# Unit Two

# Chemistry of Lipids

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# Unit 2. Chemistry of Lipids

## Definition of Lipids

Lipids constitute a heterogeneous group of compounds of biochemical importance. Lipids may be defined as compounds which are relatively insoluble in water, but freely soluble in non-polar organic solvents, such as acetone.

# Unit 2. Chemistry of Lipids

## Functions of Lipids

1- Storage form of energy.

2- Structural components of bio-membranes.

3- Metabolic regulators.

4- Act as surfactants, detergents and emulsifying agents.

5- Act as electric insulators in neurons.

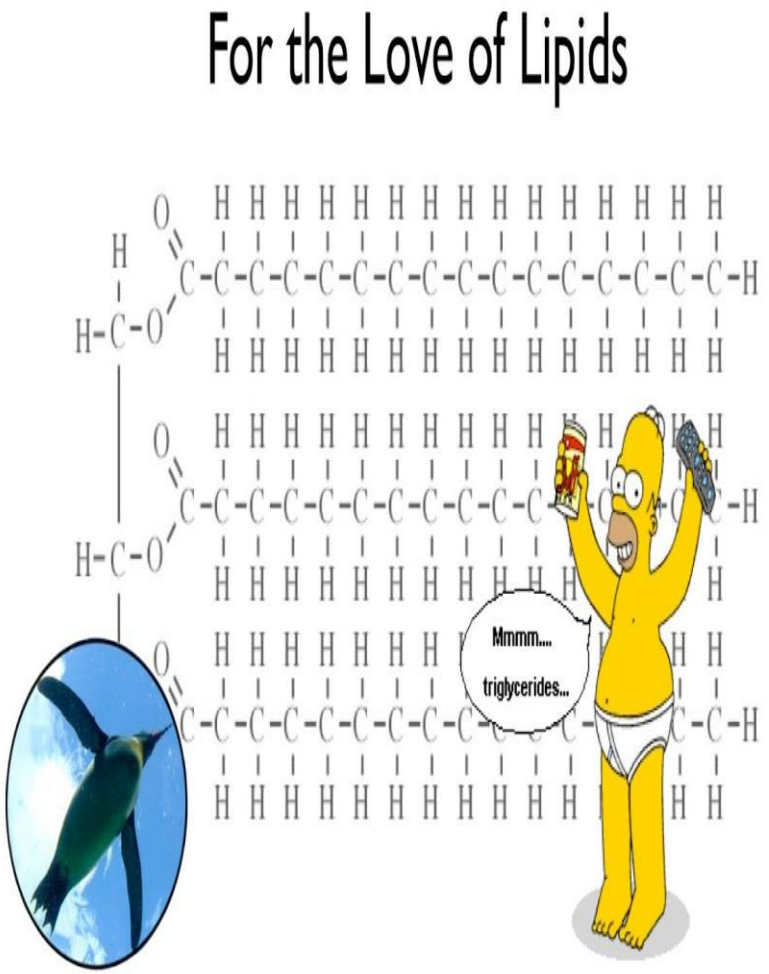
6- Provide insulation against changes in external temperature.

7- Give shape and contour to the body.

8- Protect internal organs by providing a cushioning effect (pads of fat).

9- Help in absorption of fat soluble vitamins (A, D, E and K).

10- Improve taste and palatability of food.



# Unit 2. Chemistry of Lipids

## Properties of Lipids

Lipids are a dissimilar group of biological compounds, but they are poised of a chain of hydrocarbons, ending with groups of bonded oxygen and hydrogen. They are essential to all forms of life and are the key constituent of every cell membrane on Earth and have the below properties:

**1- Solubility:** Lipids are soluble in non-polar solvent such as acetone or ether.
**2- Consistency:** They are colorless, odorless and tasteless. Being lighter than water they have a specific gravity of 0.86.
**3- Hydrolysis:** Acid hydrolysis results in the formation of glycerol and long chain of fatty acid whereas alkaline hydrolysis of fats results in the formation of sodium or potassium salts of fatty acids called as Soaps and the process is called as saponification.
**4- Hydrogenation.**
**5- Emulsification:** When fats are rubbed with water, the large molecules of lipids broke into smaller ones forming the emulsion
**6- Rancidity:** When lipids are exposed to atmosphere (heat, light, air, moisture) for more than 30 days, an unusual and undesirable odor is developed.

# Unit 2. Chemistry of Lipids

## Classification of Lipids

Based on the chemical nature, lipids are classified as:

**1- Simple lipids:** They are esters of fatty acids with glycerol or other higher alcohols such as: Triglycerol (TG or triglycerides or triacylglycerols "TAG" or neutral fat) and Waxes.

