

BIOC 801 - Dr. Tischler
Lecture 28 – March 23, 2005

LIPIDS: DIGESTION AND ABSORPTION

Tucson



FAT FACTS

- Fat (lipid) makes up 37% of the calories in the American diet
- Fat is energy rich and provides 9 kcal/gm
- Dietary lipids are 90% triacylglycerols; also include cholesterol esters, phospholipids, essential unsaturated fatty acids; fat soluble vitamins (A,D,E,K)
- Normally essentially all (98%) of the fat consumed is absorbed, and most is transported to adipose for storage.

SIX STEPS OF LIPID DIGESTION AND ABSORPTION

- + **Minor digestion** of triacylglycerols in mouth and stomach by lingual (acid-stable) lipase
- + **Major digestion** of all lipids in the lumen of the duodenum/jejunum by pancreatic lipolytic enzymes
- + **Bile acid** facilitated formation of *mixed micelles* that present the lipolytic products to the mucosal surface, followed later by enterohepatic bile acid recycling
- + **Passive absorption** of the lipolytic products from the mixed micelle into the intestinal epithelial cell
- + **Reesterification** of 2-monoacylglycerol, lysolecithin, and cholesterol with free fatty acids inside the intestinal enterocyte
- + **Assembly and export** from intestinal cells to the lymphatics of chylomicrons coated with Apo B48 and containing triacylglycerols, cholesterol esters and phospholipids

