Lipid Metabolism

Lipids

The body lipids include:

- Triglycerides (provide energy for the different metabolic processes).
- Phospholipids & Cholesterol (used to form the membranes of the body cells and to perform other cellular functions).

Chemical Structure of Triglycerides:

Three long-chain fatty acid are bound with one molecule of glycerol.

Lipid Transportation

- During digestion the fats are absorbed from the intestines into the intestinal lymph as droplets called **chylomicrons**.
- A small amount of apoprotein B is adsorbed to the outer surfaces of the chylomicrons to prevent the chylomicrons of adherence to the lymphatic walls.
- After that, the chylomicrons are transported into the circulating venous blood.
- After one hour of a fatty meal the chylomicrons concentration in the plasma rise to 1% to 2% of the plasma.
- The plasma becomes clear again after few hours.

- The chylomicrons is removed from the plasma by the following way:
- The chylomicrons are removed of the plasma by passing the three tissues (adipose tissue, muscle & heart).
- Then, these tissues synthesize enzyme called **Lipoprotein Lipase**.
- This enzyme hydrolyzes chylomicrons triglycerides and releases fatty acids & glycerol.
- The fatty acids is stored in the adipose tissue to use as energy or again synthesized into triglycerides.
- When the body needs the fat to provide energy, the stored fat is transported from the adipose tissue to the other tissue in the blood in the form of free fatty acids combines with albumin.

The Use of Fatty Acids

- The body oxidizes the transported free fatty acids for normal energy requirements, so the half of fatty acid plasma is replaced by new fatty acid every 2 to 3 minutes.
- In some condition (starvation and in diabetes mellitus) the cell utilization of fat for energy increase, for that, the concentration of free fatty acids in the blood increase.

Formation and Function of Lipoproteins

- After the removed of the chylomicrons from the blood 95% of the lipids in the plasma are in the form of Lipoproteins which are smaller than the chylomicrons but similar in it's composition (triglycerides, cholesterol, phospholipids, and protein).
- Almost all the lipoproteins are formed in the liver.
- The function of the lipoproteins is to transport their lipid components in the blood (from the liver to the tissues or the opposite).

The Types of Lipoproteins:

Types of Lipoproteins	Abbreviation	composition
1/ very low density lipoproteins	VLDLs	- high concentrations of triglycerides - moderate concentrations of both cholesterol and phospholipids
2/ intermediate-density lipoproteins	IDLs	Part of the triglycerides are removed, so the concentrations of cholesterol and phospholipids are increased.
3/ low-density lipoproteins	LDLs	All the triglycerides are removed , leaving high concentration of cholesterol and phospholipids
4/ high-density lipoproteins	HDLs	high concentration of protein much smaller concentrations of cholesterol and phospholipids.

The Functions of The Liver in Lipid Metabolism

- Degrade fatty acids into small compounds that can be used for energy.
- Synthesize triglycerides from carbohydrates & lesser from proteins.
- Synthesize other lipids from fatty acids, such as cholesterol and phospholipids.

The Use of Triglycerides for Energy

- The triglycerides is hydrolyzed into fatty acids and glycerol. Then, both fatty acids and glycerol are transported in the blood to the active tissues.
- When **the glycerol** enter the active tissues, is changed into glycerol-3- phosphate then enter the glycolytic pathway to use for energy.
- **The fatty acids** enter into mitochondria and degraded in 5 steps to form (acetyl-CoA) in process called the beta-oxidation.
- After that, the acetyl-CoA enter into the citric acid cycle. Large amounts of adenosine triphosphate (ATP) are formed by oxidation of fatty acids.
- The final breakdown of degradation of fatty acids to acetyl-CoA, is the same as the acetyl-CoA formed from pyruvic acid during the metabolism of glucose.

The Formation of Acetoacetic Acid in the Liver

- A large part of the degradation of fatty acids occurs in the liver.
- After the fatty acid chains split into acetyl-CoA, every two molecules of acetyl-CoA form one molecule of acetoacetic acid, which is transported in the blood to the other cells to be used for energy.
- Part of the acetoacetic acid converted into B-hydroxybutyric acid, and acetone.
- The **acetoacetic acid**, **β-hydroxybutyric acid**, and **acetone** are transported by the blood to the tissues. Then, reverse reactions occur and acetyl-CoA are formed. Acetyl-CoA enter the citric acid cycle, and are oxidized for energy.

Ketosis

- The concentrations of acetoacetic acid, β-hydroxybutyric acid, and acetone rise in the blood. This condition is called (**Ketosis**) because acetoacetic acid is a keto acid.
- This condition occurs in starvation, in diabetes mellitus, and with the high fat diet without carbohydrates.
- When the carbs not available for energy, the body uses the fat to provide energy. So, the rate of removal of fatty acids from fat tissues increase. As a result, quantities of fatty acids become available.
- When changing slowly from a carbs' diet to a complete fat diet, the body adapts to use more acetoacetic acid than usual. So, ketosis normally does not occur.
- The rate of acetoacetic acid metabolism by the cells enhance after a few weeks. Also, the brain cells, which usually derive all their energy from glucose, can derive 50 to 75 % of their energy from fats.

