

ANSC/NUTR 618
LIPIDS & LIPID METABOLISM
Digestion of Lipids

I. Intake and initial processing of dietary fats

A. Intake of cholesterol and fat in three human populations

Item	Older men	Men	PM women
Age, <i>yr</i>	49	36	58
Body weight, <i>kg</i>	86	86	71
LDL cholesterol, <i>mg/dL</i>	143	122	124
HDL cholesterol, <i>mg/dL</i>	41	47	62
Triacylglycerols, <i>mg/dL</i>	205	102	92
Total energy intake, <i>kcal</i>	2,293	2,085	1,633
Cholesterol, <i>mg/d</i>	276	353	202
Saturated fat, <i>g/d</i>	28	39	20
Monounsaturated fat, <i>g/d</i>	29	26	15
Polyunsaturated fat, <i>g/d</i>	14	10	8
Total fat, <i>g/d</i>	92	87	62

B. Mastication and digestion of dietary fats

1. Saliva of rats (not humans) contains lingual lipase, which digests milk fats.
 - a. Primary products – 2,3-diacylglycerols
 - b. pH optimum – 4.5 - 5.4, so lingual lipase is active in stomach
 - c. Does not require bile salts for activity.
 - d. ***Lingual lipase probably does not exist in human infants.***
2. Lipase from human breast milk, bile salt-stimulated lipase, is taken up by human infants and activated by bile salts in the small intestine.

C. Digestion of fat in the stomach

1. Stomach causes physical reduction in fat particle size.
2. Gastric lipase
 - a. Responsible for up to 25% of TAG hydrolysis in adults and ***infants***.
 - b. pH optimum around 4.0.

II. Digestion of fats in the small intestine

A. Secretion of cholecystokinin from the intestinal mucosal cells (stimulated by fat in the intestine) causes:

1. Gall bladder contraction.

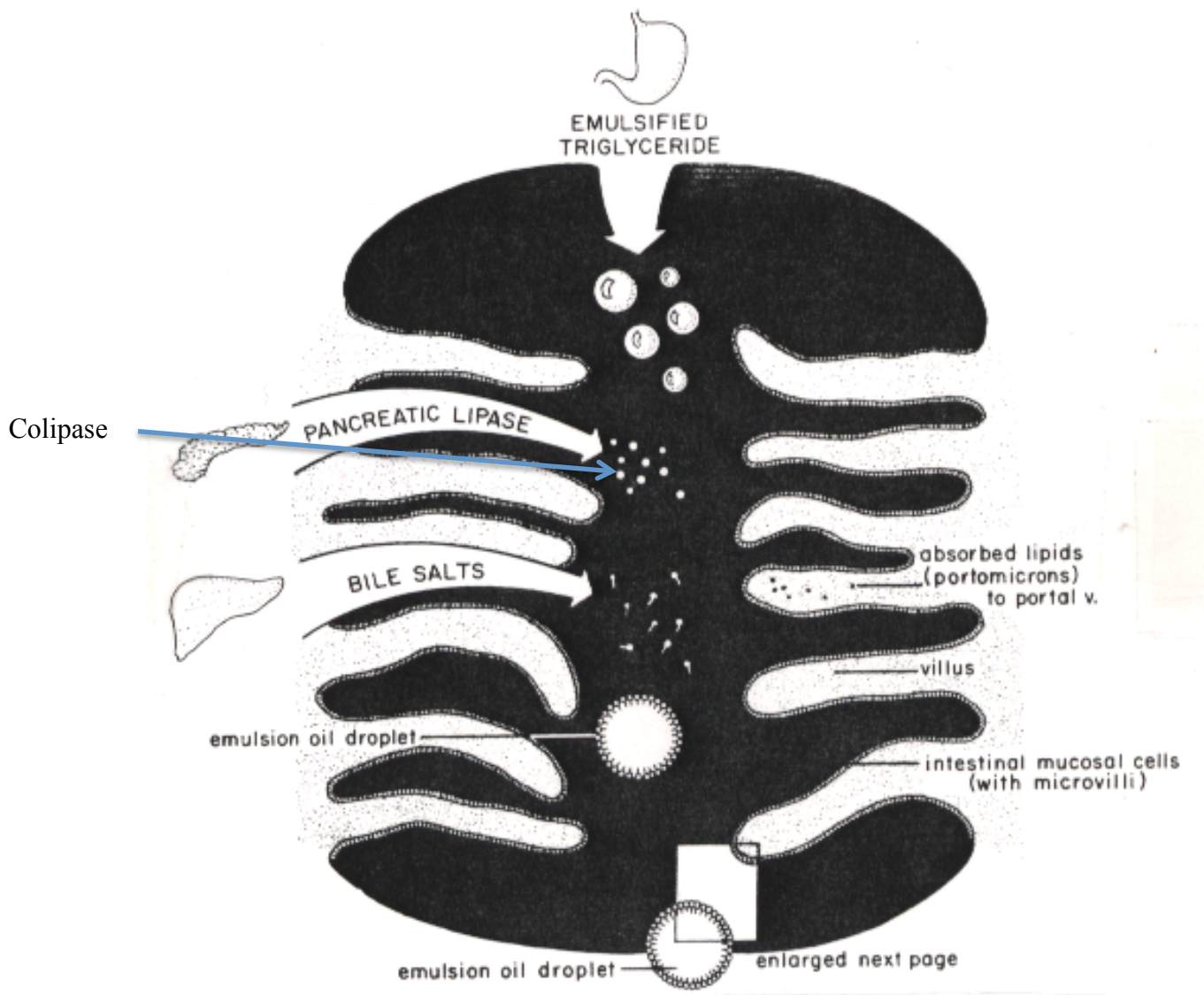
a. The gall bladder contains 40 to 70 mL.

