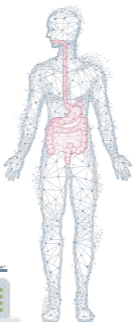




L3:

Biochemical aspects of digestion of lipids

GNT Block



Color Index:

- Main text
- Female slides
- Male slides
- Important
- Doctor's notes
- Extra notes

Editing file:



Objectives:



Understand the process of digestion of dietary lipids including, the organs involved, the enzymes required, and the end products.



Study the synthesis, secretion and fate of chylomicron



Understand the clinical manifestations of diseases that involve defective lipid digestion and/or absorption (indigestion and malabsorption syndrome)

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Dr. Usman Ghani



Science Bites



Ninja Nerd

Dietary lipids

Overview

Dietary lipid: organs and enzyme

Lipid degradation by the pancreatic enzymes

Lipid digestion in the stomach and intestine

Lipid absorption, re-synthesis and secretion. ⁴³⁹: Lipid molecules are hard to absorb so the body breaks them down to smaller molecules, absorbs them then rebuilds the molecules.

Control of lipid digestion

Pancreatic insufficiency

Lipid malabsorption

Use of dietary lipid by the tissues

Dietary lipids

Dietary lipids intake is ~78-81 g/day.

Triacylglycerol is >90%, The remainder includes: Cholesterol, Cholesterol Ester ⁴³⁹: There is fatty acid bonded to the cholesterol molecule, Phospholipids, Glycolipids and Free fatty acids.

For lipids, digestion begins when they reach the stomach. However, the amount of lipids digested in the stomach is minimal. The majority of the digestion occurs in the small intestine and is completed there.

Stomach

1. **Lingual lipase.** This enzyme is secreted in the mouth, but it starts working in the stomach because it needs an acidic medium to work.
2. **Gastric lipase.**

Organs & Enzymes:

Small intestine

1. **Pancreatic Lipase / CO-lipase.**
2. **Cholesterol esterase.**
3. **Phospholipase A2.**
4. **Lysophospholipase.**

They are produced in the pancreas, but their main function is in the small intestines.



Extra note:

- Lipase plays a crucial role in lipid digestion by breaking down triglycerides into fatty acids and glycerol.
- Co-lipase aids lipase in this process by enhancing its activity.
- Cholesterol esterase is responsible for hydrolyzing cholesterol esters into free cholesterol and fatty acids.
- Phospholipase A2 acts on phospholipids, breaking them down into lysophospholipids and free fatty acids.
- Lysophospholipase further contributes by converting lysophospholipids into glycerophospholipids and fatty acids

Lipid digestion

In Stomach

- Catalyzed by an **acid-stable lipase** (lingual lipase & gastric lipase) 439: Acid stable means that the enzyme doesn't get denatured in an acidic environment like the stomach.
- Triacylglycerols (TAGs) are hydrolyzed (They will hydrolyze the TAGs which have short to medium chain fatty acids (12 carbon atoms or less.) by the lipases secreted under the tongue and gastric mucosa
- Acid lipases are important for lipid (milk fat is full of short and medium chain fatty acids) digestion in:

-**neonates** Their primary food is milk.

-**patients with pancreatic insufficiency** pancreatic secretions are either not produced or fail to reach the small intestine.



In Small intestine

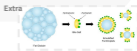
Emulsification: breaking down big lipid droplets into smaller ones in an aqueous medium which increases the surface area.

- Occurs in the **duodenum**
 - Increases surface area of lipid droplets
 - To maximize the effect of digestive enzymes
- Let's imagine the enzyme and fat like the water (enzyme) and oil (fat). We need a spoon to mix them (mechanical mixing) and also we need a detergent (bile salts) because Bile salt and phospholipids are amphipathic which means they have two ends, hydrophilic and hydrophobic that will make lipids (hydrophobic) available for the enzyme (hydrophilic)

-Two mechanisms:

1-Detergent properties of bile salts in the bile (bile salts emulsify dietary lipid particles)

2-Mechanical mixing by peristalsis



By Pancreatic enzymes

TAG degradation:

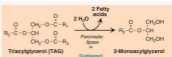
- Performed by pancreatic lipase, colipase.

If somebody asks you which enzyme cleaves the fatty acid groups from the triacylglycerol, it is pancreatic lipase. But pancreatic lipase requires co-lipase for the activity of pancreatic lipase.