**2- Compound lipids:** They are fatty acids esterified with alcohol; but in addition they contain other groups. Depending on these extra groups, they are sub-classified to:

a. Phospholipids containing phosphoric acid.

b. Non-phosphorylated lipids.

**3- Derived lipids:** They are compounds, which are derived from lipids or precursors of lipids, e.g. fatty acids, steroids.

**4- Miscellaneous Lipids:** they are lipids complexed to other compounds such as Proteolipids and lipoproteins.

# Unit 2. Chemistry of Lipids

## Fatty Acids (FA's)

It is the most common component of lipids in the body. They are generally found in ester linkage in different classes of lipids. In the human body, free fatty acids (FFA's) are formed only during metabolism. Fatty acids are aliphatic carboxylic acids and have the general formula, R—COOH, where COOH (carboxylic group) represents the functional group. Depending on the R group (the hydrocarbon chain), the physical properties of fatty acids may vary. FA divided to:

**1- Saturated Fatty Acids:** such as Palmitic acid CH3—(CH2)14—COOH.

**2- Unsaturated Fatty Acids:** this type divided to:

A- Monounsaturated Fatty Acids: such as Oleic acid & Elaidic acid.

B- Polyunsaturated Fatty Acids (PUFA): They are called essential fatty acids, because they cannot be synthesized by the body and have to be supplied in the diet such as Omega-3. Many clinical and epidemiologic studies have shown positive roles for omega-3 FA's in infant development; cancer; cardiovascular diseases; and more recently, in various mental illnesses, including depression, attention-deficit hyperactivity disorder, and dementia. These FA's are known to have pleiotropic effects, including effects against inflammation, platelet aggregation, hypertension, and hyperlipidemia.

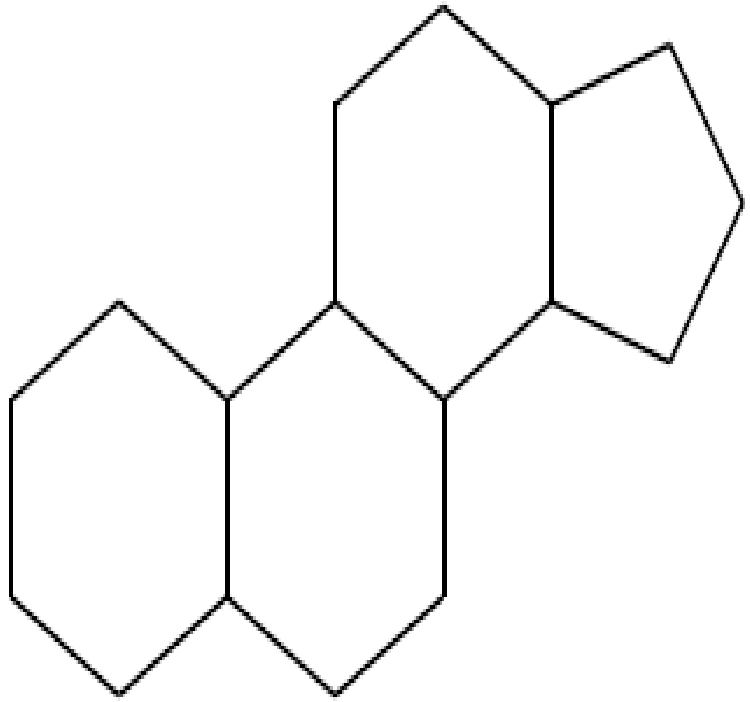
**3- Trans Fatty Acids (TFA's):** They are present in dairy products, fast food and in hydrogenated edible oils. They are generally considered to be injurious to health. However, they are used in food industry as they increase the shelf life of the fried food. TFA's adversely affects multiple risk factors for chronic diseases, including composition of blood lipids and lipoproteins, systemic inflammation, endothelial dysfunction, insulin resistance, diabetes and adiposity. It is high in processed foods and bakery products, where partially hydrogenated vegetable oils are used for cooking.

# Unit 2. Chemistry of Lipids

## Steroids

**Steroid** are biologically active organic compounds with four rings arranged in a specific molecular configuration. Steroids have two principal biological functions: as important components of cell membranes which alter membrane fluidity; and as signaling molecules. Hundreds of steroids are found in plants, animals and fungi. All steroids are manufactured in cells from the lanosterol (animals) or cycloartenol (plants). Steroids vary by the functional groups attached to this four-ring core and by the oxidation state of the rings. Steroids can also be more radically modified to form new compounds such as by changing the ring structure to get vitamin D3. Examples include cholesterol, the sex hormones estradiol, testosterone and the anti-inflammatory drug dexamethasone.

