Biochemical aspects of digestion of lipids

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Editing File

Objectives:

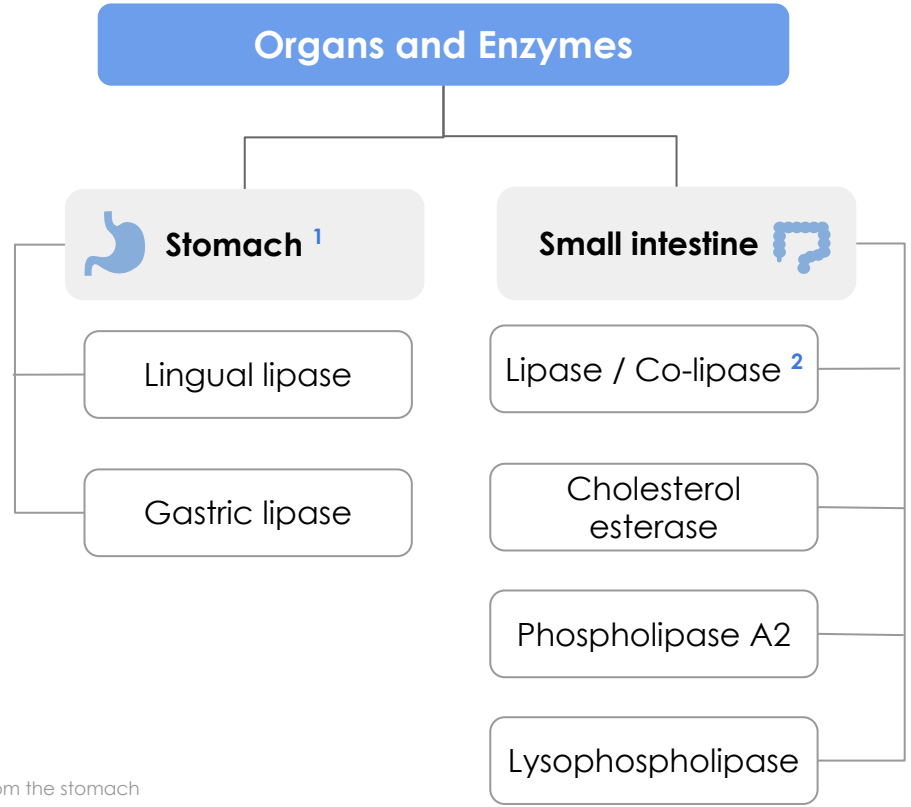
- Understand the process of digestion of dietary lipids including, the organs involved, the enzymes required, and the end products.
- Study the synthesis, secretion and fate of chylomicron
- Understand the clinical manifestations of diseases that involve defective lipid digestion and/or absorption (indigestion and malabsorption syndrome)

Overview:

- Dietary lipid: organs and enzymes
- Lipid digestion in the stomach and intestine
- Lipid degradation by the pancreatic enzymes
- Pancreatic insufficiency
- Control of lipid digestion
- Lipid absorption, re-synthesis and secretion
- Lipid malabsorption
- Use of dietary lipid by the tissues

Dietary lipids

- **Dietary lipids intake is ~81 g/day**
  - Triacylglycerol is >90%
  - The remainder includes:
    - Cholesterol
    - Cholesterol ester
    - Phospholipids
    - Glycolipids
    - Free fatty acids



1-carbohydrates digestion starts in the mouth but lipid digestion starts from the stomach
2-co-lipase activates lipase enzyme

Dietary lipids

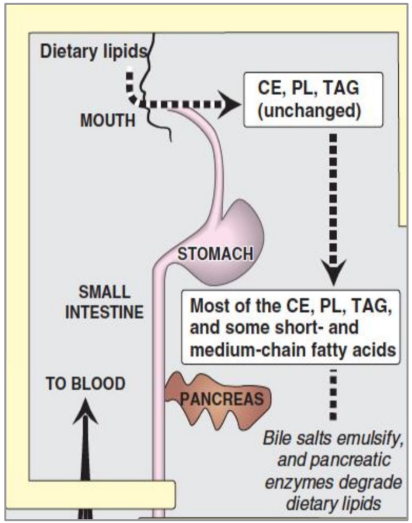
Lipid digestion

Stomach

- Catalyzed by an acid-stable lipase (lingual lipase)
- Triacylglycerols [1] (TAGs) are hydrolyzed by the lipases secreted:

- Under the tongue and gastric mucosa

- Acid lipases are important for lipid (milk fat) digestion in neonates and patients with pancreatic insufficiency.



