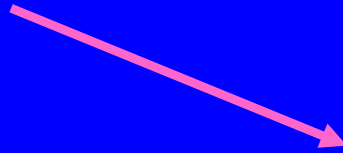
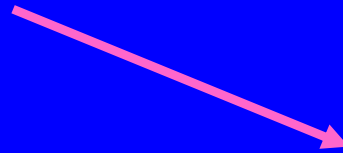


# Steps in Processing Dietary Lipids

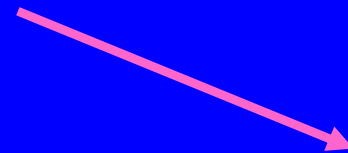
**Emulsification**



**Hydrolysis**

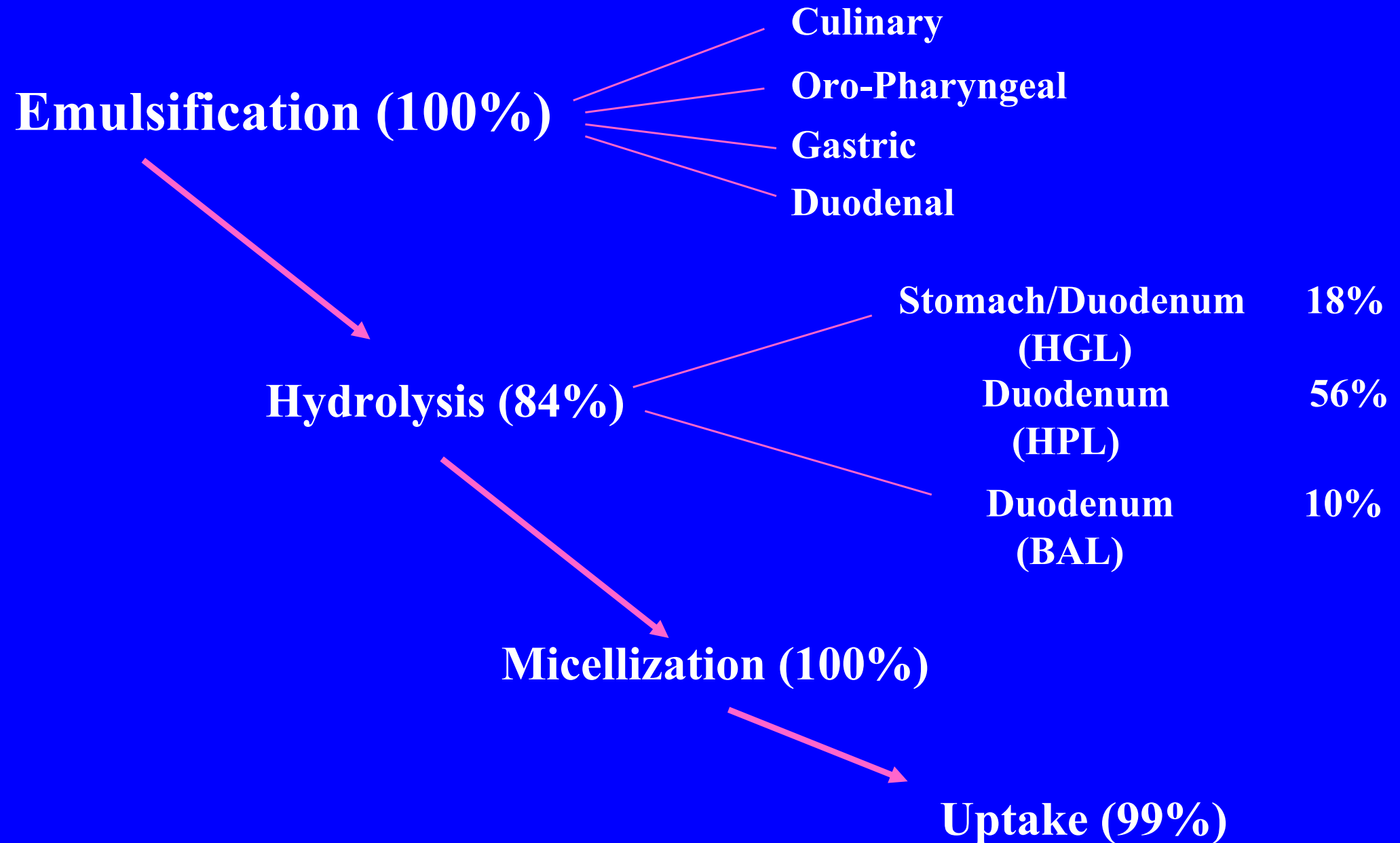


**Micellization**

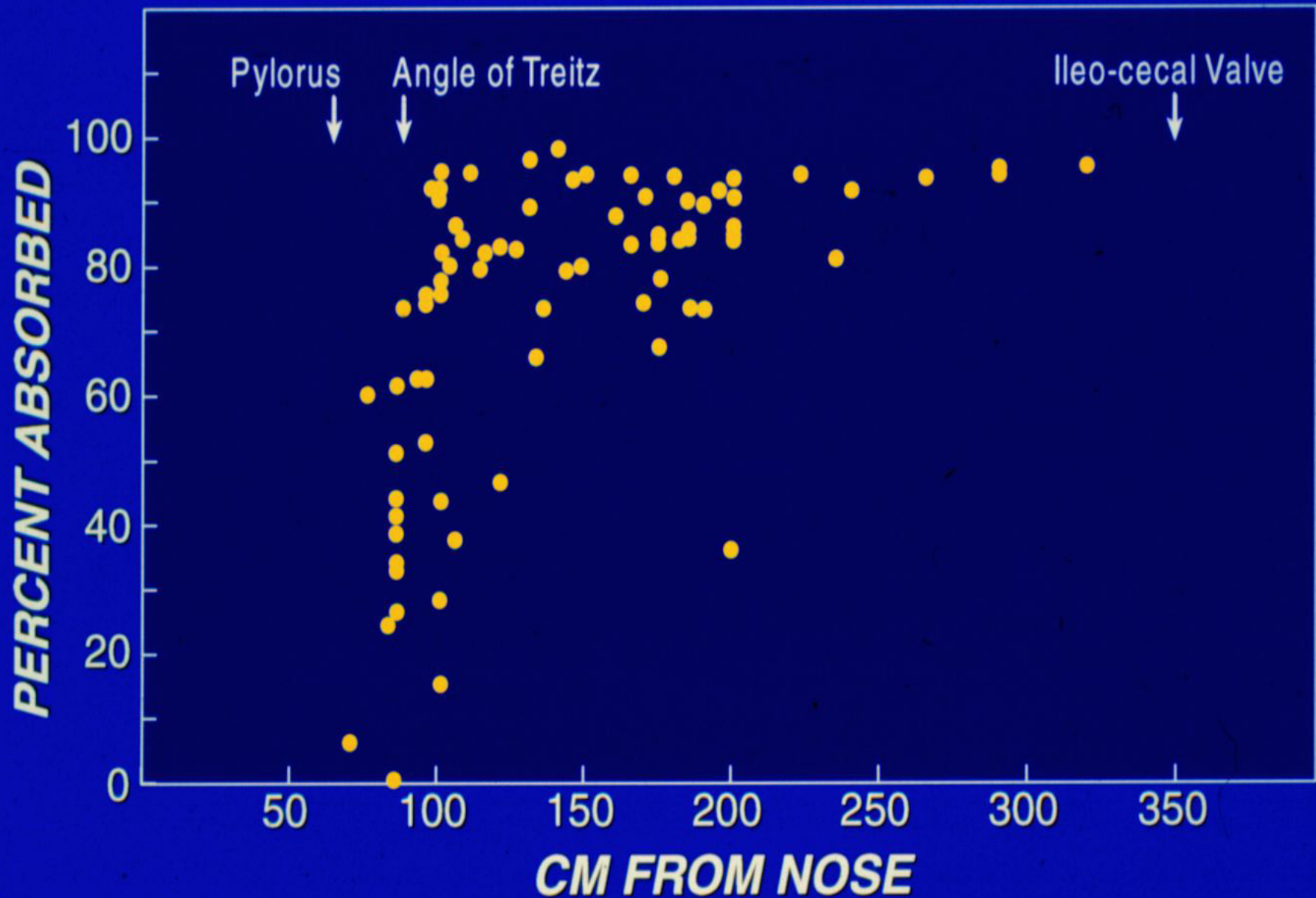