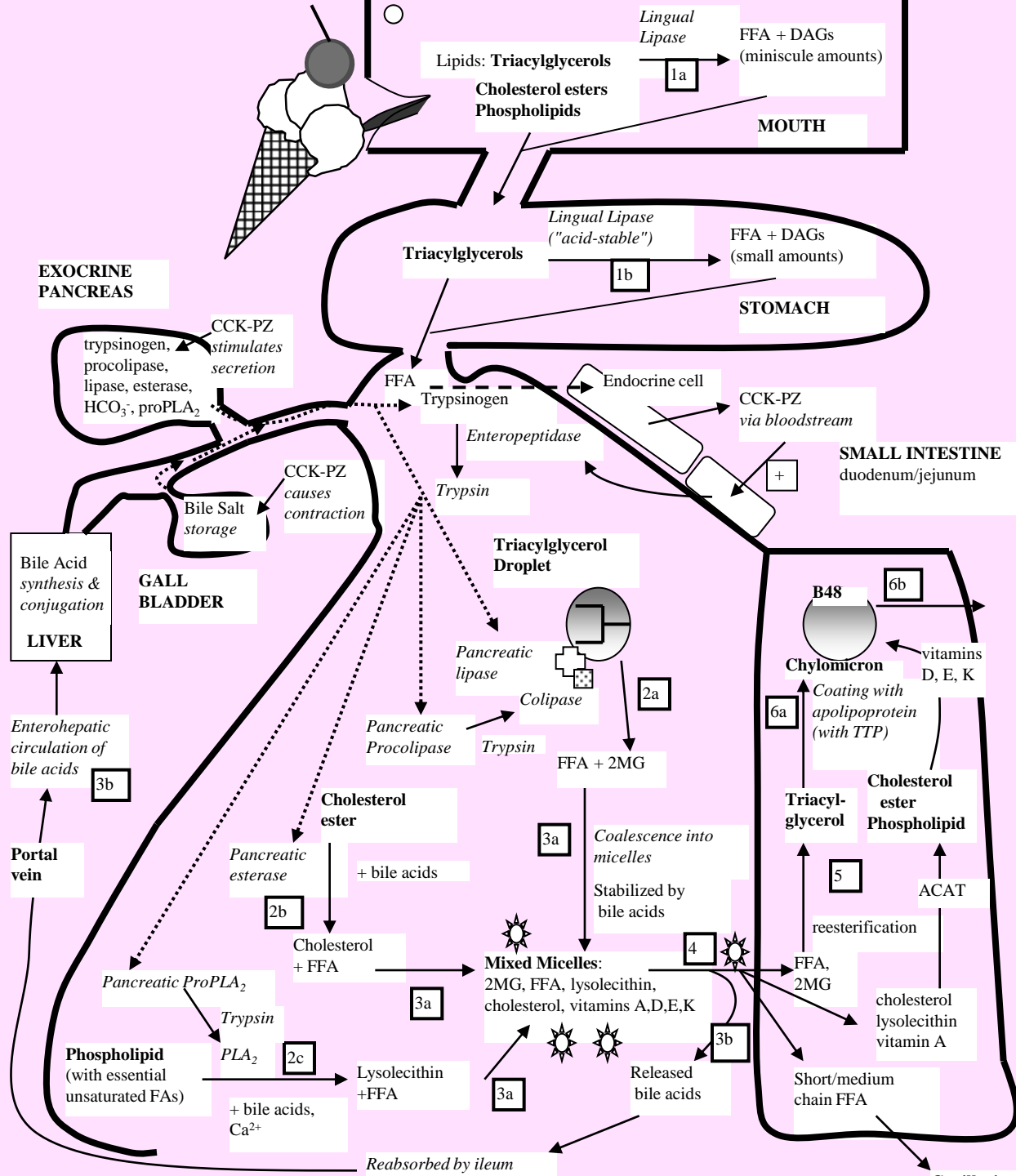