Small intestine

Emulsification[2]:

- Occurs in the duodenum
- **Increases** surface area of lipid droplets
- To maximize the effect of digestive enzymes
- Two mechanisms [3]:

1. Detergent properties of bile salts in the bile (Bile salts emulsify dietary lipid particles)
2. Mechanical mixing by peristalsis

1- Not all , only short & medium Fatty acids " that have 12 or less carbons"
- Most of dietary fatty acids are long chain fatty acids, so the contribution of these enzymes is minimal

2-Emulsification is a process that forms a liquid, known as an emulsion, containing very small droplets of fat or oil suspended in a fluid

3- Enzyme > hydrophilic. Lipids > hydrophobic .. so, how do they come in contact with each other? By two mechanisms:
- When peristaltic movement mixes the fat and the fluid together, the fat particles break up and become smaller.
- The bile also separates and keeps the small particles of lipid separated by its detergent physical properties, Which allows the enzymes to work with more surface area.

Lipid degradation by pancreatic enzymes

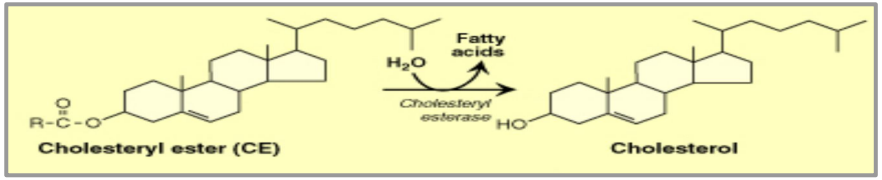
TAG degradation:

1. Performed by pancreatic lipase, colipase [1]
2. Removes fatty acids at **C1** and **C3**
3. Leaving 2-monoacyglycerol [4] **and** free fatty acids (FFAs) [2]

Pancreatic lipase :

Found in high conc. in pancreatic secretion (2-3% of total proteins)
Inhibited by Orlistat, an antiobesity drug [3]

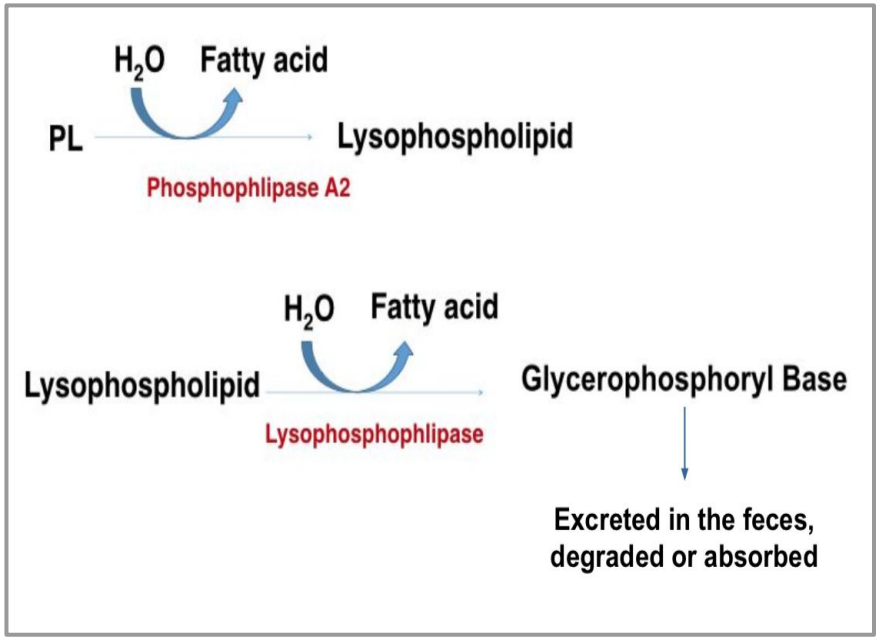
Cholesteryl ester degradation:



1. Hydrolyzed by cholesterol esterase
2. Produces cholesterol **+** FFAs

1- co-lipase is activated by trypsin when needed.
2- The free fatty acids which have been removed from 1st & 3rd C .
3- The drug inhibits the degradation of lipid by inhibiting pancreatic lipase thus decreasing lipid absorption and body weight
4- Number 2 refers to the location of the attachment