**Sterols** are forms of steroids with a hydroxy group and a skeleton derived from cholestane.



steroid ring system

# Unit 2. Chemistry of Lipids

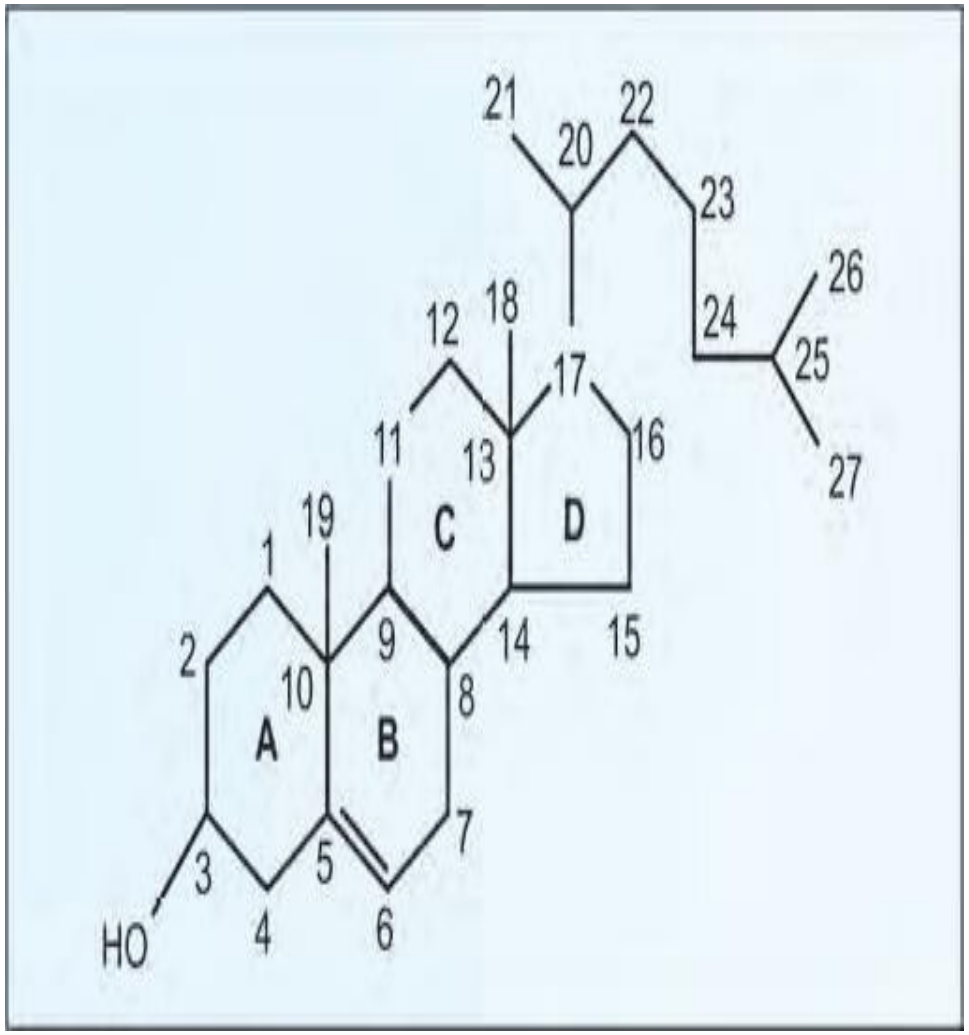
## Cholesterol

The word cholesterol is derived from Greek words, chole = bile; steros = solid; ol = alcohol. The major sites of synthesis of cholesterol are liver, adrenal cortex, testis, ovaries and intestine. All nucleated cells can synthesize cholesterol, including arterial walls. It is widely distributed in the body. In a 70 kg man, a total of about 140 g of cholesterol is available; which is distributed as about 30 g in brain and nerves, 30 g in muscles, 30 g in adipose tissue, 20 g in skin, 10 g in blood, 10 g in liver and spleen, 5 g in bone marrow, 3 g in alimentary tract, and 2 g in adrenal gland. Cholesterol is a light yellow crystalline solid. When the crystals are examined under the microscope, they show a notched appearance. Cholesterol is soluble in chloroform and other fat solvents. It is the most important animal steroid from which other steroid compounds are formed. Cholesterol is widely distributed in animal tissues. The level of cholesterol in blood is related to the development of atherosclerosis and myocardial infarction. Abnormality of cholesterol metabolism may lead to cardiovascular accidents and heart attacks.