**Uptake**

# Absorption Efficiency of Dietary Lipids

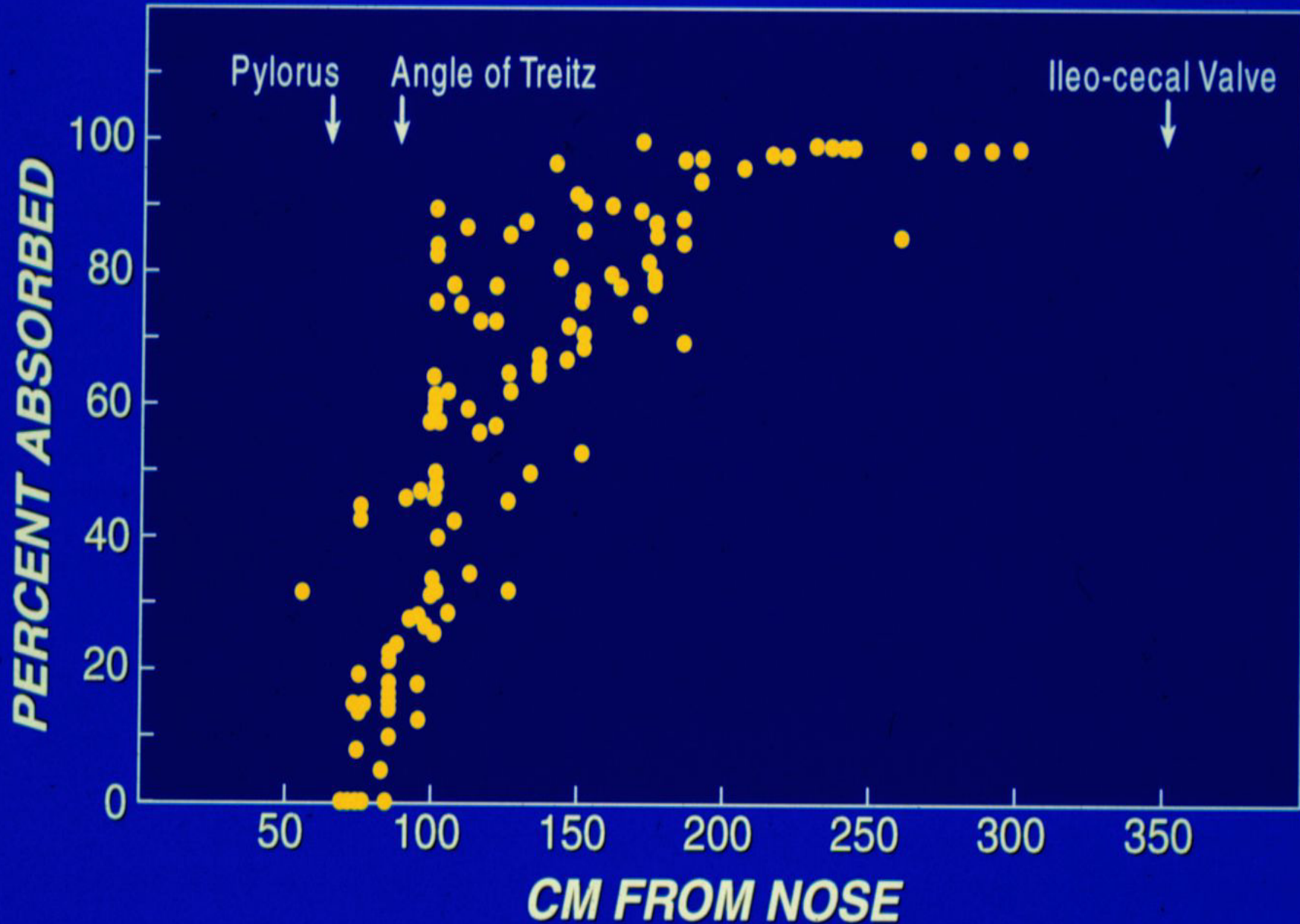


# ABSORPTION OF FAT OVER LENGTH OF HUMAN SMALL INTESTINE



Adapted from: Figure 2 in Borgstrom, B., et al. "Studies of Intestinal Digestion and Absorption in the Human." *J Clin Invest* 36 (1957): 1525.