Digestion of Phospholipids (PL)by Phospholipase A2 & Lysophospholipase



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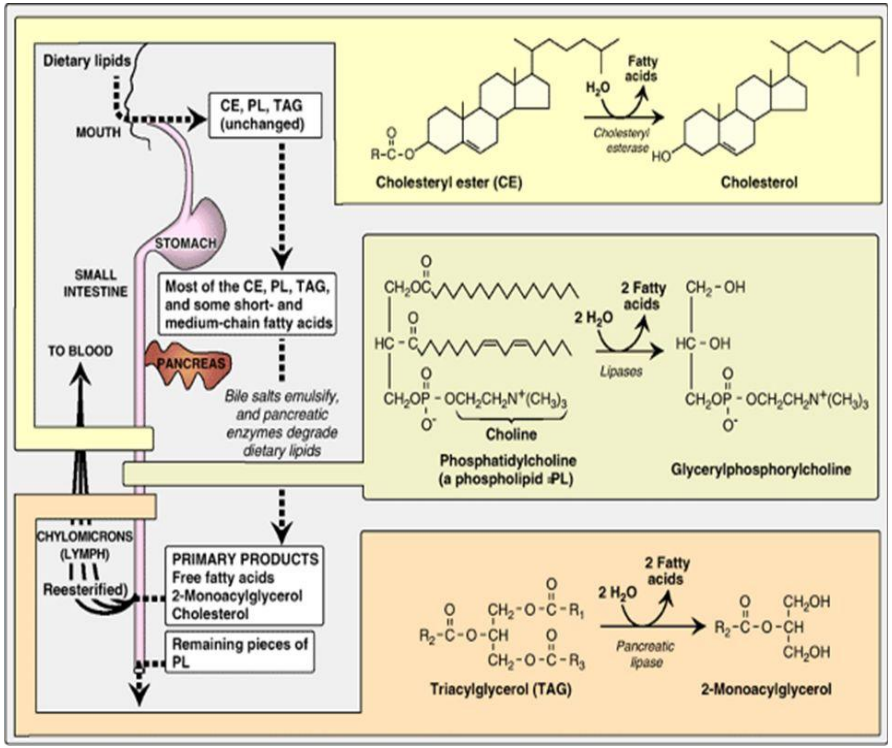
Two enzymes are responsible for digestion of phospholipids,
- Phospholipase A2
- Lysophospholipase

How do they work?
- 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

Overview of Lipid Digestion



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After Ingestion of dietary lipids:

- In the mouth→ Unchanged.
- In the stomach: some of the short, medium chain fatty acids are removed by lingual and gastric lipases, the remaining are the same
- The undigested long chain fatty acids reach the small intestine, Bile salts are released from the gallbladder to emulsify the lipids, then the pancreatic enzymes work on them.
- Pancreas also secretes bicarbonate to neutralize the chyme, because the pancreatic enzymes cannot work in an acidic media.
- End product [primary products]: free fatty acids, 2-monoacylglycerol, cholesterol.
- The end product molecules are taken into the enterocytes by mixed micelles "discussed in another slide" , then they will be synthesized to complexes again :to TAG, which is carried by chylomicrons.
- Chylomicrons carry dietary TAGs in the blood.
- The presence of lipids in the GIT stimulates the secretion of and for the glands to secrete them.

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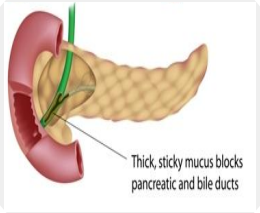
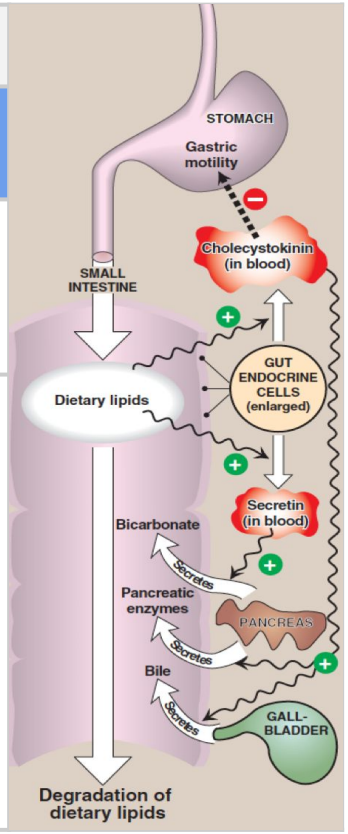
Pancreatic insufficiency in cystic fibrosis (CF)