# Unit 2. Chemistry of Lipids

## Functions of Cholesterol

1- Cell membranes: Cholesterol is a component of membranes and has a modulating effect on the fluid state of the membrane.
2- Nerve conduction: Cholesterol is used to insulate nerve fibers.
3- Bile acids and bile salts are derived from cholesterol. Bile salts are important for fat absorption.
4- Steroid hormones: Glucocorticoids, androgens and estrogens are from cholesterol.
5- Vitamin D3 is from 7-dehydro-cholesterol.
6- Esterified to fatty acids to form cholesterol esters for storage.
7- Esterified with poly-unsaturated fatty acids (PUFA) and finally excreted through liver.



# Unit 2. Chemistry of Lipids

## Excretion of Cholesterol

Average diet contains about 300 mg of cholesterol per day. Body synthesize about 700 mg of cholesterol per day. Out of this total 1000 mg, about 500 mg of cholesterol is excreted through bile. This cholesterol is partly reabsorbed from intestines. Vegetables contain plant sterols which inhibit the re-absorption of cholesterol. The unabsorbed portion is acted upon by intestinal bacteria to form cholestanol and coprostanol. These are excreted (fecal sterols). Another 500 mg of cholesterol is converted to bile acids, which are excreted in the bile as bile salts.

## Liver and Cholesterol

The liver has a major role in controlling the plasma levels of LDL cholesterol:
1. Liver synthesizes cholesterol
2. Liver removes cholesterol from lipoproteins (LP) remnants.
3. Liver is the only organ that can excrete cholesterol through bile.
4. Liver converts cholesterol to bile acids.

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## Plasma Lipids

Total plasma lipid is 400—600 mg/dL. Out of this, 40% is cholesterol; 30% is phospholipids; 20% is triglycerides. Since lipids are insoluble in water, they need the help of carriers in plasma. Therefore, they are complexed with lipoproteins. Lipoproteins in plasma are classified into five major types:

1. Chylomicrons: they are the transport form of dietary TG from intestines to the adipose tissue for storage; and to muscle or heart for their energy needs.
2. Very low density lipoproteins (VLDL): It synthesized in the liver from glycerol and fatty acids. VLDL carries triglycerols (endogenous triglycerols) from liver to peripheral tissues for energy needs.
3. Intermediate density lipoproteins (IDL).
4. Low density lipoproteins (LDL).
5. High density lipoproteins (HDL).

# Unit 2. Chemistry of Lipids

## Low density lipoproteins (LDL)

About 75% of the plasma cholesterol is incorporated into the LDL particles. LDL transports cholesterol from liver to the peripheral tissues. In addition, LDL concentration in blood has positive correlation with incidence of cardiovascular diseases. LDL infiltrates through arterial walls, and are taken up by macrophages or scavenger cells. This is the starting event of atherosclerosis leading to myocardial infarction. When these cells become engorged with cholesterol, foam cells are formed, that get deposited in the sub-endothelial space triggering formation of atheromatous plaque. Procoagulant changes are induced in the endothelium resulting in increased chances of thrombosis and coronary artery disease. So, LDL creates a pro-coagulant surface on the endothelium, causing blood clot formation. LDL is found in higher levels in cigarette smokers, patients with diabetes mellitus and in insulin resistance. Since LDL-cholesterol is thus deposited in tissues, the LDL (low density lipoprotein) variety is called “bad cholesterol” in common parlance.

# Unit 2. Chemistry of Lipids

## High density lipoproteins (HDL)

It transport cholesterol from peripheral tissues to the liver. The intestinal cells synthesize components of HDL and release into blood. So, the functions of HDL are:

1- HDL is the main transport form of cholesterol from peripheral tissue to liver, which is later excreted through bile. This is called reverse cholesterol transport by HDL.

2- The only excretory route of cholesterol from the body is the bile.

3- Excretion of cholesterol needs prior esterification with PUFA. Thus PUFA will help in lowering of cholesterol in the body, and so PUFA is anti-atherogenic.

In addition, The level of HDL in serum is inversely related to the incidence of myocardial infarction. As it is “anti-atherogenic” or “protective” in nature, HDL is known as “good cholesterol” in common parlance. It is convenient to remember that "H" in HDL stands for "Healthy". HDL level below 35 mg/dL increases the risk, while level above 60 mg/dL protects the person from coronary artery diseases.

# Unit 2. Chemistry of Lipids

## Bile

It is the chief secretion of liver, the largest gland in the body. Daily volume of secretion is about 500 mL. The secreted bile is stored in the gallbladder and released on demand. The pH of bile in hepatic duct is 7.8, and in gall bladder is 7.4. An enzyme present in bile is alkaline phosphatase. Bile is a yellowish brown or green fluid produced in the liver and stored in the gall bladder. Bile salts act like soaps and other emulsifiers: they contain both polar and nonpolar regions, helping to break fats in foods into smaller pieces, allowing them to be hydrolyzed more easily. So, Functions of Bile are:

1. The alkaline pH of the bile serves to neutralize the acidity of the gastric juice.
2. The bile salts are efficient surfactants and detergents.
3. Bile is the only route of excretion for bilirubin, the end product of heme catabolism.
4. It serves to excrete cholesterol, thus regulating the body cholesterol pool.
5. Bile serves as the medium of excretion for several drugs, which are detoxified by the liver.