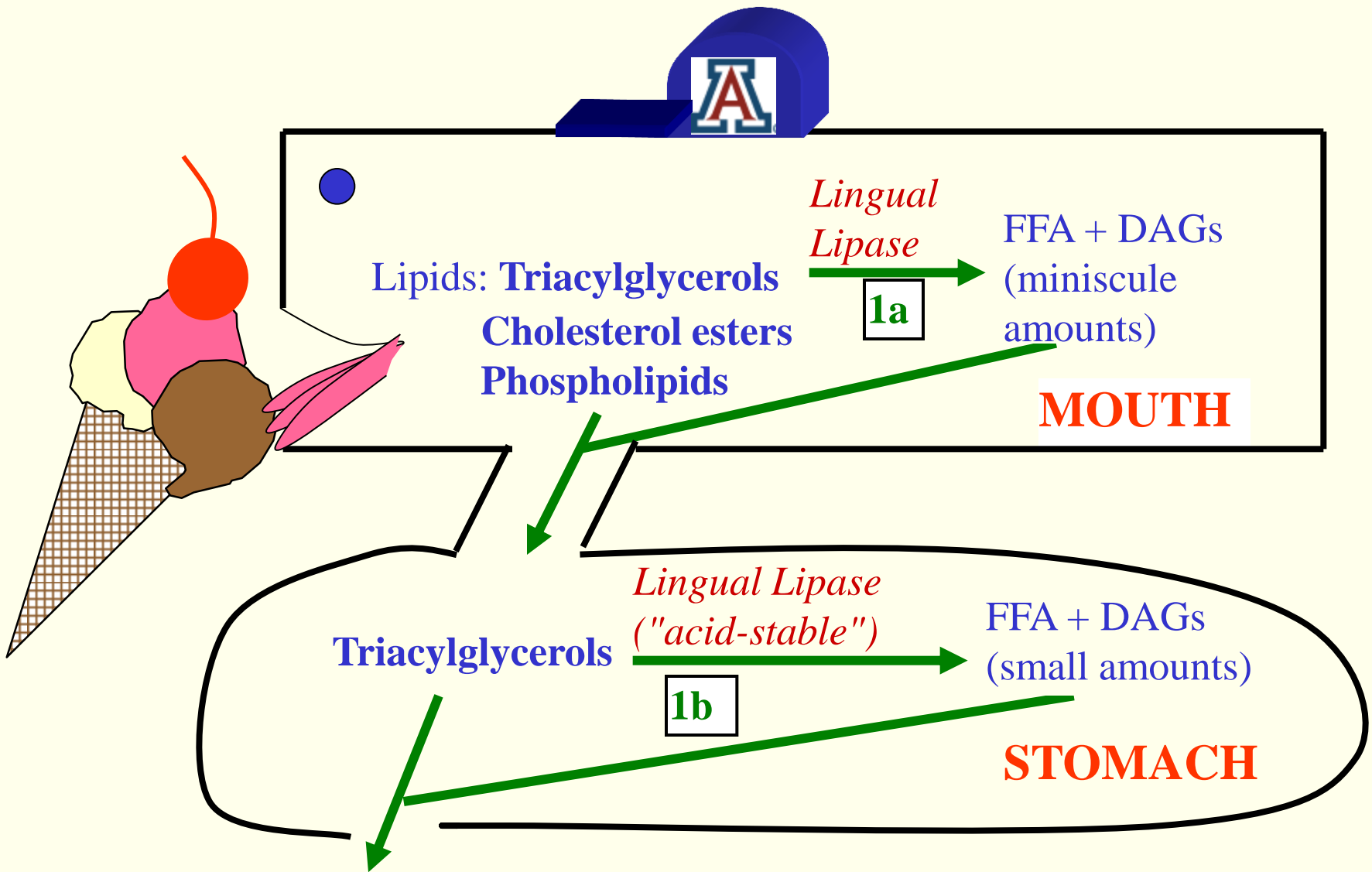