1. **CF is due to genetic mutations in CFTR (transmembrane conductance regulator protein)**
2. **Functions as chloride channel on epithelium**
3. **Defective CFTR causes:**
   - Decreased secretion of chloride
   - Increased reabsorption of sodium and water
4. **Decreased hydration in pancreas thickens the pancreatic secretions**
5. **Pancreatic enzymes are unable to reach the intestine**
6. **Treatment: enzyme and fat-soluble vitamin supplementation**



Control of lipid digestion

Controlled by hormones:	
Cholecystokinin (CCK)	**Secretin**
Acts on gallbladder to release bile	Low pH stimulates its secretion
Acts on pancreas to release enzymes	Acts on pancreas to release bicarbonate and acts on liver to release bile To Neutralizes the pH of the contents before entering the small intestine
Decreases gastric motility (slow release of gastric contents)	

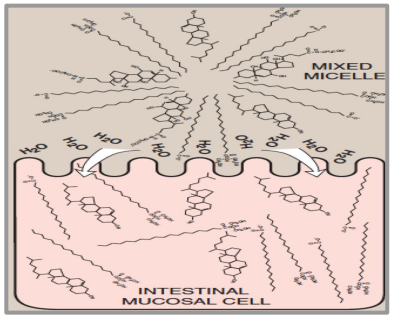


Lipid absorption by enterocytes

1. Products of lipid digestion (FFAs, free cholesterol, 2-monoacylglycerol.) combine with bile salts and fat-soluble vitamins
2. They form mixed micelles (disk-shaped particles)
3. Absorbed by brush border membrane of enterocytes
4. Short and medium chain length fatty acids are absorbed directly

Mixed micelles are hydrophobic inside and hydrophilic outside

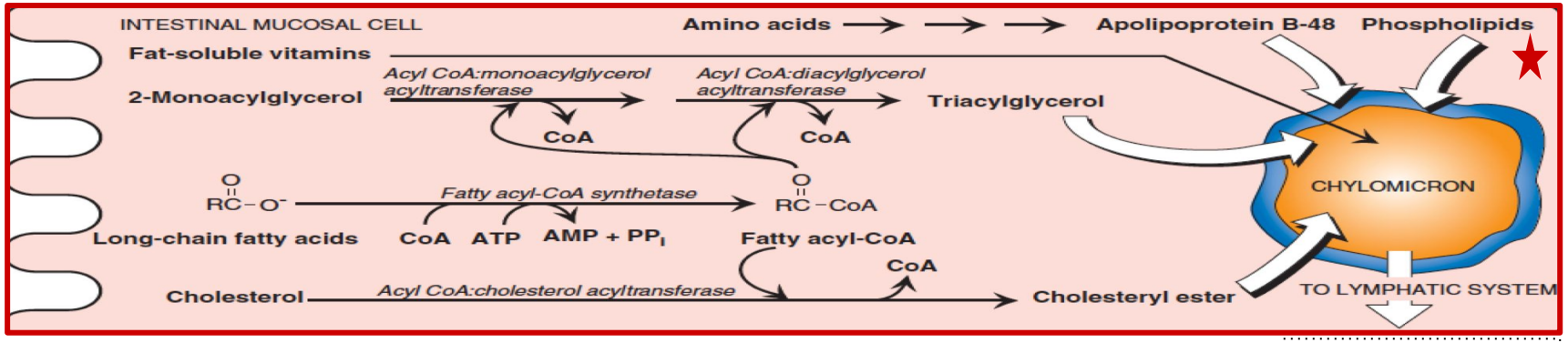
Intestinal mucosal cells have a thin water layer, which will attract the hydrophilic outer portion of the micelles for absorption



Resynthesis of TAG / Cholesteryl esters

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

Fatty acids → activated to acyl CoA form → 2-Monoacylglycerols → TAGs



The whole picture is important.