b. The gall bladder releases approximately 700 mL/d (extensive recirculation).

2. Secretion of pancreatic digestive enzymes (approximately 1,200 mL/d).

a. Pancreatic lipase

b. Colipase (activates lipase in the presence of bile salts)

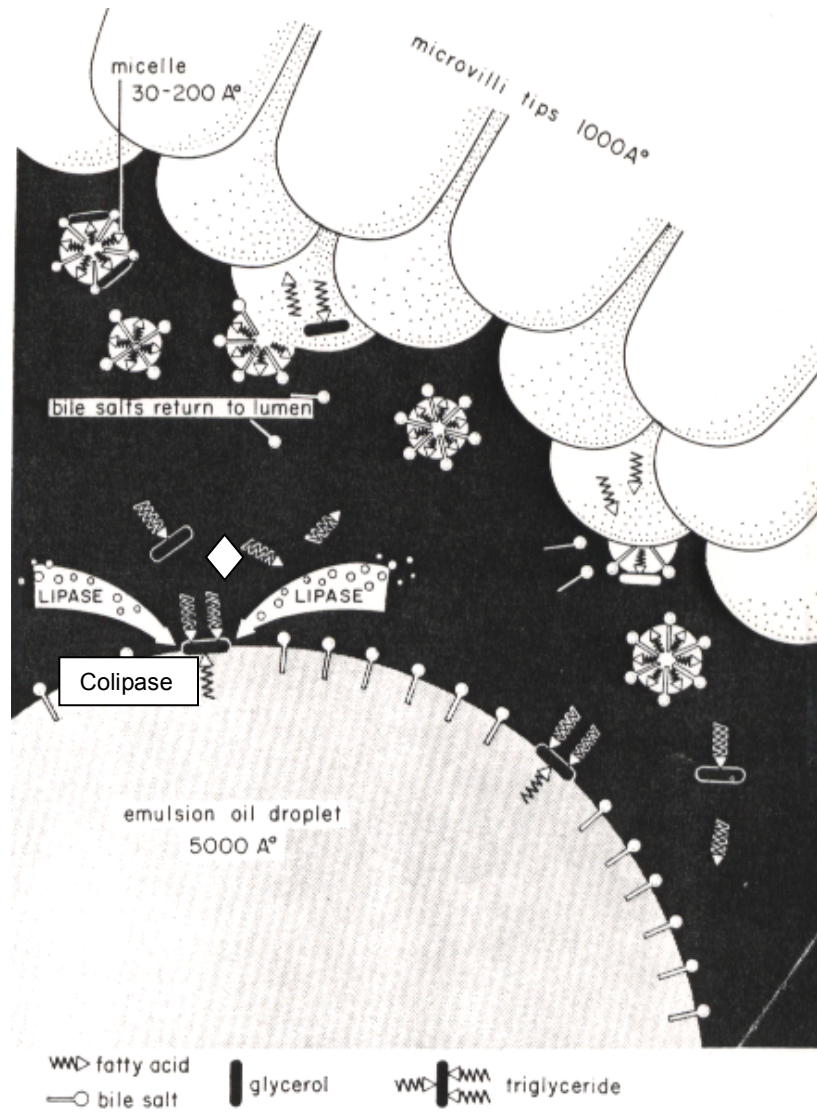


B. Functions of bile acids

1. Emulsification of fats, leading to increased surface area of fats.
2. Activation of pancreatic lipase (at low concentrations).
3. Formation of mixed micelles.

C. Emulsification by bile salts

1. Bile acids and glycine or taurine conjugates serve as detergents.
2. Bile salts cause the formation of triacylglycerol particles of 1 μm or less (which greatly increases surface area).
3. Other emulsifiers: phospholipids (especially lysolecithin [lysophosphatidyl choline]) and 2-monoacylglycerols.



D. Hydrolysis of dietary fat by pancreatic lipase

1. Pancreatic lipase works at lipid-water interface.
2. Pancreatic lipase is activated by bile salts at low concentrations.
3. Inhibited by bile salts at high concentrations.
4. Co-lipase:
 - a. Secreted by pancreas with lipase.
 - b. Binds to bile salt micelles.
 - c. Reduces inhibitory action of bile salts on pancreatic lipase.
5. Pancreatic lipase hydrolyzes TAG to fatty acids and 2-monoacylglycerol (**2-MAG**).

III. Absorption from small intestine**A. Formation of mixed micelles**

1. Mixed micelles *are not small chylomicrons*.
2. Mixed micelles are 4-6 nm in diameter.
3. Formed when bile salts and fatty acids reach a critical micellar concentration (2 – 5 mM for bile salts).
4. Mixed micelles incorporate 2-MAGs, lysolecithin, cholesterol, and long-chain fatty acids.

B. Absorption into the enterocytes (intestinal mucosal cells).

1. 2-MAG, lyso-phospholipids, FAs, and cholesterol dissociate at the surface of the mucosal cells.
2. Produce locally high concentrations of 2-MAG, lyso-phospholipids, and fatty acids.
3. These are absorbed by the epithelial cells of the *duodenum* and *proximal jejunum*.