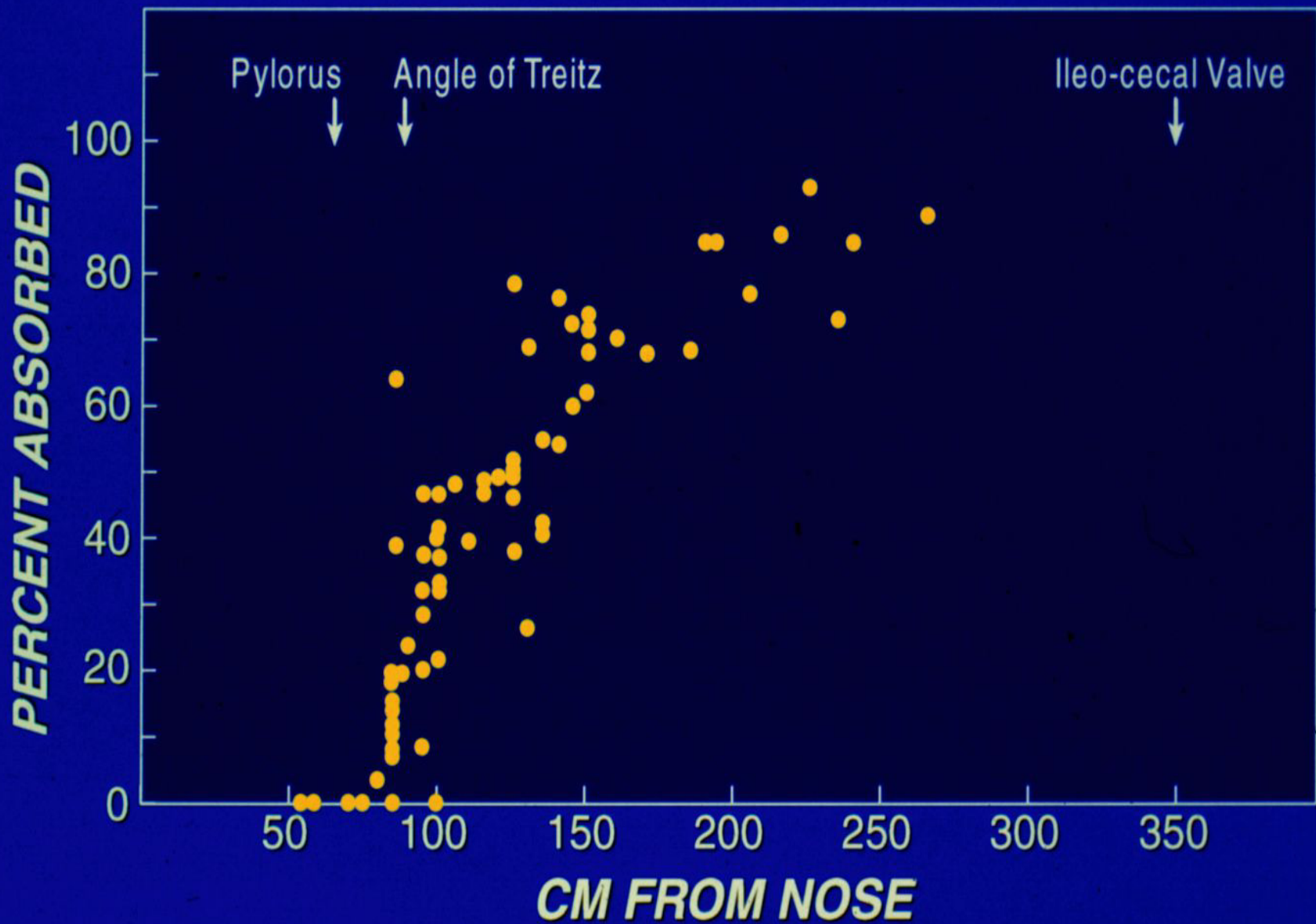
# ABSORPTION OF CARBOHYDRATE OVER LENGTH OF HUMAN SMALL INTESTINE



Adapted from: Figure 2 in Borgstrom, B., et al. "Studies of Intestinal Digestion and Absorption in the Human." *J Clin Invest* 36 (1957): 1525.



# ABSORPTION OF PROTEIN OVER LENGTH OF HUMAN SMALL INTESTINE

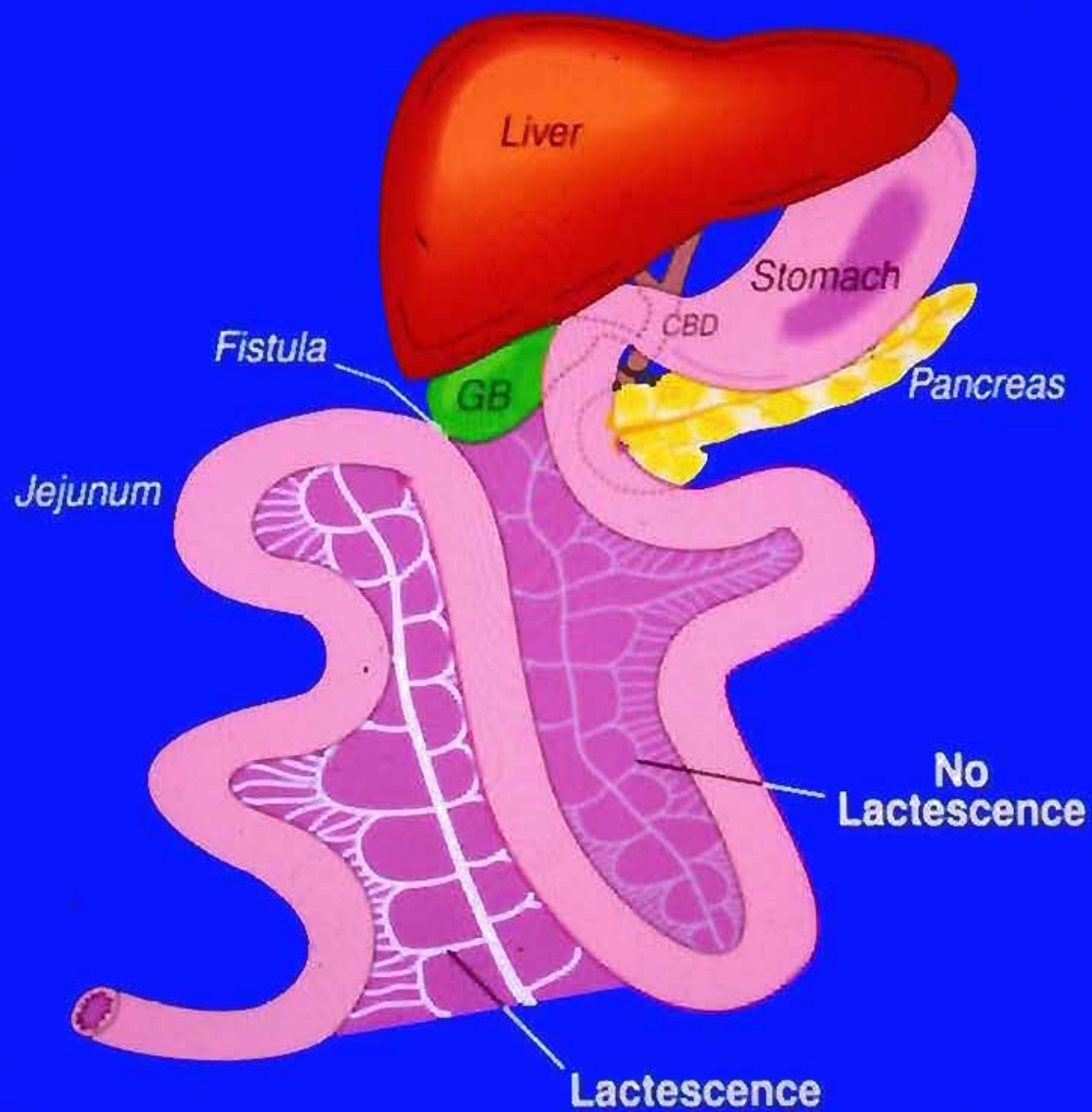


Adapted from: Figure 2 in Borgstrom, B., et al. "Studies of Intestinal Digestion and Absorption in the Human." *J Clin Invest* 36 (1957): 1525.

Figure removed due to copyright reasons. Please see:

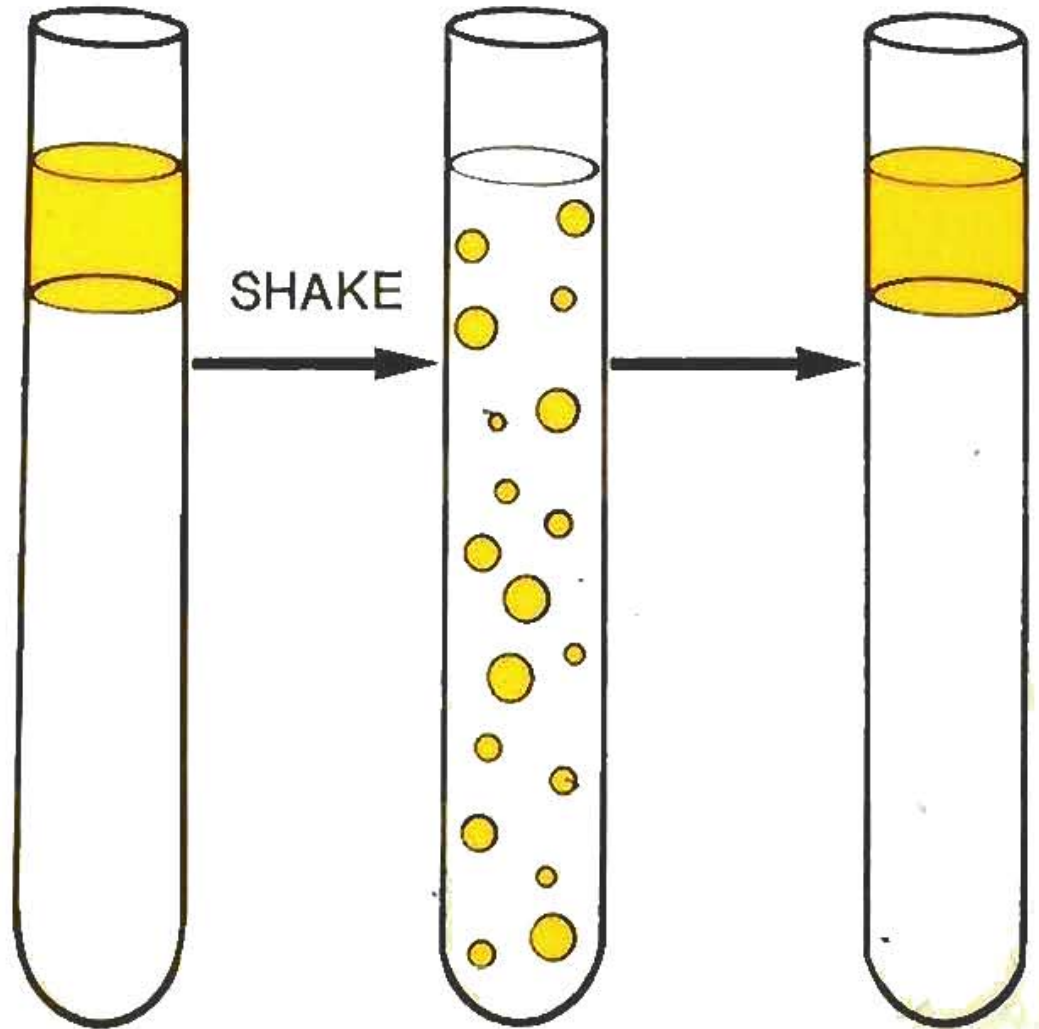
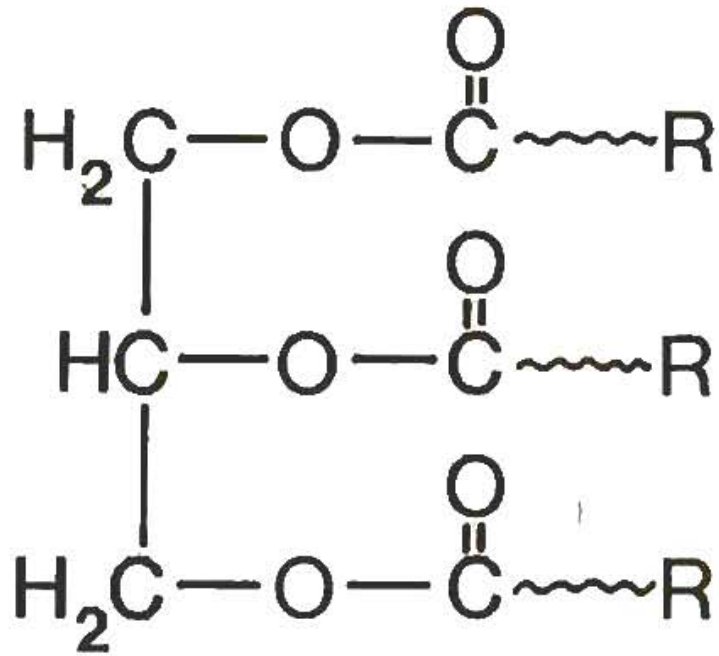
Claude Bernard's *Memoire sur le Pancreas*, Bailliére, Paris, 1856, color plate No. 7-8.

# CANINE FAT ABSORPTION WITH CHOLECYSTO-INTESTINAL FISTULA



# DIETARY FAT

95% TG





# FAT DIGESTION

## 24 HR. INPUT-OUTPUT BALANCE

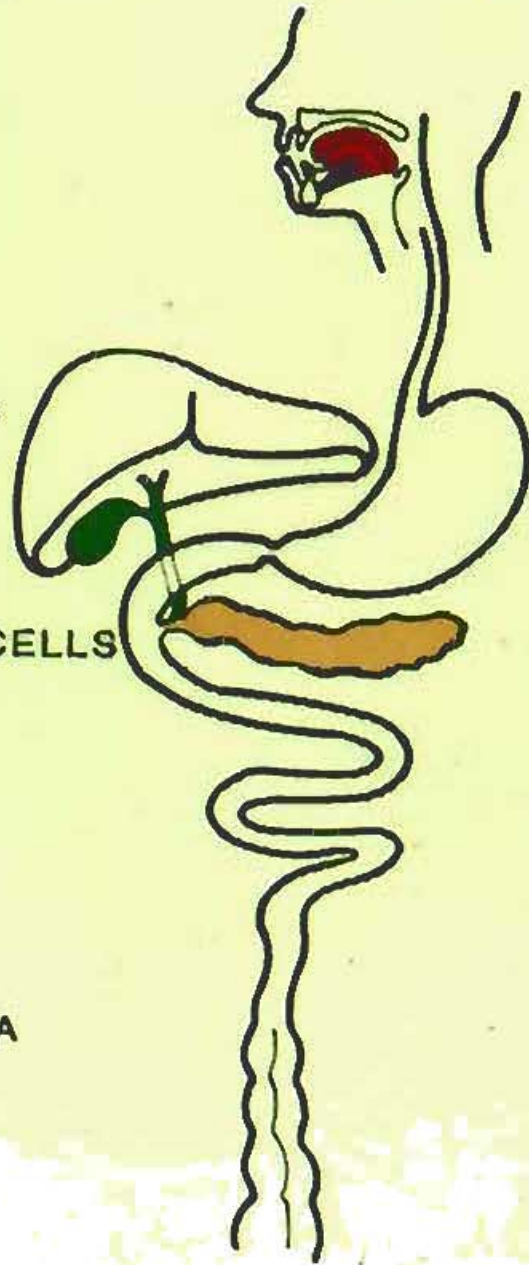
DIETARY FAT  
100 g IN

BILIARY LIPIDS  
30g BILE SALTS  
10-15g P'LIPIDS  
1-2g CHOL.

DESQUAMATED CELLS  
2-6g LIPIDS

DEAD BACTERIA  
10g LIPIDS

FECAL FAT  
4g OUT



TONGUE

ESOPHAGUS

STOMACH

BILIARY TREE

DUODENUM

PANCREAS

JEJUNUM

ILEUM

COLON

# PHYSICAL STATES OF MAJOR DIETARY LIPIDS

Figure removed due to copyright reasons. Please see:

Figure 1 in Carey, M. C., D. M. Small, and C. M. Bliss. "Lipid Digestion and Absorption." *Annual Review of Physiology* 45 (1983): 651-677.