Newly synthesized **TAG** and **cholesterol ester** are packaged as lipid droplets surrounded by 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 chyle

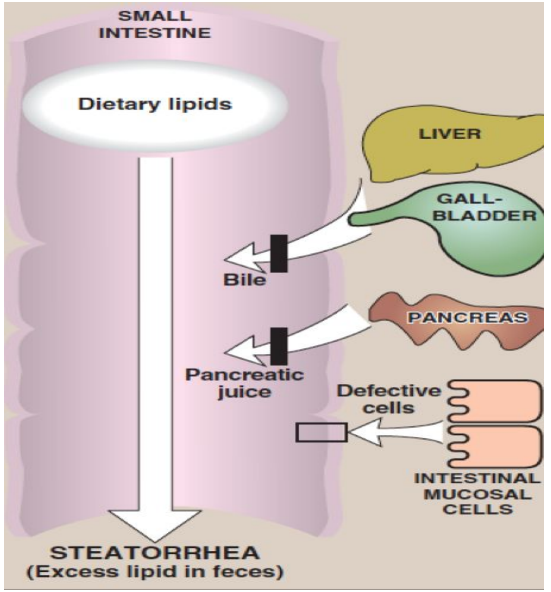
Serum becomes milky after a fatty meal

Once chyme reaches the intestine its called chyle , and chyle contains some undigested lipids , those lipids are gonna stimulate the release of CCK hormone.

Lipid malabsorption

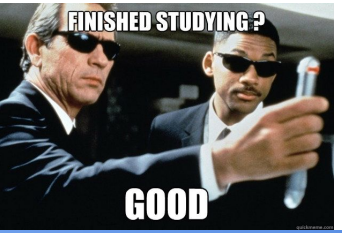
Due to defects in lipid digestion or absorption

1. Increased excretion of lipids, fat-soluble vitamins and essential FAs in the feces
2.
3. Can be caused by CF (cystic fibrosis) or shortened bowel