C. Bile salts

1. Bypass the duodenum and jejunum.
2. Bile salts are reabsorbed almost entirely in the ileum (*water soluble*).

IV. Synthesis of TAG and phospholipids in enterocytes**A. Triacylglycerols**

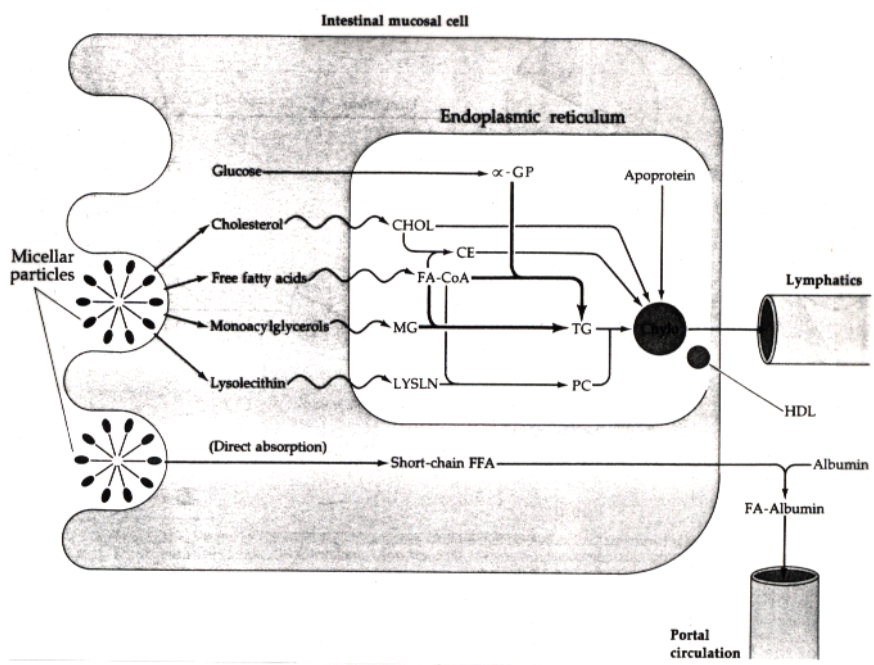
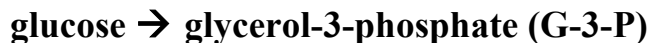
1. 75% of TAGs are synthesized via the 2-monoacylglycerol pathway *located on the smooth endoplasmic reticulum*.



($\rightarrow 2\text{P}_i$; This pulls the reaction to the right.)



2. 25% of TAGs are synthesized via the standard TAG biosynthetic pathway *located on the rough endoplasmic reticulum*.