# Unit 2. Chemistry of Lipids

## Bile Acids

Bile acids are synthesized in the liver from cholesterol. They facilitate the digestion of lipids. They can form molecular aggregates called micelle which bring about the absorption of lipids. Bile salt micelle also plays an important role in keeping the cholesterol in solution. Bile acid-controlled signaling pathways are promising novel drug targets to treat common metabolic diseases, such as obesity, type 2 diabetes, hyperlipidemia, and atherosclerosis. The relative concentration of cholesterol in the bile favors the precipitation and resultant stone formation; it is referred to lithogenic bile. Bile salts and phospholipids in the bile play a significant role in keeping the cholesterol in solution by forming mixed micelle. Infections of the gallbladder may predispose to stone formation. Dehydration may also lead to precipitation of cholesterol crystals.

Dietary fat leaves the stomach and enters the small intestine, where it is emulsified (suspended in small particles in the aqueous environment) by bile salts. The bile salts are amphipathic compounds (containing both hydrophobic and hydrophilic components). The contraction of the gallbladder and secretion of pancreatic enzymes are stimulated by the gut hormone cholecystokinin, which is secreted by the intestinal cells when stomach contents enter the intestine. Bile salts act as detergents, binding to the globules of dietary fat as they are broken up by the peristaltic action of the intestinal muscle. This emulsified fat, which has an increased surface area compared with emulsified fat, is attacked by digestive enzymes from the pancreas.

# Unit 2. Chemistry of Lipids

## Metabolism of Lipids

Most of the lipids found in the body fall into the categories of fatty acids and TAG; glycerophospholipids and sphingolipids; eicosanoids; cholesterol, bile salts, steroid hormones; and fat-soluble vitamins. These lipids have very diverse chemical structures and functions. However, they are related by a common property: their relative insolubility in water. Fatty acids are a major fuel in the body. After eating, we store excess fatty acids and carbohydrates that are not oxidized as fat (TAG) in adipose tissue. Between meals, these fatty acids are released and circulate in blood bound to albumin. In muscle, liver, and other tissues, fatty acids are oxidized to acetyl coenzyme A (acetyl-CoA) in the pathway of β-oxidation to generate energy. Small amounts of certain fatty acids are oxidized through other pathways that convert them to either oxidizable fuels or urinary excretion products (e.g., peroxisomal β-oxidation). Not all acetyl-CoA generated from β-oxidation enters the tricarboxylic acid (TCA) cycle. In the liver, acetyl-CoA generated from β-oxidation of FA's can also be converted to the ketone bodies. Ketone bodies are taken up by muscle and other tissues, which convert them back to acetyl-CoA for oxidation in the TCA cycle. They become a major fuel for the brain during prolonged fasting.

# Unit 2. Chemistry of Lipids

1- Cholesterol adds stability to the phospholipid bilayer of membranes. It serves as the precursor of the bile salts, detergent like compounds that function in the process of lipid digestion and absorption. Cholesterol also serves as the precursor of the steroid hormones, which have many actions, including the regulation of metabolism, growth, and reproduction.
2- The initial digestive products (free FA's and 2-monoacylglycerol) are reconverted to TAG in intestinal epithelial cells, packaged in lipoproteins known as chylomicrons (so they can safely enter the circulation), and secreted into the lymph. Ultimately, chylomicrons enter the blood, serving as one of the major blood lipoproteins.
3- VLDL is produced in the liver, mainly from dietary carbohydrate. Lipogenesis is an insulin-stimulated process through which glucose is converted to FA's, which are subsequently esterified to glycerol to form the TAG that are packaged in VLDL and secreted from the liver. Thus, chylomicrons primarily transport dietary lipids, and VLDL transports endogenously synthesized lipids. The FA's that are released are taken up by muscle and many other tissues and are oxidized to $CO_2$ and water to produce energy. After a meal, these FA's are taken up by adipose tissue and stored as TAG. 4-
4- The principal function of HDL is to transport excess cholesterol obtained from peripheral tissues to the liver. During fasting, FA's and glycerol are released from adipose TAG stores. The glycerol travels to the liver and is used for gluconeogenesis. Only the liver contains glycerol kinase, which is required for glycerol metabolism. The FA's form complexes with albumin in the blood and are taken up by muscle, kidney, and other tissues, where ATP is generated by their oxidation to $CO_2$ and water. Liver also converts some of the carbon to ketone bodies, which are released into the blood. Ketone bodies are oxidized for energy in muscle, kidney, and other tissues during fasting, and in the brain during prolonged starvation.