Table 1. Summary of the physiologically important lipases

Lipase	Site of Action	Regulation	Preferred Substrate	C cleaved	Product(s)
lingual/acid-stable lipase	mouth, stomach	----	TAGs with med. chain FAs	3	FFA+DAG
pancreatic lipase	small intestine	colipase (+)	TAGs with long-chain FAs	1 and 3	FFA+2MG
milk lipase	small intestine	bile acids (+)	TAGs with med. chain FAs	1 and 2 and 3	FFA+ glycerol
phospholipase A₂ (PLA₂)	small intestine	bile acids (+) Ca²⁺ (+)	PLs with unsat. FA on position 2	2	Unsat FFA lysolecithin
lipoprotein lipase	capillary walls	apo CII (+) insulin (+)	TAGs in chylo-micron or VLDL	1 and 2 and 3	FFA+ glycerol
Hormone-sens. Lipase	adipose cell	insulin (-) glucagon (+) Epineph. (+)	TAG stored in adipose cells	3	FFA+DAG



STEP 1: Digestion in the Mouth and Stomach

**EXOCRINE
PANCREAS**

*CCK-PZ
stimulates
secretion*

from stomach

trypsinogen,
procolipase,
lipase, esterase,
 HCO_3^- , proPLA₂

FFA

**Endocrine
cell**

**CCK-PZ
via bloodstream**

Trypsinogen

**SMALL
INTESTINE
duodenum/jejunum**

Bile Salt
storage

Bile Acid
Synthesis
Conjugation
LIVER

**GALL
BLADDER**

**Pancreatic
lipase**

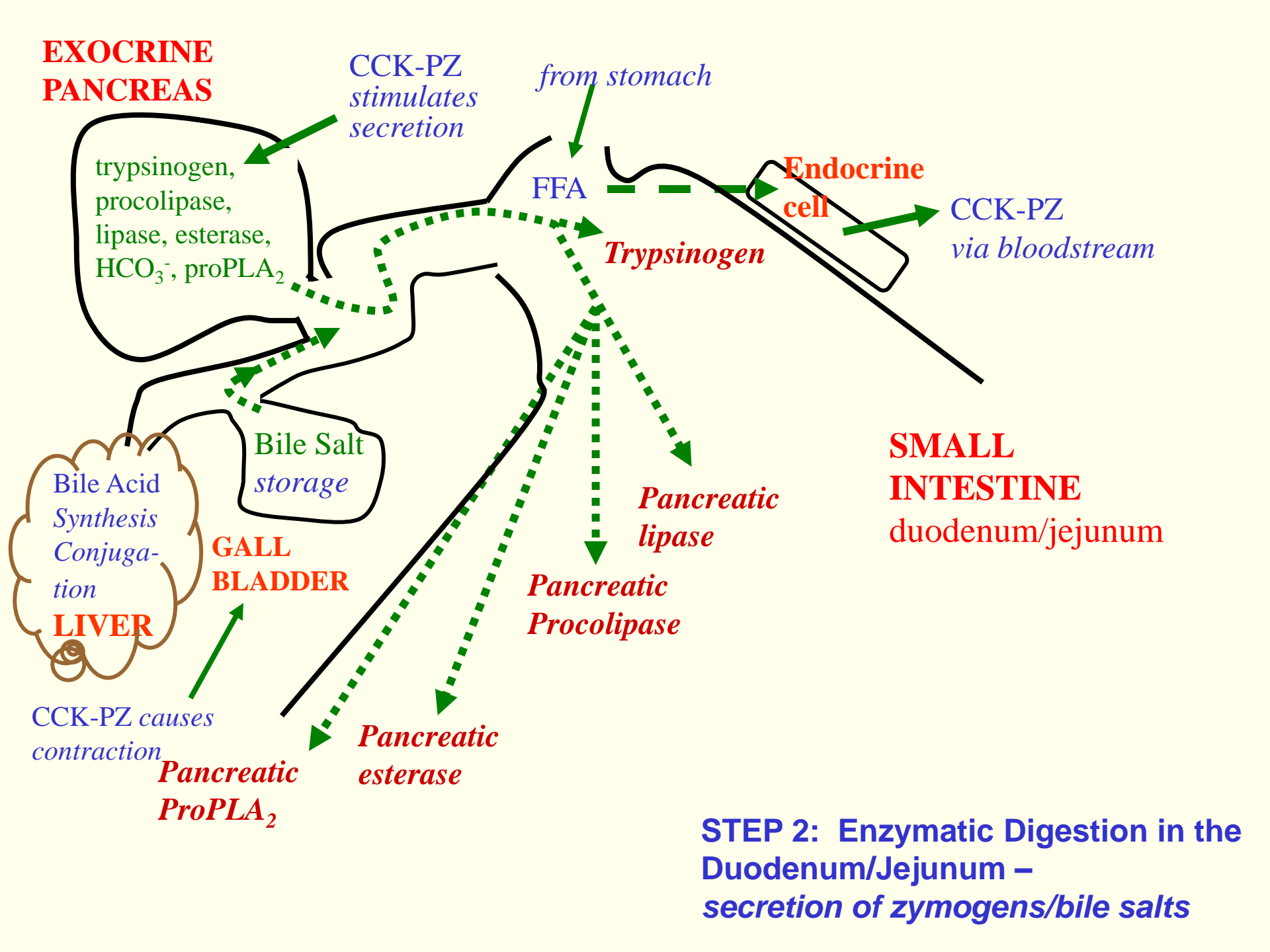
**Pancreatic
Procolipase**

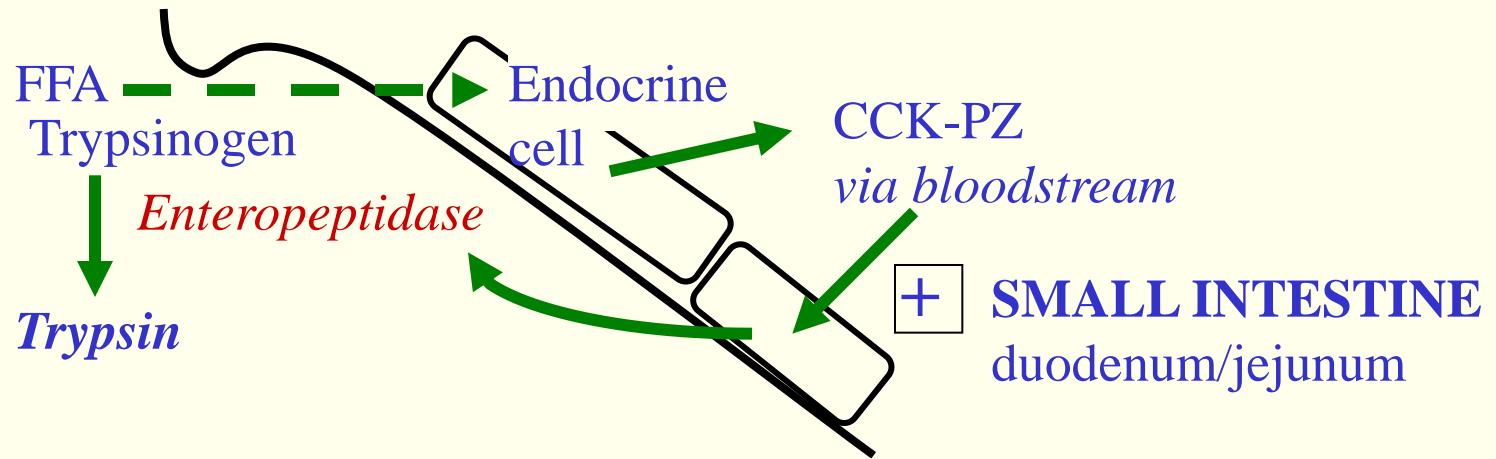
**Pancreatic
esterase**

**Pancreatic
ProPLA₂**

*CCK-PZ causes
contraction*

**STEP 2: Enzymatic Digestion in the
Duodenum/Jejunum –
secretion of zymogens/bile salts**





**STEP 2: Enzymatic Digestion in the Duodenum/Jejunum –
*activation of trypsinogen***

Triacylglycerol Droplet

Pancreatic lipase

Pancreatic Procolipase

Colipase

Trypsin catalyzed activation

FFA + 2MG

2a

2b

Cholesterol ester

Pancreatic esterase

+ bile acids

Cholesterol + FFA

Pancreatic ProPLA₂

Trypsin catalyzed activation

2c

Phospholipid
(with essential unsaturated FAs)