B. Phospholipids

1. Phosphatidylcholine (lecithin)



2. Others – Phosphatidylethanolamine, phosphatidyl serine

C. Cholesterol esters: $\text{Cholesterol} + \text{FACoA} \rightarrow \text{Cholesterol ester}$

V. Chylomicrons

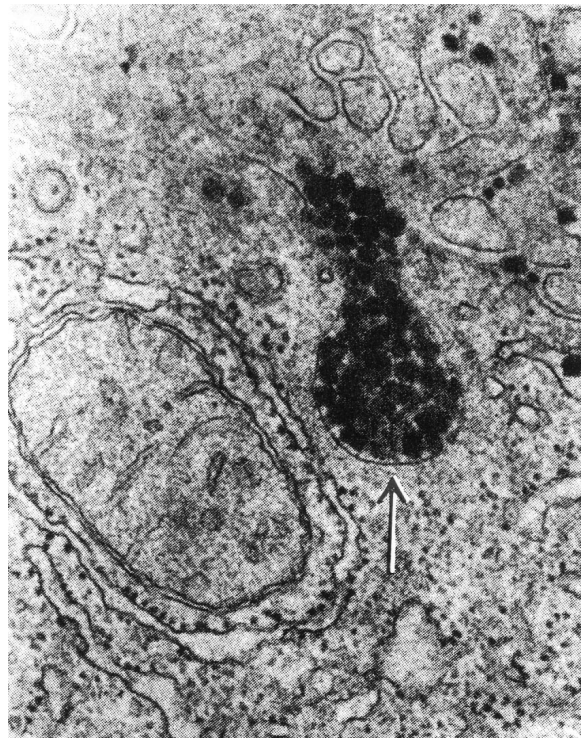
A. Synthesis

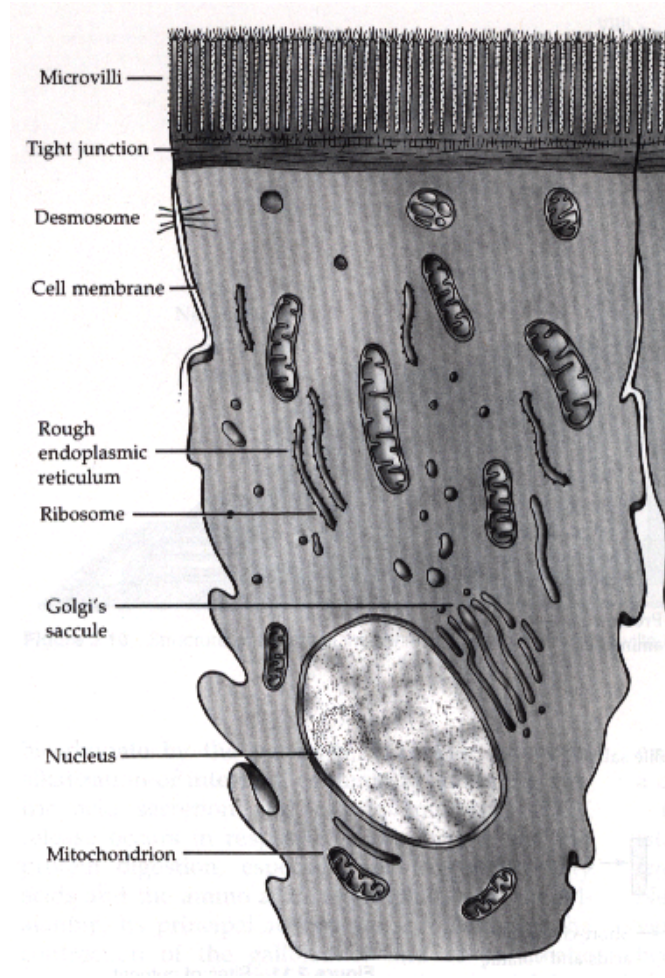
1. Lipid droplets form within the endoplasmic reticulum and Golgi apparatus.
2. Lipid droplets contain TAG, phospholipid, cholesterol, cholesterol ester, and apolipoprotein (with carbohydrate) complexes.
 - a. Apolipoproteins and phospholipids are formed in the rough endoplasmic reticulum.
 - b. TAG are formed in the smooth endoplasmic reticulum and are transferred to ApoB₄₈ to form a developing core for the chylomicron.
 - c. After accumulating TAG and CE, Golgi vesicles form and carbohydrate moieties are added to the apolipoproteins.
2. Golgi vesicles fuse with the cell membrane and are extruded into the lacteals.
3. Chylomicrons are transported via the lymphatics to the subclavian vein.

B. Composition

- 70 – 90% TAG
- 4 – 8% phospholipid
- 3% cholesterol
- 4% cholesterol ester
- 2% protein (apolipoprotein B)

(The figure at right is actually a micrograph of liver, showing subcellular structures and lipoprotein particles (VLDL), which are similar to chylomicrons.)





VI. Cholesterol absorption

A. Sources of cholesterol in the small intestine

1. **Dietary:** In humans, this accounts for 0.4 - 0.5 g/d.