# Unit 2. Chemistry of Lipids

## Fat Oxidation

FA's are a major fuel for humans and supply our energy needs between meals and during periods of increased demand, such as exercise. During overnight fasting, FA's become the major fuel for cardiac muscle, skeletal muscle, and liver. The liver converts fatty acids to ketone bodies which also serve as major fuels for tissues (e.g., the gut). The brain, which does not have a significant capacity for FA oxidation, can use ketone bodies as a fuel during prolonged fasting. The route of metabolism for a FA depends somewhat on its chain length. ATP is generated from oxidation of FA's. Between meals and during overnight fasting, FA's are released from adipose tissue TAG. They circulate through blood bound to albumin. In cells, they are converted to fatty acyl coenzyme A (fatty acyl-CoA). The activated acyl group is transported into the mitochondrial matrix bound to carnitine, where fatty acyl-CoA is regenerated. In the pathway of β-oxidation, the fatty acyl group is sequentially oxidized to yield (FAD[2H]), (NADH), and acetyl coenzyme A (acetyl-CoA). Subsequent oxidation of NADH and FAD(2H) in the electron transport chain, and oxidation of acetyl-CoA to CO2 in the tricarboxylic acid (TCA) cycle, generates adenosine triphosphate (ATP) from oxidative phosphorylation.

# Unit 2. Chemistry of Lipids

## Fat Oxidation

The rate of FA oxidation is linked to the rate of NADH, FAD(2H), and acetyl-CoA oxidation and thus to the rate of oxidative phosphorylation and ATP use. FA's and ketone bodies are used as fuel when their level increases in the blood, which is determined by hormonal regulation of adipose tissue lipolysis. Between meals, a decreased insulin level and increased levels of insulin counter-regulatory hormones (e.g., glucagon) activate lipolysis, and free FA's are transported to tissues bound to serum albumin. Within tissues, energy is derived from oxidation of FA's to acetyl-CoA in the pathway of β- oxidation. The acetyl-CoA produced from FA oxidation is principally oxidized in the TCA cycle or converted to ketone bodies in the liver.

# Unit 2. Chemistry of Lipids

## Metabolic Disorders of Lipids Metabolism

The study of hyperlipidaemia is of considerable importance, mainly because of the involvement of lipids in cardiovascular disease. It gives little clue as to the aetiology of the disorder; indeed, all of the phenotypes can be either primary or secondary. Nowadays, a more descriptive classification is used for the primary hyperlipidaemia, as follows:

**1- Chylomicron syndrome:** This can be due to familial lipoprotein lipase deficiency, an autosomal recessive disorder affecting about 1 in 1,000,000 people. Lipoprotein lipase is involved in the exogenous lipoprotein pathway by hydrolysing chylomicrons to form chylomicron remnants, and also in the endogenous pathway by converting VLDL to IDL particles. There is probably no increased risk of coronary artery disease. Gross elevation of plasma triglycerides due to the accumulation of uncleared chylomicron particles occurs. Treatment of the chylomicron syndrome involves a low-fat diet, aiming for less than 20 g of fat a day, if possible, although compliance on such a diet may be difficult. Some clinicians supplement the diet with medium-chain triglycerides and also give 1 per cent of the total calorie intake as linoleic acid.

**2- Familial hypercholesterolaemia:** This condition is usually inherited as an autosomal dominant trait resulting in impaired LDL catabolism and hypercholesterolaemia. Familial hypercholesterolaemia (FH) is defined as a plasma cholesterol concentration of more than 7.5 mmol/L in an adult (more than 6.7 mmol/L in children under 16 years) or a plasma LDL cholesterol concentration of more than 4.9 mmol/L in an adult in the presence of tendon xanthoma.

**3- Familial defective apoB3500.**

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**4- Familial combined hyperlipidaemia:** In familial combined hyperlipidaemia (FCH), the plasma lipids may elevated, plasma cholesterol concentrations often being between 6 mmol/L and 9 mmol/L and plasma triglyceride between 2 mmol/L and 6 mmol/L. The diagnosis of FCH is suspected if there is a family history of hyperlipidaemia, particularly if family members show different lipoprotein phenotypes. There is often a family history of cardiovascular disease.

**5- Familial hypertriglyceridaemia:** Familial hypertriglyceridaemia is often observed with low HDL cholesterol concentration. The condition usually develops after puberty and is rare in childhood. overproduction of VLDL or a decrease in VLDL conversion to LDL is likely. There may be an increased risk of cardiovascular disease. Acute pancreatitis may also occur, and is more likely when the concentration of plasma triglycerides is more than 10 mmol/L. Some patients show hyperinsulinaemia and insulin resistance. Dietary measures, and sometimes lipid-lowering drugs such as the fibrates or omega-3 are used to treat the condition.