PLA₂

+ bile acids, Ca²⁺

Lysolecithin + FFA

STEP 2: Enzymatic Digestion in the Duodenum/Jejunum – pancreatic lipase (2a), esterase (2b) and phospholipase A₂ (2c)

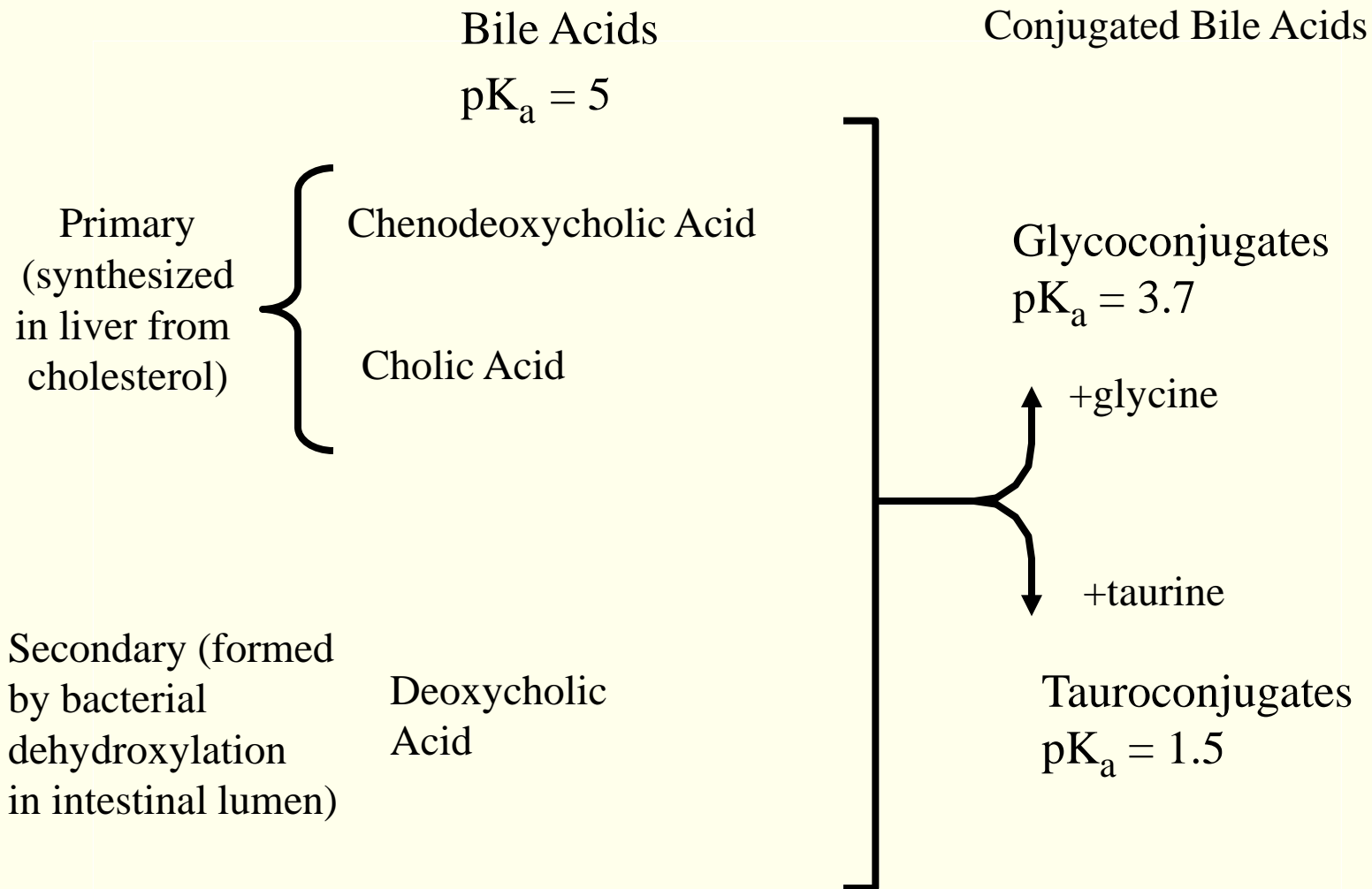
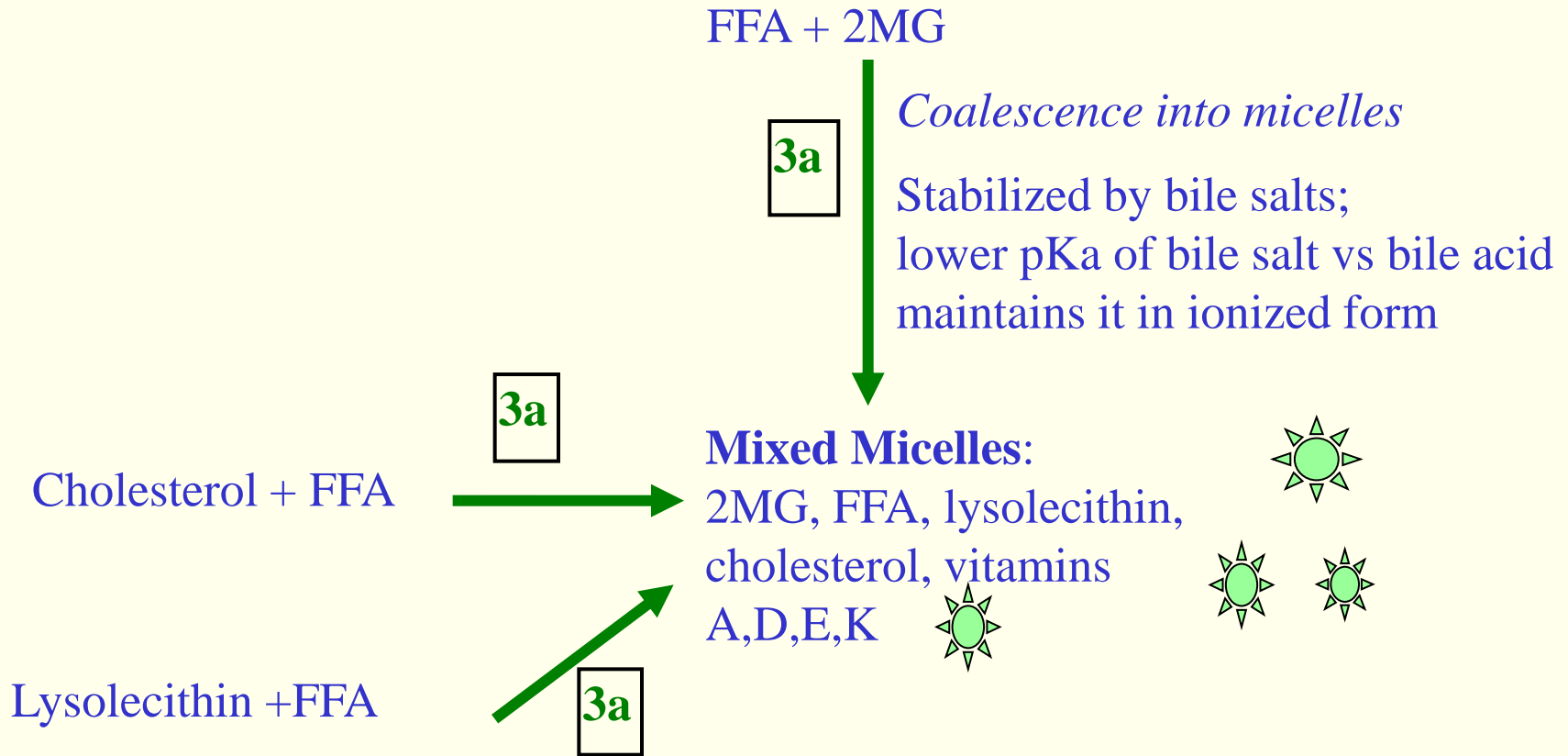
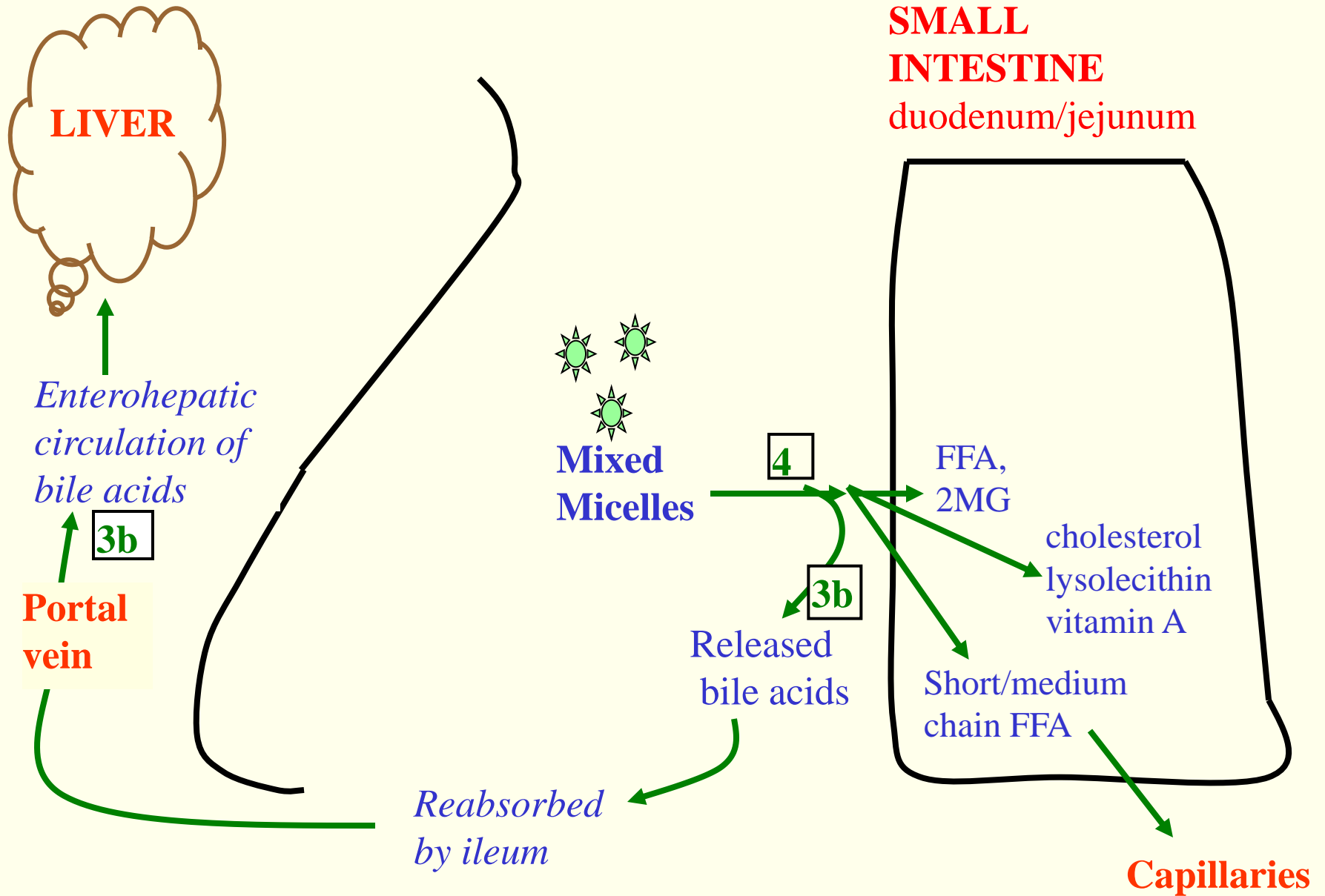