SOURCES OF CHOLESTEROL  
ENTERING THE  
GASTROINTESTINAL TRACT

	<u>MG/D</u>	<u>%</u>
DIET	300-500	20
BILE	720-1920	65
CELLS	<u>180-480</u>	15
	1200-2900	

# **For Effective Hydrolysis...**

**Dietary fats must be dispersed  
as stable emulsion particles**

# DISPERSED STATES OF MAJOR DIETRY LIPIDS IN WATER

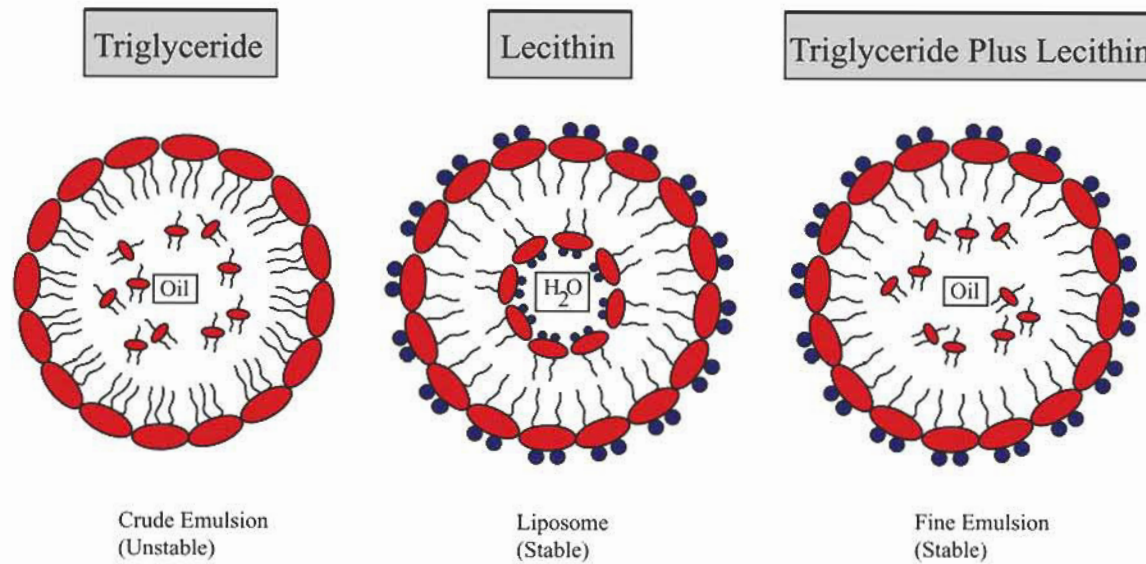
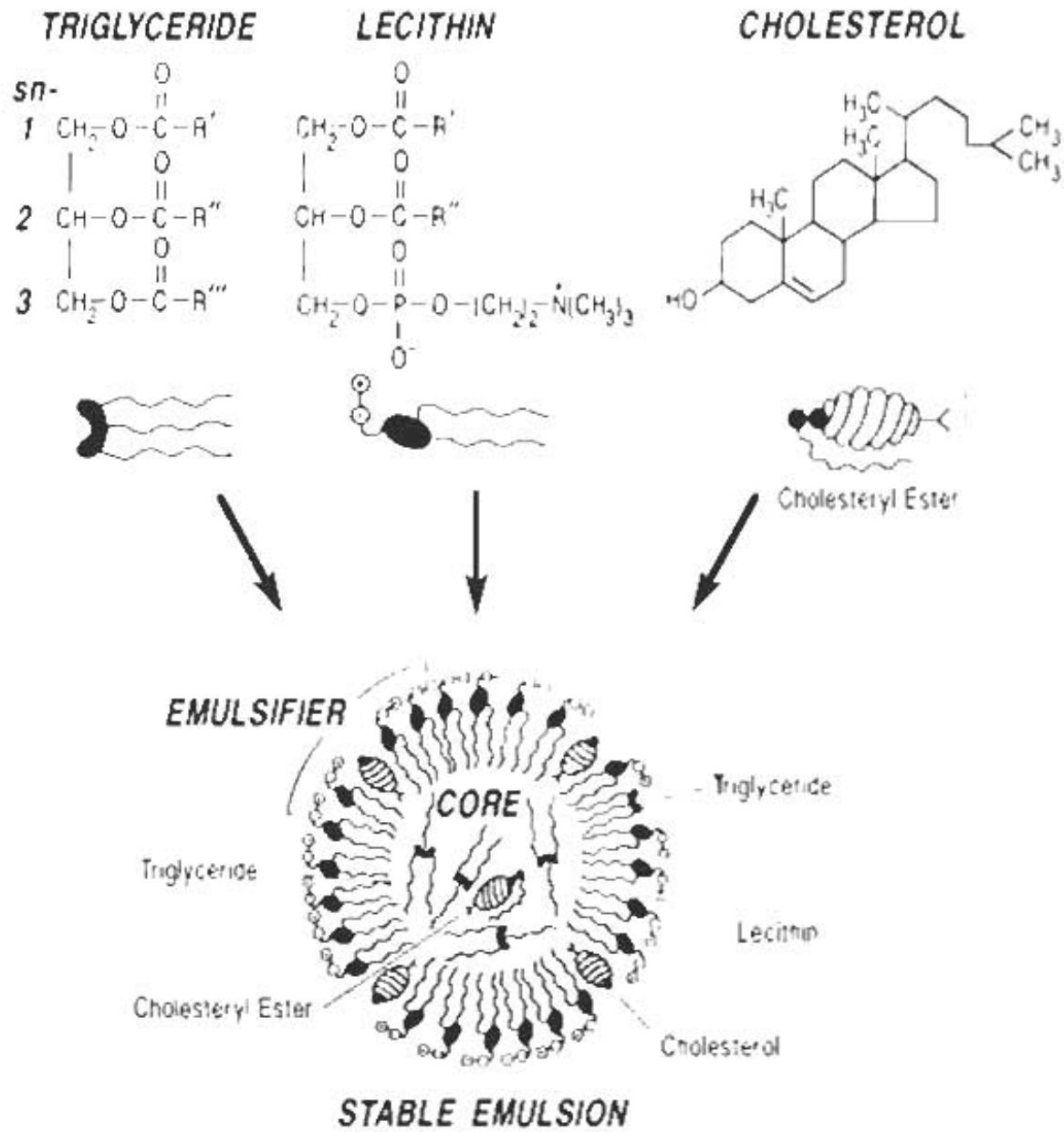


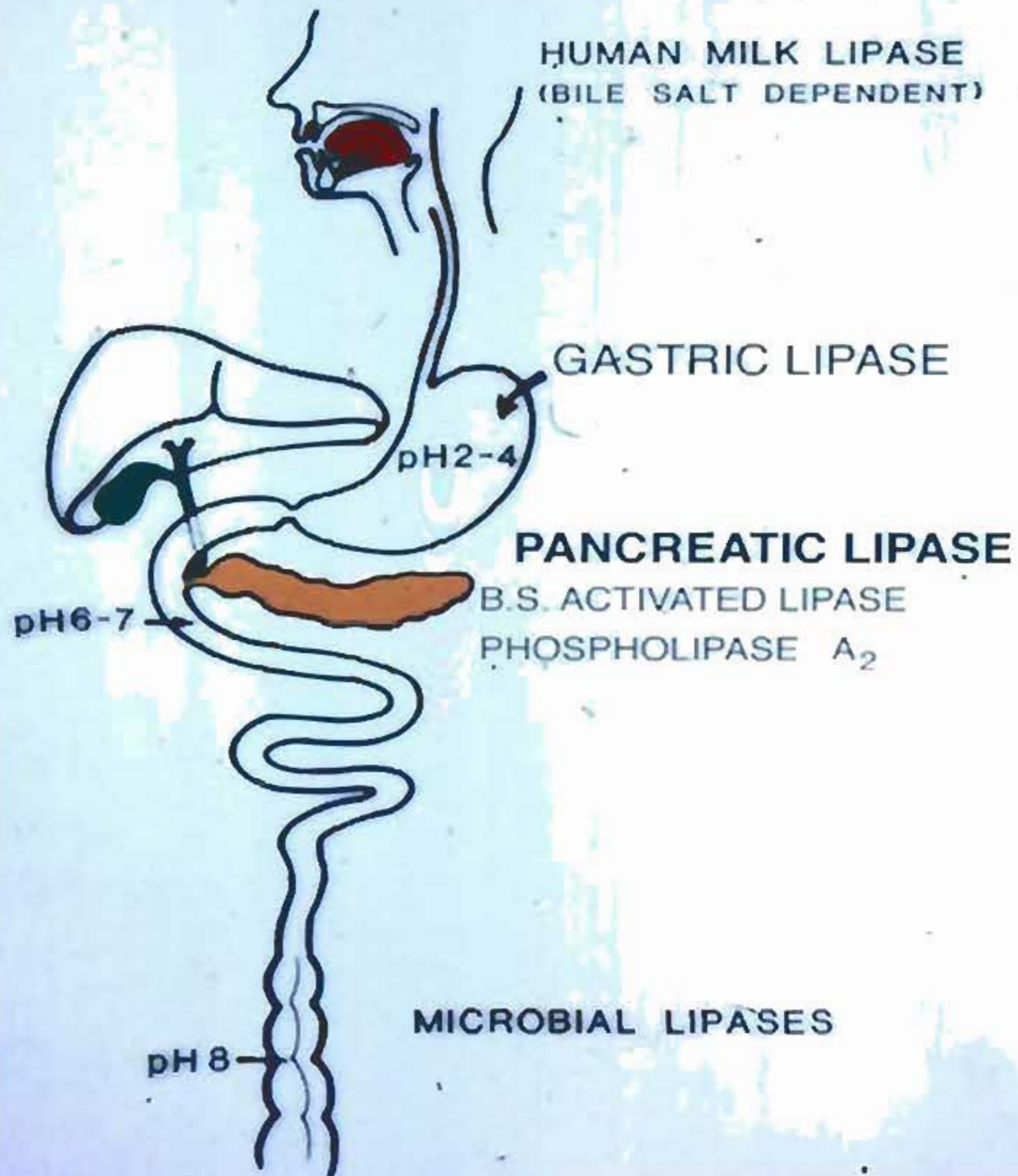
Figure by MIT OCW.