**6- Type III hyperlipoproteinaemia.**

**7- Polygenic hypercholesterolaemia:** This is one of the most common causes of a raised plasma cholesterol concentration. This condition is the result of a complex interaction between multiple environmental and genetic factors. In other words, it is not due to a single gene abnormality, and it is likely that it is the result of more than one metabolic defect. There is usually either an increase in LDL production or a decrease in LDL catabolism. The level of cholesterol in blood is related to the development of atherosclerosis. Abnormality of cholesterol metabolism may lead to cardiovascular accidents and heart attacks.

# Unit 2. Chemistry of Lipids

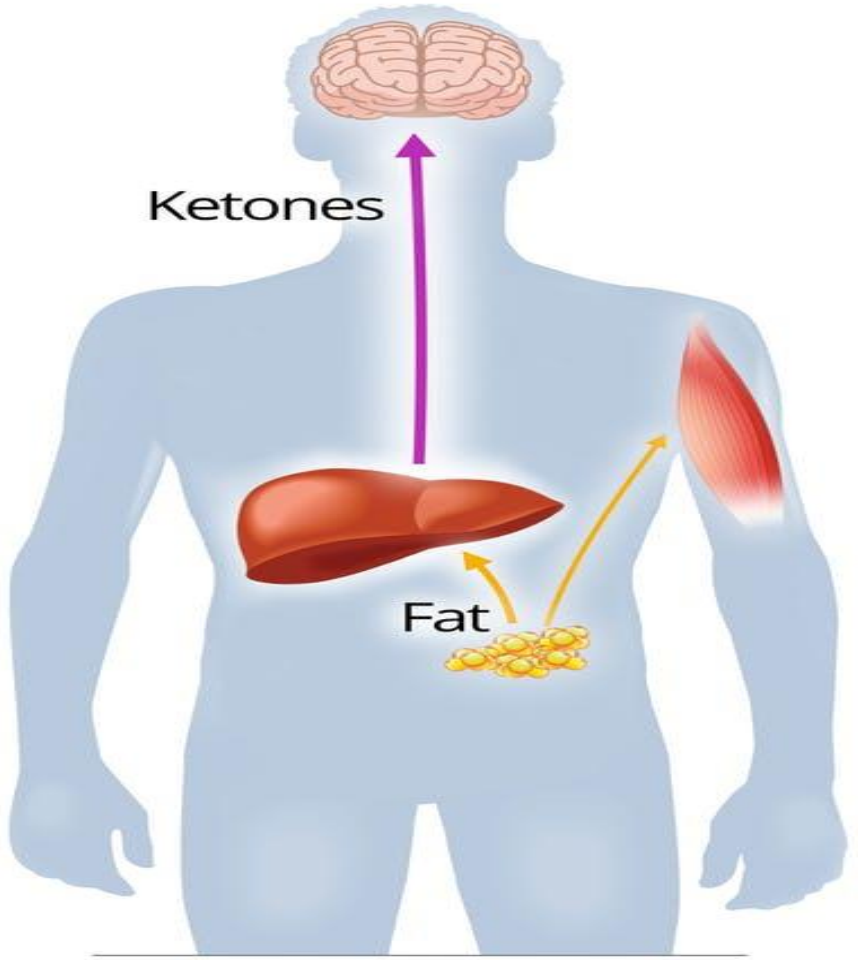
**8- Hyperalphalipoproteinaemia:** Hyperalphalipoproteinaemia results in elevated plasma HDL cholesterol concentration and can be inherited as an autosomal dominant condition or, in some cases, may show polygenic features. The total plasma cholesterol concentration can be elevated, with normal LDL cholesterol concentration. There is no increased prevalence of cardiovascular disease in this condition; in fact, the contrary probably applies, with some individuals showing longevity. Plasma HDL concentration is thought to be cardioprotective, and individuals displaying this should be reassured.

**9- Secondary hyperlipidaemias:** it occurs due to many causes such as Hypothyroidism, Diabetes mellitus and metabolic syndrome, etc.

# Unit 2. Chemistry of Lipids

## Ketosis

Normally the rate of synthesis of ketone bodies by the liver is such that they can be easily metabolized by the extrahepatic tissues. Hence, the blood level of ketone bodies is less than 1 mg/dL and only traces are excreted in urine (not detectable by usual tests). But when the rate of synthesis exceeds the ability of extrahepatic tissues to utilize them, there will be accumulation of ketone bodies in blood. This leads to ketonemia, excretion in urine (ketonuria) and smell of acetone in breath. This will constitute a condition called Ketosis. So, Ketosis is a metabolic state characterized by elevated levels of ketone bodies in the blood or urine. Physiologic ketosis is a normal response to low glucose availability, such as low-carbohydrate diets or fasting, that provides an additional energy source for the brain in the form of ketones.



