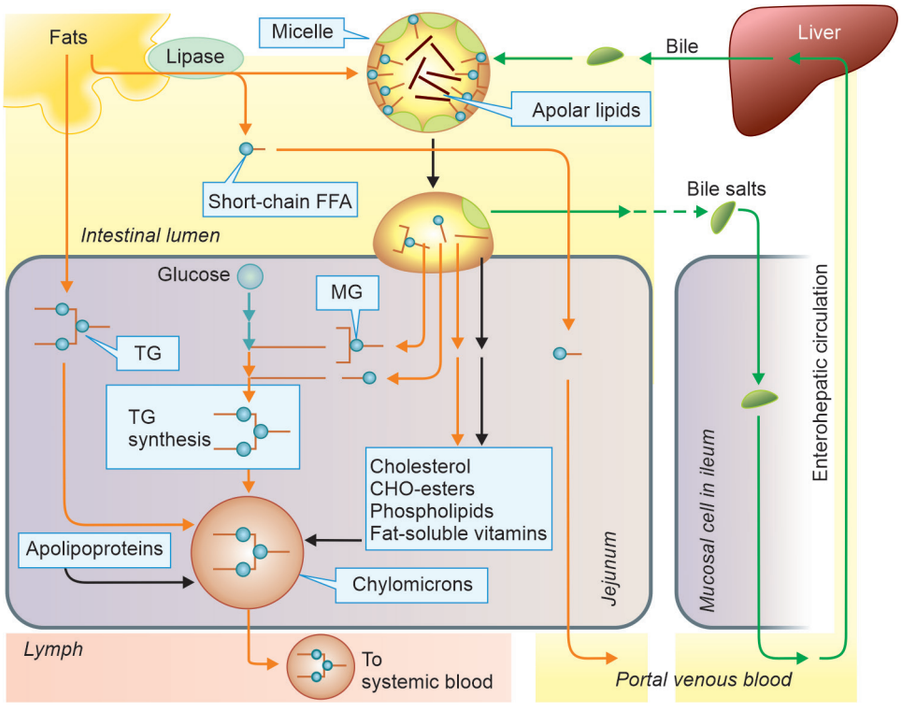

Fig. 16.2: Lipid absorption from intestine

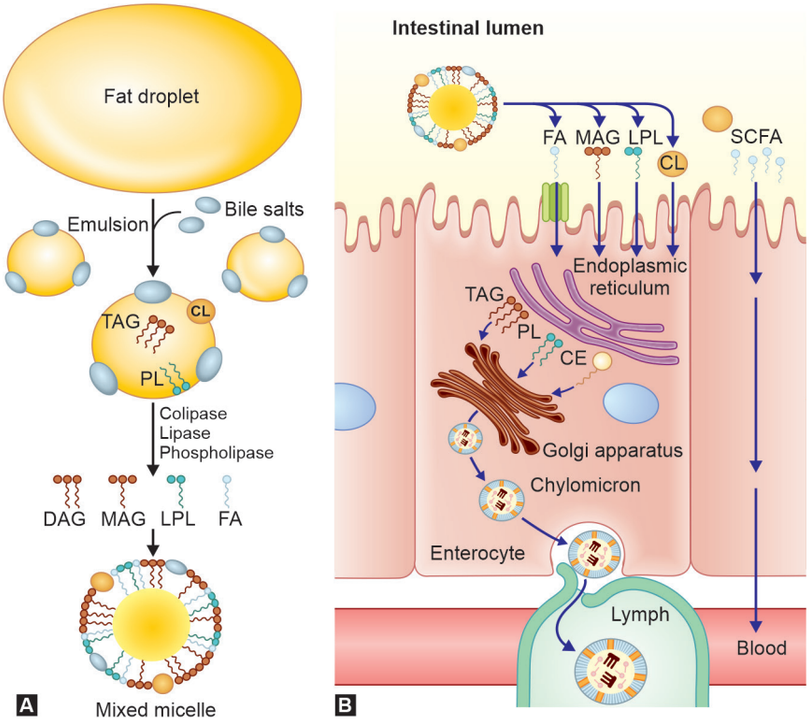

Fig. 16.3: Mixed micelle at the brush border of enterocyte

Clinical Application

Steatorrhea

Due to defect in lipid digestion and/or absorption, excess of it comes out in the feces along with fat-soluble vitamins. It results in increased bulk of stool which additionally is of foul smelling.