- **Removes fatty acids at C1 and C3**
- Leaving **2-monoacylglycerol and free acids (FFAs)**

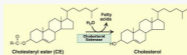
Pancreatic lipase:

- Found in high conc. In pancreatic secretion (2-3% of total proteins)
- It is inhibited by **Orlistat**, an antiobesity drug (so lipids are not digested; instead they are excreted with stool, causing fatty stools).



Cholesteryl ester degradation:

- Hydrolyzed by cholesterol esterase
- Produces cholesterol + FFAs



Digestion of Phospholipids(PL)



Doctor's note:

- Phospholipase A2 removes one fatty acid from the phospholipid and we get lysophospholipid
- Lysophospholipase acts on lysophospholipids to give us glycerophosphoryl base which can be excreted. Example of phospholipid digestion:
- Phosphatidylcholine →
- Lysophosphatidylcholine → choline



IMPORTANT Doctor's note:

In the digestive process, dietary lipids undergo minimal changes in the stomach; only short and medium-chain fatty acids are removed. In the small intestine, bile salts emulsify lipids, and pancreatic enzymes break them down into free fatty acids, 2-monoacylglycerol, and cholesterol. The remaining pieces of phospholipid, which consist of a glycerophosphoryl base, are excreted. These primary products are taken up by enterocytes, where they undergo reesterification, get repackaged as chylomicrons, and are transported via the lymphatic system.

For Triacylglycerols you need pancreatic lipase & co-lipase.
 For cholesterol esters you need cholesterol esterase.
 For phospholipids, you need two enzymes, phospholipase A2 and lysophospholipase.

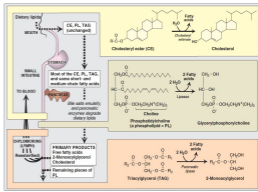


Figure 15.2
 Overview of lipid digestion.

Pancreatic insufficiency in cystic fibrosis (CF)

- ◆ CF is due to genetic mutations in CFTR (transmembrane conductance regulator protein)
- ◆ Functions as chloride channel on epithelium. The normal function of CFTR gene is increases the secretion of Chloride from epithelial cells, once the secretion of Cl^- increased from epithelial cells the Sodium reabsorption will decrease
- ◆ Defective CFTR causes: Decreased secretion of chloride & Increased reabsorption of sodium and water. Then water goes inside the epithelial cells which means pancreatic secretions now have less water available for them which means...
- ◆ Decreased hydration in pancreas thickens the pancreatic secretions When they become thick they go and block the pancreatic duct. (Pancreas secretion becomes paste like)
- ◆ Pancreatic enzymes are unable to reach the intestine. Because Pancreatic duct is blocked. Which causes malnutrition and fatty stool. And this is called Pancreatic insufficiency.
- ◆ Treatment: enzyme and fat-soluble vitamin supplementation. 1- Because enzymes can't reach the intestine. 2- Because fat soluble vitamins also get affected.

Control of lipid digestion

◆ Controlled by **hormones**:

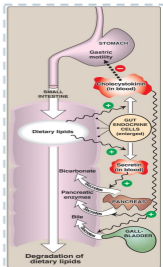
⚠ Important

1. Cholecystokinin (CCK):

- Acts on gallbladder to release bile.
- Acts on pancreas to release enzymes.
- Decreases gastric motility (slow release of gastric contents). (If you have undigested food already in the small intestine, you do not want stomach to be pushing more and more food into the small intestine because then the digestion process is going to be less efficient)

2. Secretin:

- **Low pH stimulates its secretion.** When acidic chyme from the stomach enters the duodenum, it stimulates the release of secretin.
- Acts on pancreas to release bicarbonate and liver to release bile.
- Neutralizes the PH of the contents before entering the small intestine.



Lipid absorption by enterocytes

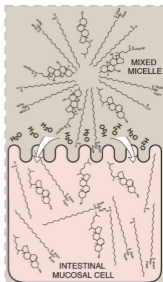
Products of lipid digestion (FFAs, free cholesterol, 2-monoacylglycerol) combine with bile salts and fat-soluble vitamins

They form mixed micelles (disk-shaped particles).
It's composed of Products of lipid digestion+ bile salts +fat-soluble vitamins

Mixed micelles are hydrophobic inside and hydrophilic outside.(Amphipathic)

Absorbed by brush border membrane of enterocytes.
Because the cell membrane is amphipathic with the hydrophilic side out.

Short and medium chain length fatty acids are absorbed directly. (They are water soluble, they do not require the assistance of mixed micelles for absorption by the intestinal mucosa).