# Unit 2. Chemistry of Lipids

## Causes of Ketosis

**1- Diabetes mellitus:** Untreated diabetes mellitus is the most common cause for ketosis. Even though glucose is in plenty, the deficiency of insulin causes accelerated lipolysis and more fatty acids are released into circulation and ketones foeming.

**2. Starvation:** In starvation, the dietary supply of glucose is decreased. The increased rate of lipolysis is to provide alternate source of fuel by converting to ketone bodies. The high glucagon favors ketogenesis. The brain derives 75% of energy from ketone bodies under conditions of fasting. Hyperemesis (vomiting) in early pregnancy may also lead to starvation-like condition and may lead to ketosis.

So, During starvation and diabetes mellitus, the blood level of glucagon is increased. Glucagon inhibits glycolysis, activates gluconeogenesis, activates lipolysis and stimulates ketogenesis. High glucagon-insulin ratio is potentially ketogenic. Insulin has the opposite effect; it favors glycolysis, inhibits gluconeogenesis, depresses lipolysis, increases and decreases ketogenesis.

# Unit 2. Chemistry of Lipids

## Salient Features of Ketosis

1. Metabolic acidosis.
2. Reduced buffers: The plasma bicarbonate is used up for buffering of these acids.
3. Kussmaul's respiration: Patients will have typical acidotic breathing due to compensatory hyperventilation.
4. Smell of acetone in patient's breath.
5. Osmotic diuresis induced by ketonuria may lead to dehydration.
6. Sodium loss: The ketone bodies are excreted in urine as their sodium salt, leading to loss of Sodium from the body.
7. Dehydration: The sodium loss further aggravates the dehydration.
8. Coma. Hypokalemia, dehydration and acidosis are contributing for the lethal effect of ketosis.

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## Management of Ketoacidosis

1- Treatment is to give insulin and glucose. When glucose and insulin are given intravenously, potassium is trapped within the cells. Hence, the clinician should always monitor the electrolytes.

2- Administration of bicarbonate, and maintenance of electrolyte and fluid balance are very important aspects.

# Unit 2. Chemistry of Lipids

## Lipid-lowering Therapy

The help of a dietitian is invariably useful in treating dyslipidaemia. Low-saturated fat/reduced cholesterol diets are instigated. Total fat intake should be less than 30 per cent of the total calorie intake, with an increase in monounsaturated fat intake up to 20 per cent of total calories. Dietary cholesterol intake should not exceed about 200 mg/day. Ideally, patients should aim to achieve their recommended body mass index. If diet and lifestyle measures fail, drug therapy may be indicated The rate-limiting enzyme of cholesterol synthesis is inhibited by the statins, which can be used to treat hypercholesterolaemia. The HDL cholesterol concentration is modestly increased and TG concentration reduced by varying degrees by these agents. The side effects notably include myalgia, myositis (and rarely rhabdomyolysis) and abnormal liver function.

Bile salt sequestrates bind bile salts in the intestinal lumen and thus interrupt their reabsorption and reutilization. The removal of bile acids stimulates hepatic cholesterol synthesis, which in turn results in an increase in hepatic LDL receptors, resulting in decreased plasma LDL concentration. The side effects include gastrointestinal symptoms, such as constipation. To avoid interference with their absorption, these drugs should not be given at the same time as other drugs. They lower plasma cholesterol concentration by about 10–20 per cent; although HDL cholesterol concentration is also modestly raised, triglyceride concentrations can be paradoxically increased.

Nicotinic acid and its derivatives have been used to reduce VLDL secretion and LDL concentration. This drug is good at raising HDL cholesterol. However, the side effects include hepatic toxicity, hyperuricaemia, impaired glucose tolerance. They also have an antiplatelet aggregatory action. They can sometimes be used to treat severe hypertriglyceridaemia.

# Unit 2. Chemistry of Lipids

## Levels of Some Lipids

| Risk Level / Lipid | Low risk (desirable level) | Borderline risk | High risk |
|---|---|---|---|
| **Total cholesterol (mg/dL)** | <200 | 200-240 | >240 |
| **LDL cholesterol (mg/dL)** | <130 | 130-160 | >160 |
| **HDL cholesterol (mg/dL)** | >60 | 35-60 | <35 |
| **Triglyceride (TG) (mg/dL)** | <200 | 200-400 | >400 |

Coronary heart disease (CHD) risk and lipid parameters