Dietary lipids & Lipid digestion
Introduction

• Lipids are a heterogeneous group of water-insoluble (hydrophobic) organic molecules that can be extracted from tissues by nonpolar solvents.

• Because of their insolubility in aqueous solutions, body lipids are generally found compartmentalized, as in the case of membrane-associated lipids or droplets of triacylglycerol in white adipocytes, or transported in plasma in association with protein, as in lipoprotein particles.
Function of lipids

- Lipids are a major storage source of energy for the body, and they also provide the hydrophobic barrier that permits partitioning of the aqueous contents of cells and subcellular structures.
- Lipids serve additional functions in the body, for example, some fat-soluble vitamins have regulatory or coenzyme functions, and the prosta glandins and steroid hormones play major roles in the control of the body’s homeostasis.
Dietary **lipids**

- Dietary **lipids** are triglycerides, phospholipids, steroids, especially cholesterol and cholesterol esters, fat-soluble vitamins, namely, vitamin A, D, E and K, and carotenoids. **Lipids** may be solid or liquid at room temperature and are referred to as **fats** and **oils**, respectively.
• **Triglycerides** or **triacylglycerols** account for about 90% of dietary **lipids**. They consist of one glycerol molecule esterified to three **fatty acids**, mostly long chain **fatty acids** (16-20 carbon atoms). They have an energy density more than twice that of **carbohydrates** (9 kcal/g) and amino acids. They must release their **fatty acids** to be used as a source of energy.
• **Phospholipids**, the main constituents of biological membranes, consist of one glycerol molecule esterified with two **fatty acids** at the *sn*-1 and *sn*-2 positions, and a phosphoric acid at the *sn*-3 position. In turn, the phosphate group binds a hydrophilic group, such as choline, serine or inositol, via ester bond.
• **Cholesterol** and its esters, together with small amounts of steroid hormones, are found only in animal products, unlike the [lipids](#) seen up to now which are also found in plant products. In the small intestine, in addition to dietary cholesterol, there is also biliary cholesterol,
• Like vitamins, even this steroid molecule is not a source of energy. A variety of plant stanols and sterols, in particular the β-sitosterol (that is not absorbed under physiological conditions), are also included among dietary steroids.
Lipid digestion

- **Lipid digestion** and **absorption** are complex processes. They involve soluble enzymes, substrates with different degree of solubility, and occur primarily in the stomach and small intestine.

- **Lipid** digestion begins in the mouth, continues in the stomach, and ends in the small intestine. Enzymes involved in **triacylglycerol digestion** are called lipase. They are **proteins** that catalyze the partial hydrolysis of triglycerides into a mixture of free **fatty acids** and acylglycerols.
Overview of lipid digestion

Lipid particles from diet (lipid-soluble vitamins, lipophilic substances, cholesterol esters, phospholipids)

Oral cavity

Lingual lipase:
- Digests short and medium-chain fatty acids

Gastric lipase:
- Digests short and medium-chain fatty acids

Bile acids

Gallbladder

Exocrine secretions from pancreas

Micelle assembly

Pancreatic lipase with colipase:
- Digests triacylglycerols

Phospholipase:
- Digests phospholipids

Cholesterol esterase:
- Digests cholesterol esters

Micelles (monomeric lipids, e.g., lipid-soluble vitamins, free fatty acids, 2-monoacylglycerol, cholesterol)

Short-chain fatty acids diffuse through stomach to enter circulatory system

Small intestine
• There are several lipases, the most important of which is produced by the exocrine pancreas; the others are lingual lipase, gastric lipase, and breast milk lipase. Other enzymes involved in lipid digestion are cholesterol esterase and phospholipases $A_1$ and $A_2$. 
Lipid digestion and lingual lipase

• In the mouth, food is broken into small particles and mixed with lingual lipase. The enzyme is produced and secreted by serous lingual glands,

• The reaction catalyzed by the enzyme releases a single fatty acid, preferably a short-chain or medium-chain fatty acid, and a 1,2-diacylglycerol, which is then hydrolyzed in the duodenum. Lingual lipase plays a modest role in the digestion of triacylglycerols
Lipid digestion and gastric lipase

• In the stomach, lipids are hydrolyzed also by a second acid lipase, the gastric lipase. This enzyme is secreted by the chief cells of the gastric mucosa, and has an optimal pH around 4, but is still quite active at less acidic pH values, 6 to 6.5. Therefore, it probably remains active even in the upper duodenum, where the pH is between 6 and 7.
Bile salts and the emulsion of lipid droplets