Synthesis of Triglycerides from Carbs

- While consuming large quantity of carbs, the body use it immediately for energy or store them in the form of glycogen, and the excess is converted into triglycerides and stored in the adipose tissue.
- The triglycerides are synthesized in the liver, and few quantities are also synthesized in the adipose tissue.

1. **First**, the carbs is converted into acetyl-CoA during the normal degradation of glucose.
2. **Second,** acetyl-CoA is converted into fatty acids in two steps.
3. **Third**, the fatty acid chains bind with glycerol to form triglycerides. the glycerol portion comes from **α-glycerophosphate**, which is another product derived from the glucose degradation.

The Importance of fat synthesis from carbohydrates:

1. The ability of the cells to store carbohydrates in the form of glycogen is slight. The body can store 150 times as much energy in the form of fat as stored in the form of carbs.

2. Each gram of fat contains nearly two and a half times the calories of energy in gram of glycogen.

The Failure to Synthesize Fats from Carbs:

- This condition happened when insufficient insulin is available. So, fats are poorly synthesized for 2 reasons:

1. The glucose does not enter the fat and liver cells, so none acetyl-CoA and NADPH are available for fat synthesis.

2. Lack of glucose in the fat cells reduces the availability of

α-glycerophosphate, which makes it hard for the tissues to form triglycerides.

The Hormonal Regulation of Fat Utilization

- During the absence of carbs decrease the pancreatic secretion of insulin decrease. This reduces the rate of glucose utilization and increase fat utilization.
- The release of epinephrine and norepinephrine activate hormone-sensitive triglyceride lipase, and this causes rapid breakdown of triglycerides and mobilization of fatty acids. For Ex. (heavy exercise, stress).
- Moreover, thyroid hormone causes rapid mobilization of fat by increasing the overall rate of energy metabolism in all cells.

Phospholipids

- In the body, there are many types of phospholipids.
- Phospholipids contain one or more fatty acid, one phosphoric acid, a nitrogenous base.
- Phospholipids are used in the body for various structural purposes, such as: cell membranes and intracellular membranes.
- Phospholipids are synthesized in all the body cells and 90% are formed in the liver cells.
- Phospholipids have many functions in the body such as: formation of structural in the cells' membranes, important constituent of lipoproteins in the blood.

Cholesterol

- Cholesterol is present in the diets of all people.
- Cholesterol is absorbed slowly from the GI tract into the intestinal lymph.
- Some Cholesterol absorbed each day from the gastrointestinal tract, called **exogenous cholesterol.**
- Greater quantity of Cholesterol is formed in the cells such as the liver, called **endogenous cholesterol.**

The Factors Affect Plasma Cholesterol Concentration

1. An increase in the amount of cholesterol ingested each day increases the plasma concentration slightly.
2. A highly saturated fat diet increases blood cholesterol concentration.
3. Ingestion of fat containing highly unsaturated fatty acids usually lower the blood cholesterol concentration.
4. Lack of insulin or thyroid hormone increases the blood cholesterol concentration.
5. Genetic disorders of cholesterol metabolism may greatly increase plasma cholesterol levels.

The Uses of Cholesterol in the Body

1. Cholesterol is converted into cholic acid which helps to form bile salts, which promote digestion and absorption of fats.
2. cholesterol is used to form some hormones such as, estrogen.
3. Cholesterol works Phospholipids in the formation of structural elements of the cells.
4. Makes the skin highly resistant to the absorption of water-soluble substances & help prevent water evaporation from the skin.

Atherosclerosis

➢ **Definition:** It is a disease in which fatty lesions called atheromatous plaques develop on the inside surfaces of the arterial walls.

➢ **The Causes of Atherosclerosis:**

Increase the plasma concentration of high-cholesterol LDLs.

➢ **The factors of high-cholesterol LDLs increasing:**

- The diet high in saturated fat.
- The diet high in cholesterol.
- Obesity.
- Decreasing in the physical inactivity.
- The defective genes for the formation of LDL Receptors.

Role of High-Density Lipoproteins in Preventing Atherosclerosis:

- It is believed that HDLs can absorb cholesterol that are beginning to be deposited in arterial walls.
- The mechanism of the prevention still not clear, but HDLs do help protect against the development of atherosclerosis.

Major Risk Factors for Atherosclerosis:

1. Physical inactivity and obesity
2. Diabetes mellitus
3. Hypertension
4. Hyperlipidemia
5. Cigarette smoking.

Prevention of Atherosclerosis

1. Maintain a healthy weight
2. Eat diet contains unsaturated fat & low in cholesterol
3. Prevent hypertension and be physically active.
4. Control blood pressure
5. Control blood glucose
6. Avoiding smoking.
7. Several types of drugs could lower plasma lipids and cholesterol.

References

- Hall, J. E. (2011). *Guyton and hall textbook of medical physiology* (12th ed.). W B Saunders.


Thank
you