Figure 2. Bile acids. The pK_a is lowered by formation of conjugates in liver. Conjugated acids more easily remain ionized in the intestine.



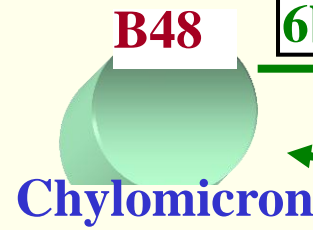
STEP 3a: Bile Acid Facilitated Formation of Mixed Micelles



STEP 3b: Bile Acid Recycling
STEP 4: Lipid Absorption

**SMALL
INTESTINE**
duodenum/jejunum

Triacylglycerol
transfer protein



To lacteals and
thoracic duct

vitamins
D, E, K

6a *Coating with
apolipoprotein
(with TTP)*

**Triacyl-
glycerol**

**Cholesterol
ester
Phospholipid**

5
reesterification

ACAT

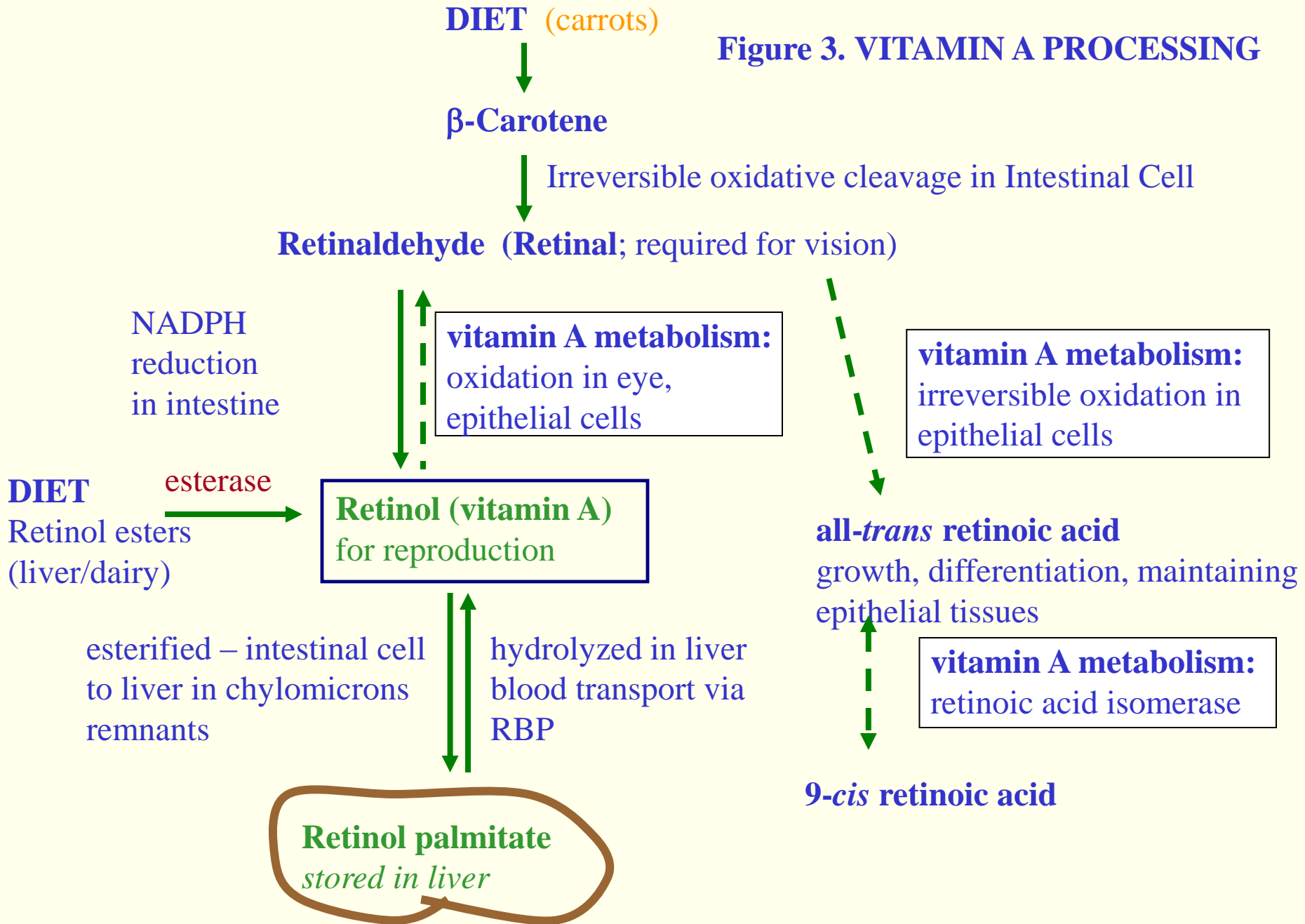
Acyl CoA:
cholesterol acyl
transferase

FFA,
2MG

cholesterol
lysolecithin
vitamin A

STEP 5: Re-esterification
**STEP 6: Chylomicron Assembly
and Export**

Figure 3. VITAMIN A PROCESSING



CLINICAL CORRELATES

Orlistat (Xenical)

- anti-obesity drug
- inhibits pancreatic and gastric lipase
- blocks about 30% of dietary fat from digestion and absorption

Olestra

- artificial fat
- chemical structure is a sucrose polyester esterified with 8 fatty acids
- not digested by gastric or pancreatic lipases (or sucrase)
- passes through the system undigested and unabsorbed
- **in excess interferes with absorption of fat-soluble vitamins**