- The chyme, containing a lipid emulsion made up of droplets of diameter less than 0.5 mm, enters the upper portion of the small intestine, the duodenum, where the hydrolysis of triglycerides continues. In the duodenum, the chyme is mixed with bile, whose release by the gallbladder is stimulated by cholecystokinin, hormone secreted by cells of the mucosa of the duodenum and jejunum in response to the ingestion of a meal, particularly if high in fat.
In the bile, among the other components, there are **bile salts**, phospholipids, and cholesterol. **Bile salts** are **bile acids** conjugated with glycine or taurine. In turn, bile acids are oxygenated derivatives of cholesterol. **Bile acids** and **bile salts** are both synthesized by the liver.
Lipid digestion and pancreatic lipase

- Cholecystokinin also stimulates the exocrine pancreas to secrete a pancreatic juice containing, among other molecules, **pancreatic lipase**. The enzyme catalyzes the digestion of the majority of ingested triglycerides, mainly in the upper portion of the jejunum, and has a optimum pH of 7.0 to 8.8.
• It catalyzes the cleavage of fatty acids, typically with 10 or more carbon atoms, primarily in \textit{sn}-1 and \textit{sn}-3 positions of the glycerol backbone. The products of the reaction are free fatty acids and 2-monoacylglycerols. The 2-monoacylglycerol, the main form in which the monoacylglycerols are absorbed from the small intestine, can undergo an isomerization process in which the remaining fatty acid moves to carbon 1 or 3.
Lipid digestion and lipase in breast milk

• This lipase has a neutral pH optimum, and is stimulated by **bile salts**. The enzyme contributes substantially to hydrolysis of the triglycerides in the intestine of breast-fed infants. Instead, there are no lipases in cow’s milk.
Lipid digestion and cholesterol esterase

• Another enzyme present in the pancreatic juice is cholesterol esterase. The enzyme, synthesized and secreted in an active form by the exocrine pancreas, is a lipase with broad specificity, being active on:

• cholesterol esters, with cholesterol and free fatty acids as reaction products;
Bile salt deficiency: cholelithiasis

- The movement of cholesterol from the liver into the bile must be accompanied by the simultaneous secretion of phospholipid and bile salts.

- If this dual process is disrupted and more cholesterol enters the bile than can be solubilized by the bile salts and lecithin present, the cholesterol may precipitate in the gallbladder, initiating the occurrence of cholesterol gallstone disease—cholelithiasis.
Lipids (risk of heart disease)
Lipid profile

• **Also known as:** Lipid Panel; Coronary Risk Panel

• Lipid profile: A pattern of lipids in the blood. A lipid profile usually includes the levels of total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, and the calculated low-density lipoprotein (LDL) 'cholesterol.
• Measurements of lipids levels are frequently used to assess the risk of future coronary heart disease or stroke. These two disease conditions are commonly termed cardiovascular disease (CVD).
The lipid profile is used as part of a **cardiac risk assessment** to help determine an individual's risk of **heart disease** and to help make decisions about what treatment may be best if there is borderline or high risk.
Lipoproteins

- Lipoproteins are the particles that transport cholesterol and triglycerides in the blood stream.
- Lipoproteins are composed of proteins (apolipoproteins), phospholipids, triglycerides and cholesterol.
Lipoproteins differ in the ratio of protein to lipids, and in the particular apoproteins and lipids that they contain. They are classified based on their density:

- **chylomicron** (largest; lowest in density due to high lipid/protein ratio; highest in triacylglycerols as % of weight)
- **VLDL** (very low density lipoprotein; 2nd highest in triacylglycerols as % of weight)
- **IDL** (intermediate density lipoprotein)
- **LDL** (low density lipoprotein, highest in cholesteryl esters as % of weight)
- **HDL** (high density lipoprotein, highest in density due to high protein/lipid ratio).
A lipid profile typically includes:

- **Total cholesterol** — this test measures all of the cholesterol in all the lipoprotein particles.
- **High-density lipoprotein cholesterol (HDL-C)** — measures the cholesterol in HDL particles; often called "good cholesterol" because it removes excess cholesterol and carries it to the liver for removal.
- **Low-density lipoprotein cholesterol (LDL-C)** — calculates the cholesterol in LDL particles; often called "bad cholesterol" because it deposits excess cholesterol in walls of blood vessels, which can contribute to **atherosclerosis**. Usually, the amount of LDL-C is calculated using the results of total cholesterol, HDL-C, and triglycerides.
- **Triglycerides** — measures all the triglycerides in all the lipoprotein particles; most is in the very low-density lipoproteins (VLDL).
• It is recommended that healthy adults with no other risk factors for heart disease be tested with a fasting lipid profile once every four to six years. Initial screening may involve only a single test for total cholesterol and not a full lipid profile. However, if the screening cholesterol test result is high, it will likely be followed by testing with a lipid profile.
Risk factors other than high \( \text{LDL-C} \) include:

- Cigarette smoking
- Being overweight or obese
- Unhealthy diet
- Being physically inactive— not getting enough exercise
- Age (if you are a male 45 years or older or a female 50-55 years or older)