# DIETARY LIPIDS AND INTRALUMINAL PHYSICAL STATE



# FAT DIGESTION : THE LIPASES

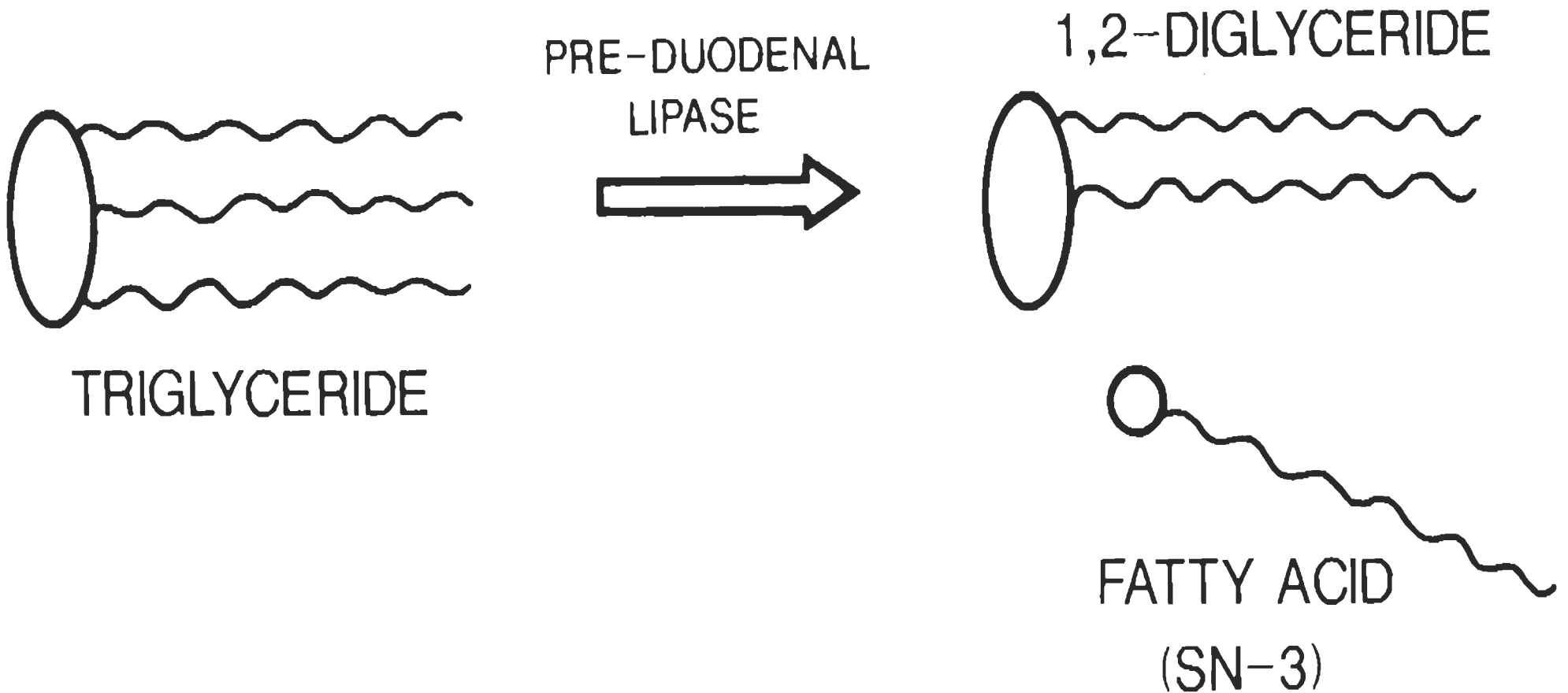


# **Humans:**

## **Luminal Triglyceride Lipases**

- **Gastric Lipase (chief cells)**
- **Bile Salt-Activated Lipase  
(breast, pancreas)**
- **Colipase-Dependent Lipase  
(pancreas)**

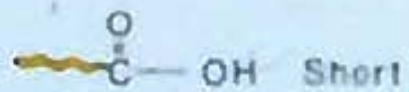
# POSITIONAL SPECIFICITY OF PRE-DUODENAL LIPASES



# RELEASED FATTY ACIDS: STOMACH

MUCOSA

GASTRIC LIPASE



[Undissociated FA]