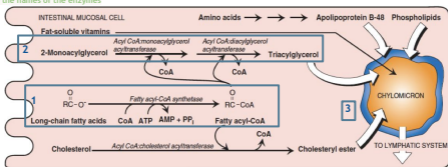


Resynthesis of TAG/Cholesterol esters

- ◆ Digested lipids absorbed by enterocytes migrate to endoplasmic reticulum for complex lipid biosynthesis



You should know the names of the enzymes



3. Chylomicrons

Assembly of chylomicrons by enterocytes

Newly synthesized TAG and cholesterol ester are packaged as lipid droplets surrounded by a thin layer of:

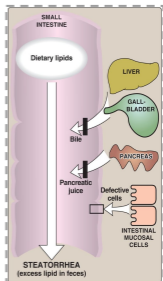
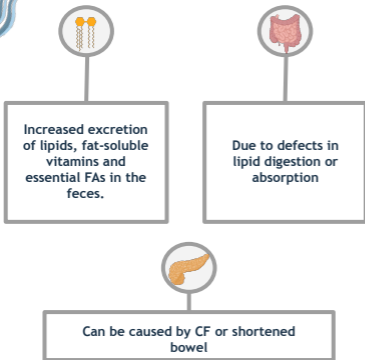
- 1- Apolipoprotein B-48 (apo B-48)
- 2- Phospholipids
- 3- Free cholesterol

Secretion of chylomicrons by enterocytes

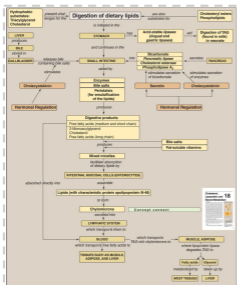
- By exocytosis into lymphatic vessels around villi of small intestine (lacteals) which enter into systemic circulation.
- Serum becomes milky after a fatty meal.



Lipid malabsorption



Key concepts for digestion and absorption of dietary lipids



#439-Extra

The big picture:

Dietary lipids **intake** (e.g. TAGs and Cholesteryl esters)

↓

Digested and broken down in intestines by pancreatic enzymes

↓

Absorbed as mixed micelles in intestinal cells (enterocytes)

↓

Resynthesis of TAGs and Cholesteryl esters in ER of enterocytes

↓

Exocytosis into lymphatic vessels as Chylomicrons (lipoprotein)

↓

Chylomicrons **circulating** in blood (milky appearance)

CVS wraps: Function of chylomicron!
Transport dietary TAGs to peripheral tissues / and cholesterol to the liver (hepatocytes)



Take home messages



Lipid digestion begins in stomach



Emulsification of lipids occurs in duodenum, helped by peristalsis and bile salts



Intestinal digestion of lipids by pancreatic enzymes




Lipid absorption by mixed micelles



Re-synthesis of TAGs, cholesterol ester and PLs inside the intestinal mucosal cells



Assembly and secretion of chylomicrons into lymphatic lacteals and then into systemic circulation



Quiz

MCQs

Q1: Which enzyme is responsible for the hydrolysis of triglycerides?

- A- Amylase
- B- Protease
- C- Pancreatic Lipase
- D- Gastric Lipase

Q2: Where does emulsification of dietary fats primarily occur?

- A- Jejunum
- B- Stomach
- C- Duodenum
- D- Ileum

Q3: Chylomicrons are synthesized in which organ?

- A- Liver
- B- Pancreas
- C- Stomach
- D- Small intestine

Q4: Where is the primary site for the absorption of the end products of lipid digestion?

- A- Stomach
- B- Small intestine
- C- Colon
- D- Esophagus

Q5: In lipid digestion, what is the primary function of phospholipase A2?

- A- Hydrolyzing cholesterol esters
- B- Activating pancreatic lipase
- C- Breaking down phospholipids
- D- Emulsifying lipids

Q6: Which organ secretes cholesterol esterase?

- A- Liver
- B- Gallbladder
- C- Small intestine
- D- Pancreas

Answers: 1-C, 2-C, 3-D, 4-B, 5-C, 6-D

SAQ

Q: How are the products of lipid digestion absorbed by enterocytes?

A: They combine with bile salts and fat-soluble vitamins to form mixed micelles. These micelles are absorbed by the brush border membrane of enterocytes in the small intestine.

Q: What is the role of cholecystokinin (CCK) in the control of lipid digestion?

A: Cholecystokinin (CCK) acts on the gallbladder to release bile and on the pancreas to release enzymes. It also decreases gastric motility, resulting in the slow release of gastric contents.

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Special Thanks to Aleen Alkulyah for the Design!

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