2. **Biliary:** 20 to 30 g bile salts enter the small intestine daily (4 to 5 g are recycled 5 to 6 times). Also, cholesterol and cholesterol ester enter the small intestine via the bile.
3. **Intestinal mucosa:** A minor contributor to total cholesterol intake.
4. **Ruminal microflora:** A minor contributor to total cholesterol intake in sheep and cattle.

B. Mechanism of absorption from the small intestine

1. Cholesterol esters are hydrolyzed by pancreatic cholesterol esterases.
2. Free cholesterol is incorporated into mixed micelles. (In the absence of bile acids cholesterol absorption is negligible.)
3. Free cholesterol is absorbed into the intestinal mucosal cells and re-esterified to form cholesterol esters.

C. Sources of loss of cholesterol from the dietary tract

1. Bile salts
 - a. 0.8 g/d bile salts are lost in the feces.
 - b. The remainder (98 - 99%) is taken up in the ileum (enterohepatic circulation).
2. Cholesterol: cholesterol is poorly absorbed.
 - a. Approximately 0.4 g/d lost in the feces
 - b. Only 30 to 60% dietary plus biliary cholesterol absorbed.
 - c. Increased cholesterol intake results in a **greater amount** of cholesterol absorbed, but a **lesser percentage** absorbed.
3. Plant sterols
 - a. 200 to 300 mg/d are ingested.
 - b. Plant sterols are absorbed only in trace amounts.
 - c. In large amounts, plant sterols inhibit cholesterol absorption (mechanism unknown).
4. 0.2 to 0.4 g/d of cholesterol is lost as sloughed skin.

