

Lipids metabolism

Introduction

- **Definition**

Organic compounds that either absorbed from food or synthesized by the liver, soluble in organic solvents and insoluble in water.

- **Functions**

- Source of energy.
- Structure of cell membranes.
- A protective cushion for many tissues and organs.
- Precursors of hormones (steroids and prostaglandins).
- They also dissolve the vitamins, which are fat soluble and assist their digestion.

- **Classification of lipids**

- Simple lipids (fat, oil and waxes).
- Complex lipids such as phospholipids and glycolipids.
- Derived lipids include hydrolytic product of the simple and complex lipids such as fat soluble vitamins and cholesterol.

Simple lipids

- Fat

Esters of fatty acids with glycerol . A fat in liquid state is known oils .

- Waxes

Simple esters of fatty acids usually saturated with long chain monohydroxy alcohols .

Fatty acids

- **Free fatty acids (normal values 10-20 mg/dl)**
 - **Transported in plasma by albumin .**
- **In fasting state , the FFA derived from the hydrolysis of TG in adipose tissues by the action of lipoprotein lipase .**
- **Fatty acid oxidation is the major source of energy for ATP synthesis in human .**

- In tissues such as muscle and kidney, fatty acids are oxidized to acetyl CoA by β -oxidation process for energy (acetyl CoA can be used as a precursor for cholesterol and other steroid).
- In the liver, fatty acids are converted to KBs that are oxidized by tissues such as muscle and kidney.

During prolonged starvation (fasting 3 days or more), the brain uses KBs for energy.

- Glycerol is used by the liver for gluconeogenesis which produces glucose for tissues such as brain and RBCs.

Fatty acids classification

Fatty acids can be classified either as:

1 - Saturated or unsaturated fatty acids .

2 – According to chain length :

A - Short chain (FA : 2-4 carbon atoms) .

B - Medium chain (FA : 6 –10 carbon atoms) .

C - Long chain (FA : 12 – 26 carbon atoms) .

3 - Essential fatty acids (EFA) vs those that can be biosynthesized in the body (NEFA) .

Unsaturated fatty acids (Essential fatty acids)

- 18: 1 ; 9 (Oleic acid)
- 18: 2 ; 6 , 9 (Linoleic acid)
- 18 : 3 ; 6 , 9 , 12 (Linolenic acid)
- 20 : 4 ; 5 , 8 , 11 , 14 (Arachidonic acid)

Functions of essential fatty acids

- 1 . The fluidity of membrane depends on length and degree of unsaturated fatty acids .**
- 2 . They are required for the synthesis of phospholipid , cholesterol ester and lipoproteins .**
- 3 . Poly unsaturated fatty acids are released from membrane , diverted for the synthesis of prostaglandin , leukotriene and thromboxane .**
- 4 . They act as fat mobilizing agent in liver and protect liver from accumulating fats (fatty liver) .**

TG

- Normal values (50 - 165 mg / dl)
- TG is a esterification of FA with glycerol , synthesized in :
 - . Liver (FA from plasma + glycerol) (endogenous TG , synthesized in the body) (This TG is incorporated into VLDL which enters the blood) .
 - . Small intestine (Monoglyceride + FA from diet) (exogenous TG , which comes from diet) (This TG becomes a component of chylomicrones) .
- They are transported in the blood as lipoproteins .
- The storage of TG in adipose tissues is mediated by insulin , which stimulates adipose cells to secrete lipase and to take up glucose , the source of glycerol for TG synthesis .