Steatorrhea may be due to empaired entery of bile from liver/gallbladder and/or digestive enzymes from pancreas.

Intake of MCFA, SCFA may help in this condition as they do not require mixed micelle formation of absorption.

Cystic Fibrosis

Cystic fibrosis is an autosomal recessive disease. It is caused by mutations in the *CFTR* (cystic fibrosis transmembrane conductance regulator) gene. The commonest mutation is the deletion of phenylalanine at codon 508.

The CFTR protein has several functions.

Normal cystic fibrosis transmembrane regulator (CFTR) protein is expressed in many cells and has multiple functions in health and disease. The primary function of the CFTR protein is as an ion channel that regulates liquid volume on epithelial surfaces through chloride secretion and inhibition of sodium absorption. It also interacts with other membrane proteins to maintain epithelial tight-junctions and barriers to fluid flow.

Many mutations in the *CFTR* gene produce abnormal or absent protein. CFTR protein dysfunction underlies the classic CF presentation of progressive pulmonary and GI pathology.

Various organs affected by cystic fibrosis is depicted in Fig. 16.4.

The mucociliary dysfunction means that a patient with cystic fibrosis cannot effectively clear inhaled bacteria. In addition, there is an excessive inflammatory response to pathogens.

According to an estimate for a given bacterial load, a person with cystic fibrosis will have up to 10 times more inflammation than a person with a lower respiratory tract infection but without the disease.

The optimal diagnostic test for cystic fibrosis is the measurement of sweat electrolyte levels. Patients with the disease have raised concentrations of sodium and chloride (>60 mmol/L, diagnostic; 40–60 mmol/L, intermediate)

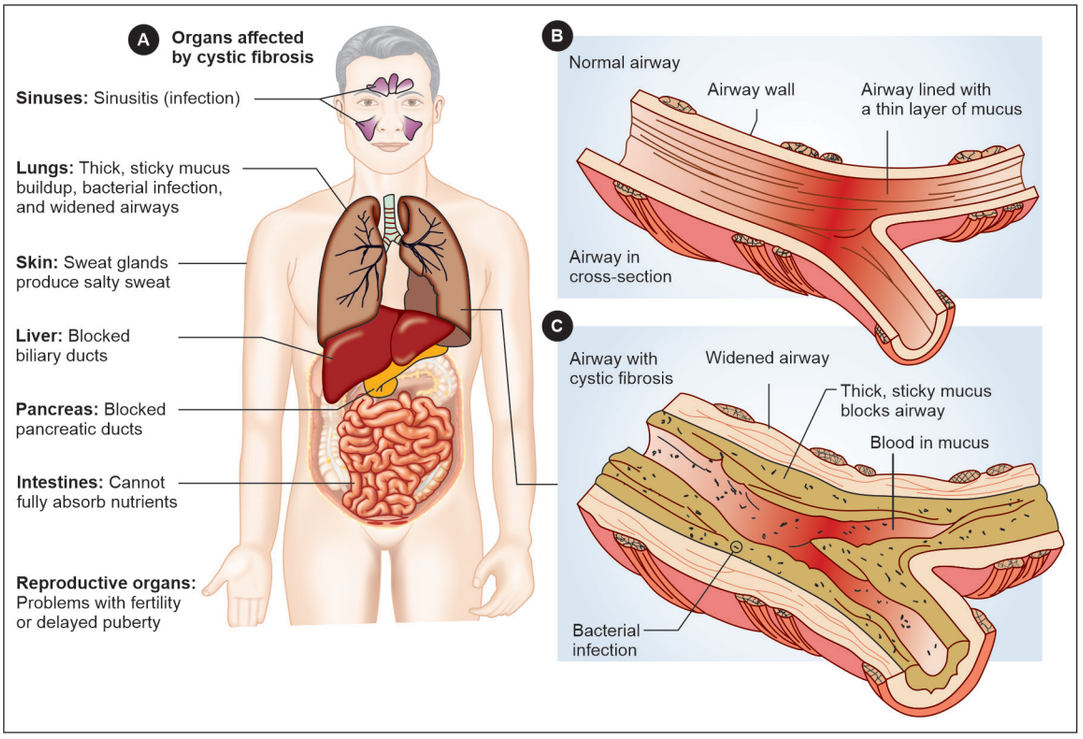

Fig. 16.4: **(A)** Shows various organs affected by cystic fibrosis; **(B)** shows normal airway; **(C)** shows airway of a patient affected with cystic fibrosis