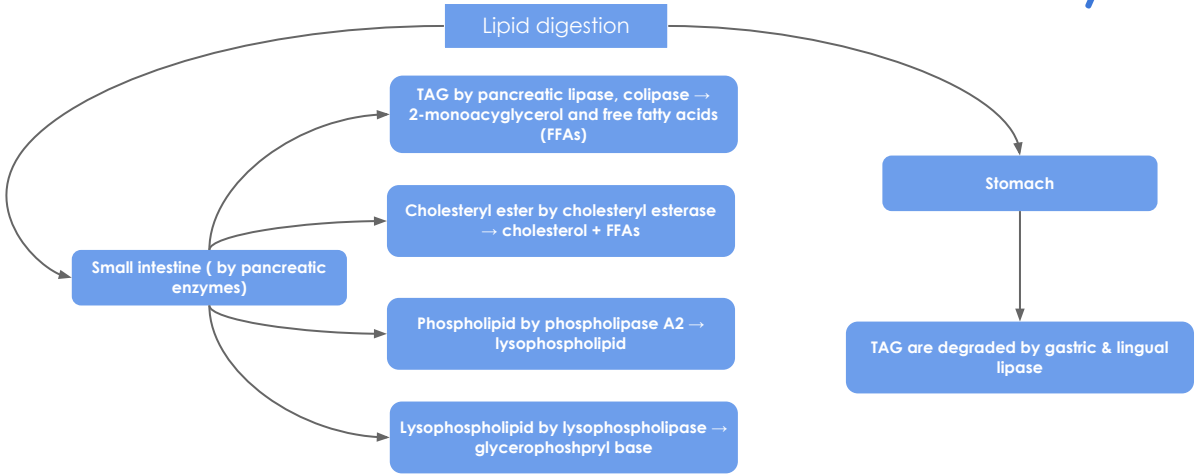


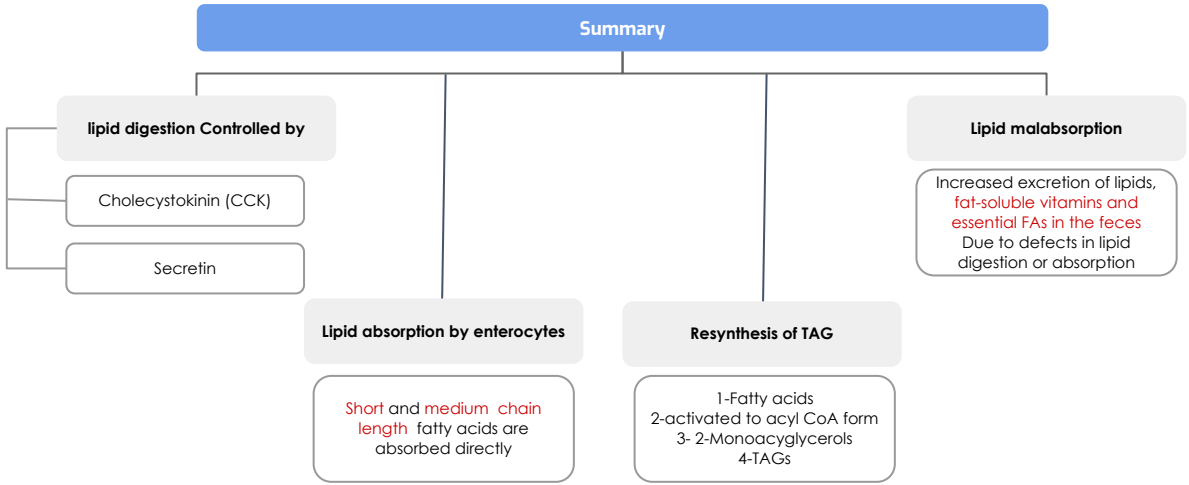
Take Home Messages

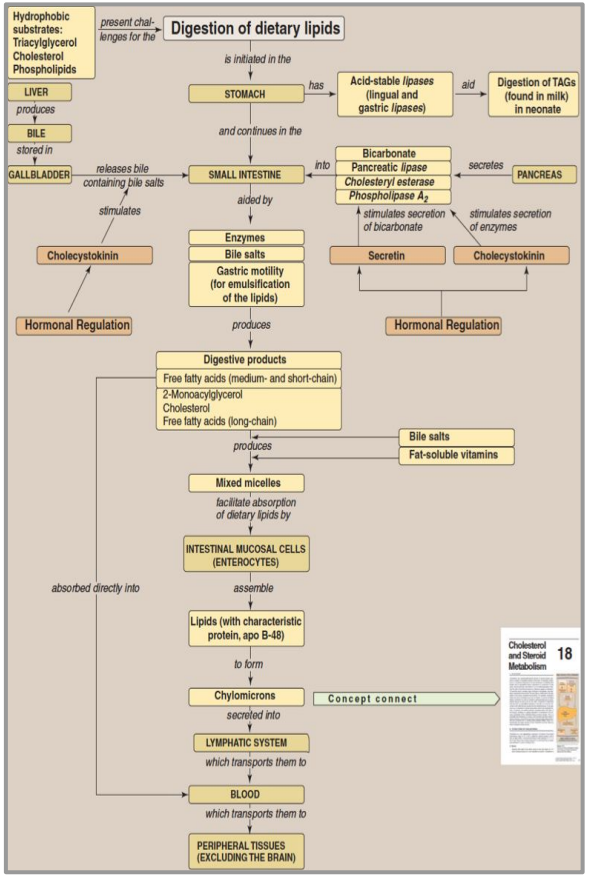
- Lipid digestion begins in stomach
- Emulsification of lipids occurs in duodenum, helped by peristalsis and bile salts
- Intestinal digestion of lipids by pancreatic enzymes
- Lipid absorption by mixed micelles
- Re-synthesis of TAGs, cholesterol ester and PLs inside the intestinal mucosal cells
- Assembly and secretion of chylomicrons into lymphatic lacteals and then into systemic circulation



Summary


Lipid digestion
TAG by pancreatic lipase, colipase → 2-monoacyglycerol and free fatty acids (FFAs)
Cholesteryl ester by cholesteryl esterase → cholesterol + FFAs
Small intestine (by pancreatic enzymes)
Phospholipid by phospholipase A2 → lysophospholipid
Lysophospholipid by lysophospholipase → glycerophoshpryl base
Stomach
TAG are degraded by gastric & lingual lipase


Summary
lipid digestion Controlled by
Cholecystokinin (CCK)
Secretin
Lipid absorption by enterocytes
Short and medium chain length fatty acids are absorbed directly
Resynthesis of TAG
1-Fatty acids
2-activated to acyl CoA form
3- 2-Monoacyglycerols
4-TAGs
Lipid malabsorption
Increased excretion of lipids, fat-soluble vitamins and essential FAs in the feces
Due to defects in lipid digestion or absorption