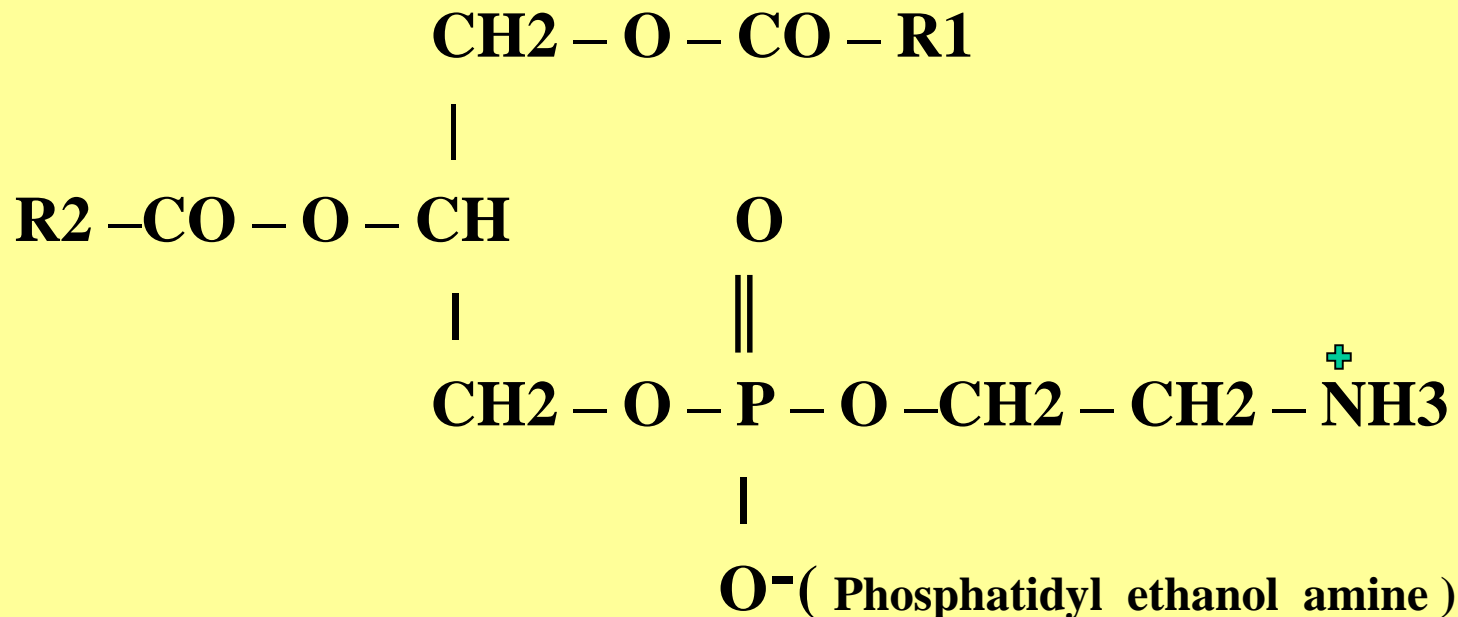
Biosynthesis of triacylglycerols

Two activate fatty acid are attached to glycerophosphate to form phosphatidic acid by acyl transferase . It is converted to diglyceride by the removal of phosphate group by phosphatase .

Another fatty acid is attached to the diglyceride to form triglyceride . The synthesis take place in adipose tissue and liver .

Phospholipids

- Normal values (150 - 250 mg / dl)

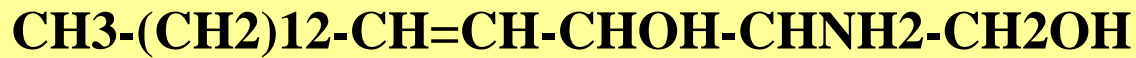


phospholipids are composed of TG esterified with phosphoric acid , which in turn , is bound as an ester to a nitrogen containing base (cholin or ethanol amine) .

- PL synthesized in the mucosa of the small intestine and liver .
- plasma PL is increased in many conditions (DM , Biliary cirrhosis , Nephrotic syndrome) that causes lipaemia .
- PLs are essential compounds of cell membrane because of their ability align them selves between water and lipid phase { PL are compounds that contain polar and non polar groups (amphipathic) }.
- Phospho ethanol amine a constituent of blood platelts , is a necessary participant in the clotting process . Solubilization of cholesterol is done by amphipathic nature of PL .

Sphingolipids

Sphingolipids are all compounds containing sphingosine (do not contain glycerol)



Sphingosine

fatty acid bind in amide linkage to the amino group .

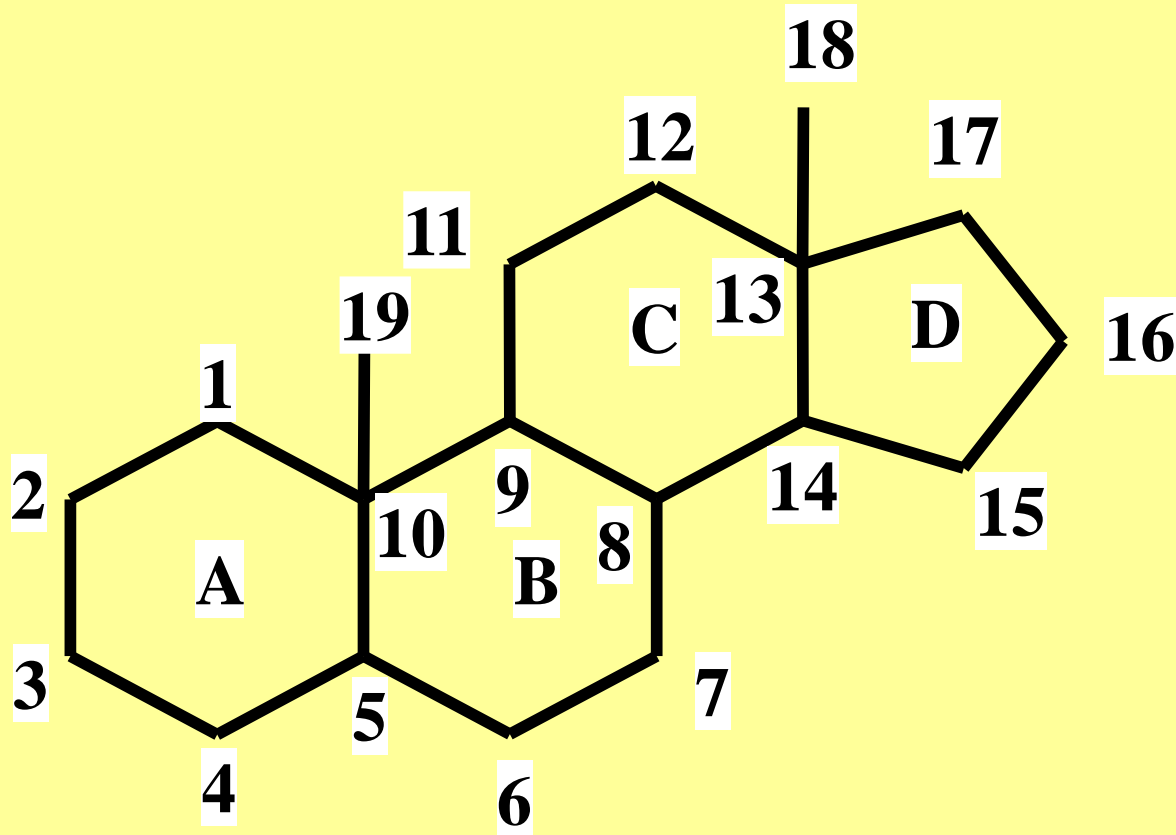
(Note)