TG → DG+FA

Solubilization

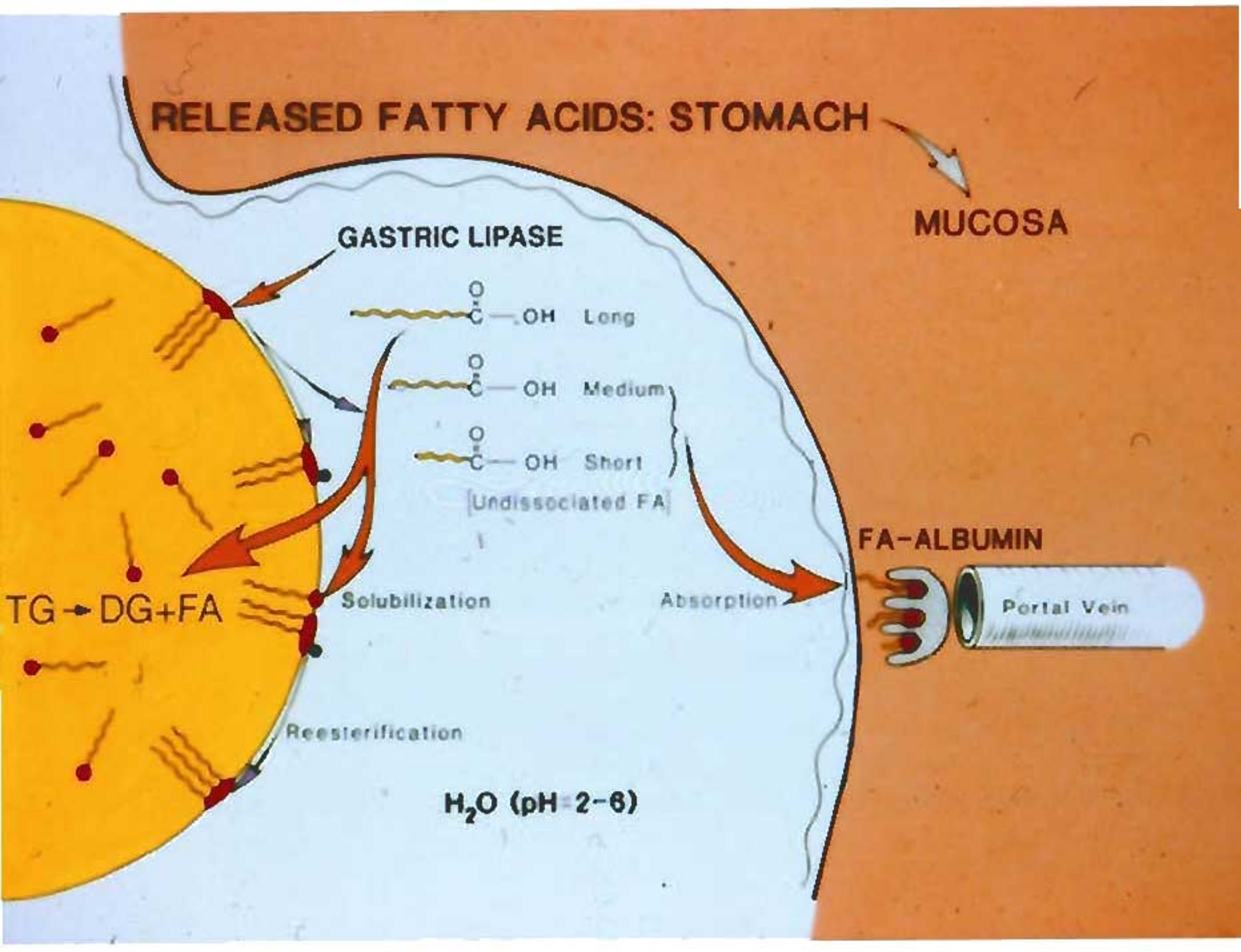
Absorption

FA-ALBUMIN

Portal Vein

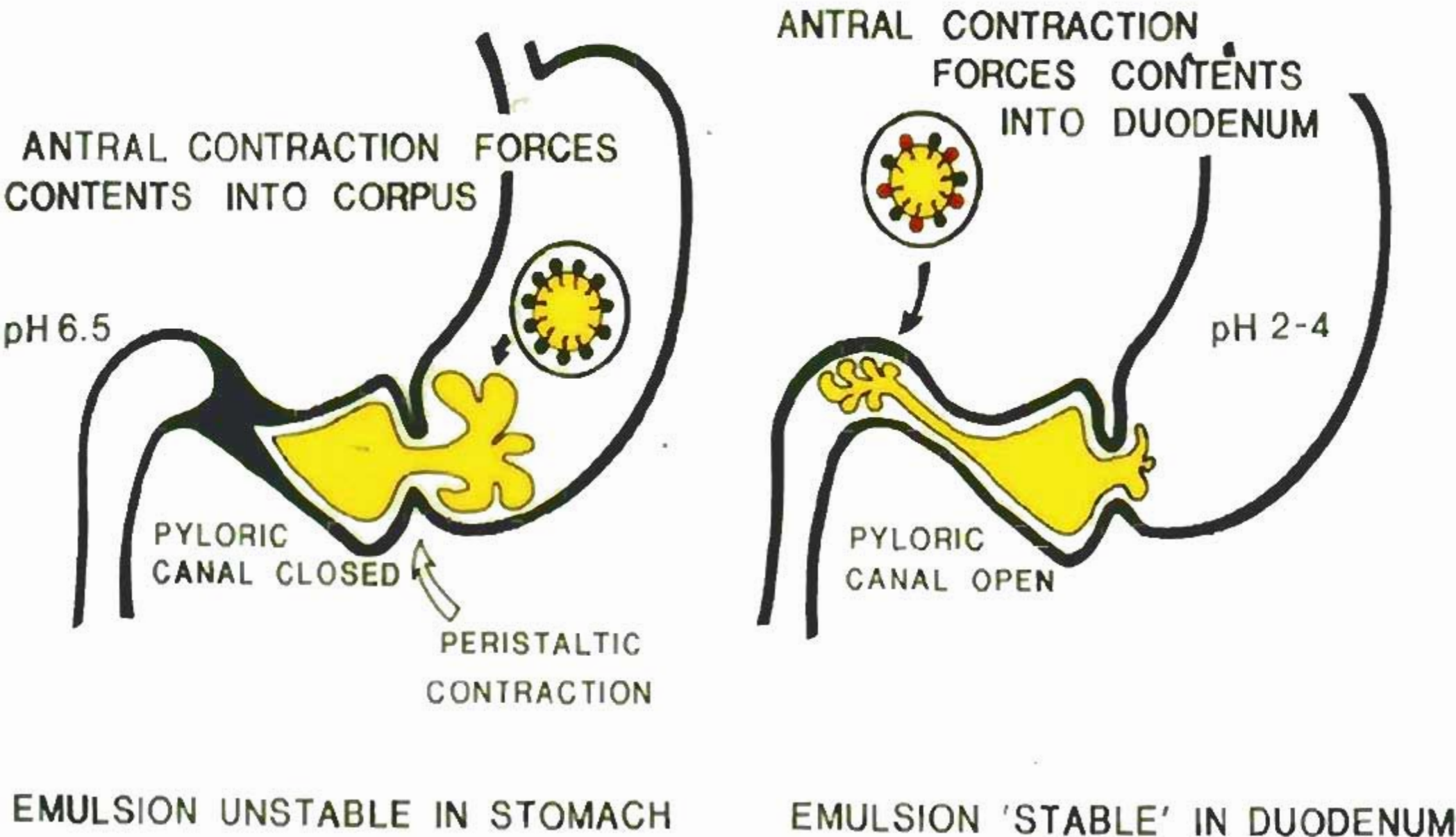
Reesterification

H<sub>2</sub>O (pH=2-6)





# EMULSIFICATION OF FAT IN STOMACH AND PYLORIC-DUODENAL REGION



## HORMONAL COORDINATION OF THE DIGESTIVE SEQUENCE : PYLORUS - DUODENUM

1. FA(NOT TG) and Acid (HCl) stimulate the release of CCK and secretin respectively.
2. Secretin
  - $\text{HCO}_3^-$  - Rich fluid from the Pancreas, Biliary tree and Brunner's glands.
  - Inhibition of gastric and duodenal motility, contracts pylorus.
  - Potentiates CCK.
3. CCK
  - Strong stimulant of enzyme secretion by the pancreas.
  - Contracts gallbladder and pylorus, stimulates intestinal motility, inhibits ODDI's sphincter.
  - Induces satiety?
4. VIP  $\uparrow 2^\circ$  Vagal activity  
GIP  $\uparrow 2^\circ$  Fat in duodenum ] ? Physiological role