Digestion of dietary lipids
Hydrophobic substrates: Triacylglycerol Cholesterol Phospholipids
present challenges for the
is initiated in the
LIVER
produces
BILE
stored in
GALLBLADDER
releases bile containing bile salts
stimulates
Cholecystokinin
Hormonal Regulation
STOMACH
has
Acid-stable lipases (lingual and gastric lipases)
aid
Digestion of TAGs (found in milk) in neonate
and continues in the
SMALL INTESTINE
aided by
Enzymes
Bile salts
Gastric motility (for emulsification of the lipids)
produces
into
Bicarbonate
Pancreatic lipase
Cholesteryl esterase
Phospholipase A2
secretes
PANCREAS
stimulates secretion of bicarbonate
stimulates secretion of enzymes
Secretin
Cholecystokinin
Hormonal Regulation
Digestive products
Free fatty acids (medium- and short-chain)
2-Monoacylglycerol
Cholesterol
Free fatty acids (long-chain)
produces
Bile salts
Fat-soluble vitamins
Mixed micelles
facilitate absorption of dietary lipids by
INTESTINAL MUCOSAL CELLS (ENTEROCYTES)
absorbed directly into
assemble
Lipids (with characteristic protein, apo B-48)
to form
Chylomicrons
Concept connect
secreted into
LYMPHATIC SYSTEM
which transports them to
BLOOD
which transports them to
PERIPHERAL TISSUES (EXCLUDING THE BRAIN)
Cholesterol and Steroid Metabolism
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Quiz

MCQs

Q1: 2-monoacyglycerol and free fatty acids is the product of degradation of:
A)Cholesteryl esters B)Phospholipids C) proteins D) TAG

Q2: Orlistat is an anti obesity drug that acts on which of the following pancreatic enzymes?
A)Lipase B)Lysophospholipase C)Phospholipase A D)Esterase

Q3: A 9-year old girl , known to have cystic fibrosis was presented in pediatric clinic complaining of distention and diarrhea with passing of foul smelling stools over the past week , which of the following explains her condition?
A) increased gastric motility B) Increased secretion of CCK
C) Pancreatic insufficiency D) Decreased reabsorption of water

Q4: Mixed micelles are classified as :
A)Hydrophilic B)hydrophobic C)Amphipathic D)fat soluble

Q5:which of the following is a primary Apolipoprotein contributed in the synthesis of chylomicrons?
A)APOE B)APO B100 C)APO B48 D)APOC

Q6: which one of the following types of fatty acids absorbed directly ?
A)Short B)Medium C)Long D) A & B

SAQs :

Q1: Mention the two mechanisms for emulsification.

Q2: Explain how Cholesteryl esters get degraded and what are the products ?

Q3: what are the hormones that control the lipid digestion and where do they act on ?

Q4: What are the enzymes involved in the resynthesis of TAG ?

★ **MCQs Answer key:**

1) D 2) A 3) C 4) C 5) C 6) D

★ **SAQs Answer key:**

1)A-Detergent properties of bile salts in the bile (Bile salts emulsify dietary lipid particles)
B-Mechanical mixing by peristalsis
2) Cholesteryl ester by cholesteryl esterase → cholesterol + FFAs
3)Slide 9
4)Acyl CoA:monoacylglycerol acyltransferase & Acyl CoA:diacylglycerol acyltransferase.

Team members

Girls Team:

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- Alwateen Albalawi
- Amirah Aldakhilallah
- Arwa Al Emam
- Deema Almaziad
- Ghaliah Alnufaei
- Haifa Alwaily
- Leena Alnassar
- Lama Aldakhil
- Lamiss Alzahrani
- Nouf Alhumaidhi
- Noura Alturki
- Sarah Alkhalife
- Shahd Alsalamah
- Taif Alotaibi

Boys Team:

- Abdulrahman Bedaiwi
- Alkassem Binobaid
- Khayyal Alderaan
- Mashal Abaalkhail
- Naif Alsolais
- Omar Alyabis
- Omar Saeed
- Omar Odeh
- Rayyan Almousa
- Yazen Bajeaifer

Team Leaders

Lina Alosaimi

Mohannad Alqarni

★ The flower doesn't dream of the bee, it blossoms and the bee comes.

We hear you