Sphingosine are major components of the membrane of brain and other nervous tissues .

Cholesterol

- Normal values (150 – 250 mg / dl) .
- Can be synthesized in all cells of the body (except RBCs) from acetyl coA .
- Ch. is present in tissues and in plasma either as free ch. or esterified with long chain fatty acid .
- Ch. is synthesized mainly in the liver and intestine from acetyl coA (ch. synthesized about 70% while dietary source of ch. is about 30%)(ch. only found in animal fat) .
- Ch. is the major constituent of gallstones .^ε

STEROID NUMBERING SYSTEM



Functions of cholesterol

Cholesterol is important in many ways :

- 1 . For the synthesis of bile salts that are important in lipid digestion and absorption .
- 2 . For the synthesis of steroid hormones that are biologically important like the six hormones estrogen and progesterone .
- 3 . For the synthesis of vitamin D3 .
- 4 . As a structural material in biological membrane .
- 5 . As a component of lipoproteins as transport form of lipid base energy .

Lipoproteins

- **particles found in plasma that transport lipids including cholesterol .**
- **lipoprotein classes and its function :**
 - **chylomicrons (CM) : Transport dietary triglycerides and cholesterol from the intestine to the liver for metabolism .**
 - **very low density lipoproteins (VLDL) : Transport endogenous triglycerides from the liver to body cells .**
 - **low density lipoproteins (LDL) : Transport cholesterol synthesized in the liver to peripheral tissues .**
 - **high density lipoproteins (HDL) : Transport excess cholesterol from peripheral tissues to the liver for degradation and removal .**

Lipoprotein class	Density (g/mL)	Diameter (nm)	Protein % of dry wt	Phospholipid %	Triacylglycerol % of dry wt
HDL	1.063-1.21	5 – 15	33	29	8
LDL	1.019 – 1.063	18 – 28	25	21	4
VLDL	0.95 – 1.006	30 - 80	10	18	50
chylomicrons	< 0.95	100 - 500	1 - 2	7	84

Composition and properties of human lipoproteins

most proteins have densities of about 1.3 – 1.4 g/mL and lipid aggregates usually have densities of about 0.8 g/mL

(Lipid malabsorption)

Resulting from the loss of lipid (including the fat soluble vitamins) in the feces .

- steatorrhoea means increased fat content of feces . It result from :

1 . Disease of pancreas .

2 . Obstruction in the flow bile into intestine .

Cardio vascular Disease(CVD)

Main type of CVD is atherosclerosis (AS) .

(factors associated with CVD)

1. Elevated levels of LDL .

More LDL around to potentially oxidize and accumulate in artery wall .

2 . Low levels of HDL

HDL carries cholesterol from artery walls back to the liver .

**3 . Low levels of antioxidant vitamins :
(vit. A , vit. C and vit. E) .**

**4 . Low levels of other dietary antioxidants
(phenolics , flavanoids , red wine ,
grape juice , vegetables , fruits) .**

5 . High blood pressure .

**(Damages the artery wall allowing LDL
to enter the wall more readily) .**

6 . Cigarette smoking .

7 . Obesity .

8 . Activity level (Exercise) .

Digestion of Dietary TG

1. Bile salts are synthesized in the liver from cholesterol and secreted into the bile, they pass into the intestine, where they emulsify the dietary triglyceride.
2. The pancreas secretes digestive enzyme and bicarbonate which neutralized stomach acid, raising the pH into the optimal range for the digestive enzyme.
3. Pancreatic lipase digests the TG to 2-monoacylglycerol and free fatty acids which is packaged into micelles.

4. The micelles travel to the microvilli of the intestinal epithelial cells which absorb fatty acids , 2-monoacyl glycerol and other dietary lipids .

5. The bile salt reabsorbed , recycled by the liver and secreted into the gut .