**Result:** Digestive milieu (pH, [lipid], [enzymes]) maintained relatively constant.

# HUMAN SPHINCTER OF ODDI

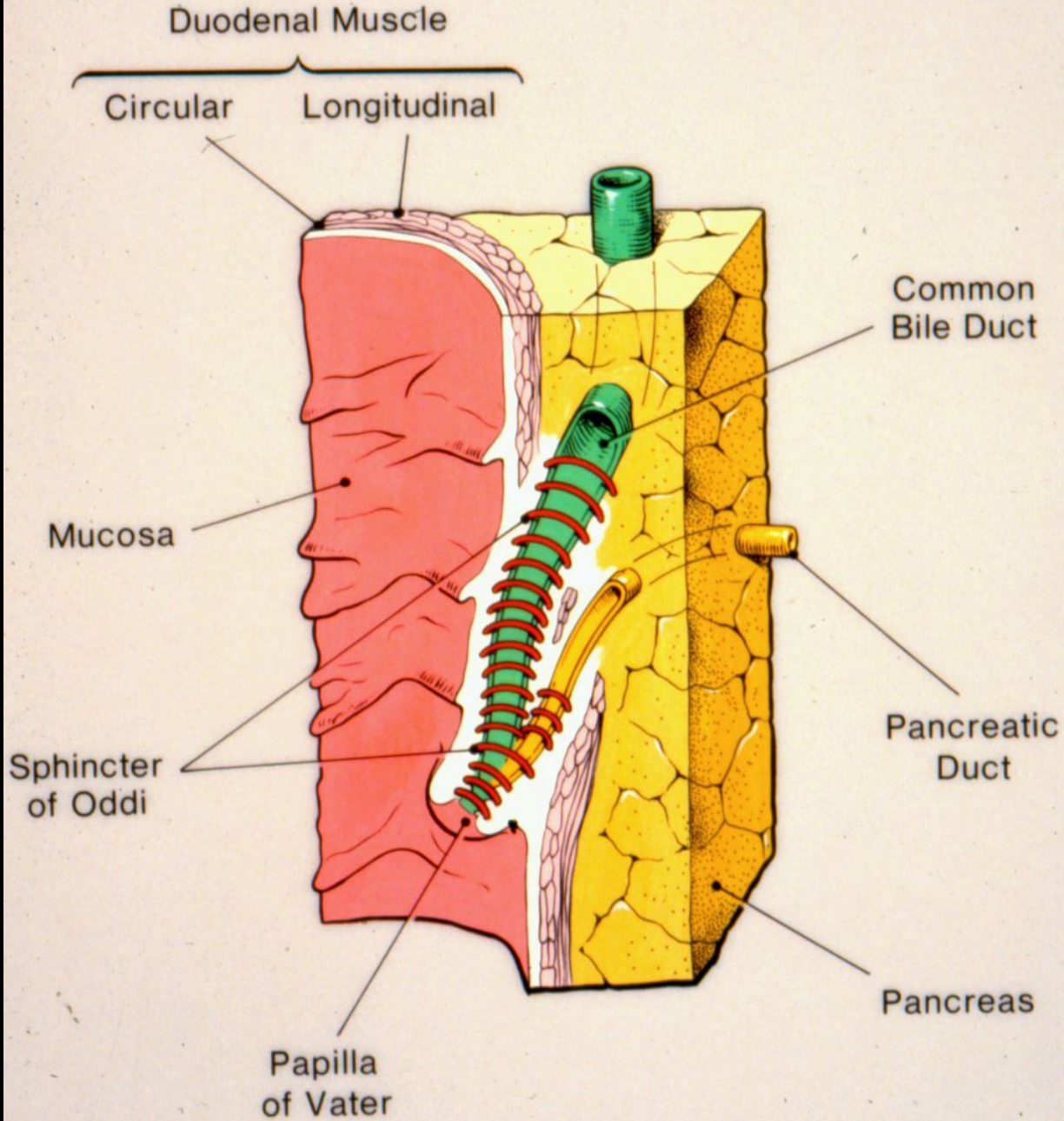
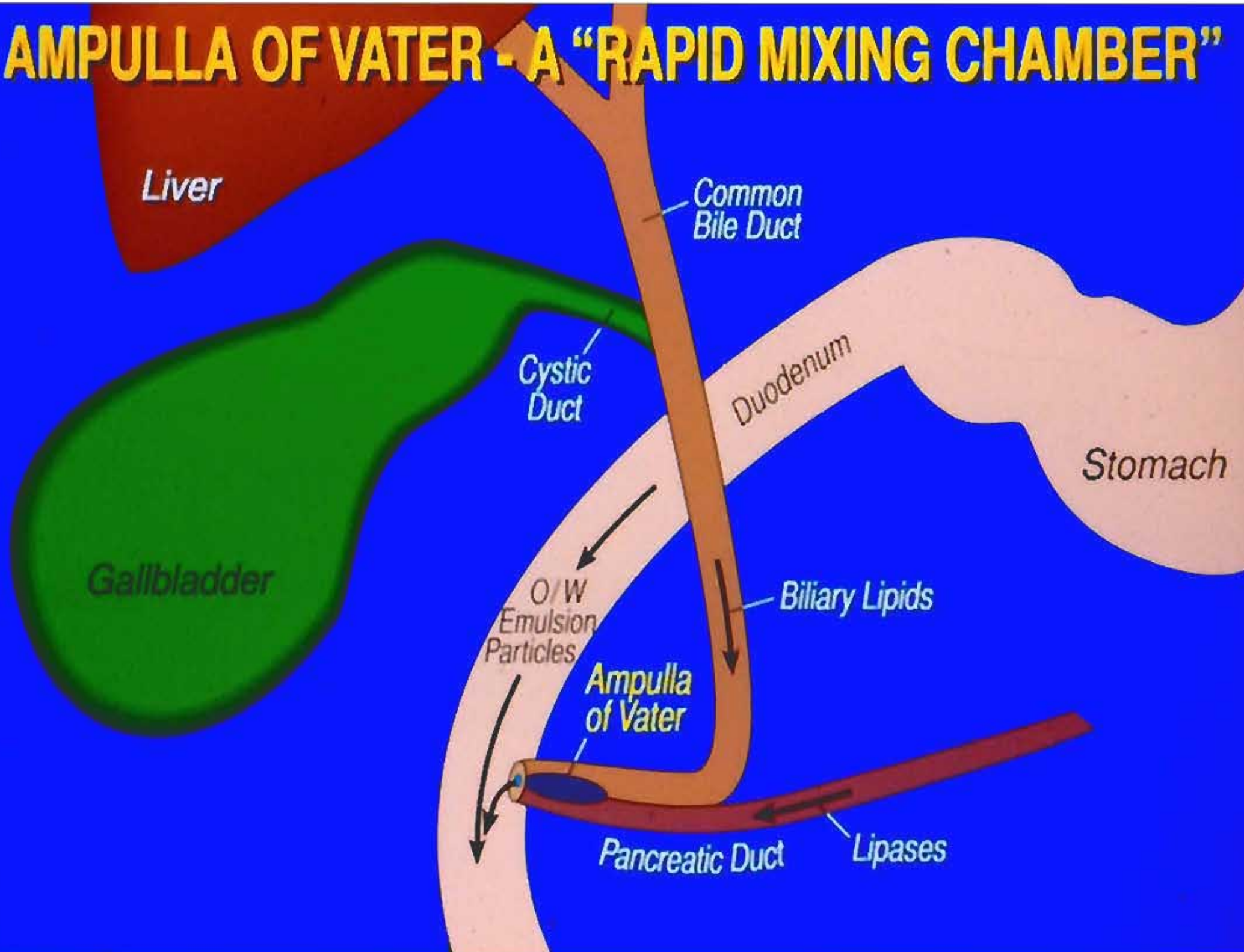


Image courtesy of Dr. James Toouli.  
Used with permission.



# AMPULLA OF VATER - A "RAPID MIXING CHAMBER"



Liver

Common Bile Duct

Cystic Duct

Duodenum

Stomach

Gallbladder

Biliary Lipids

O/W Emulsion Particles

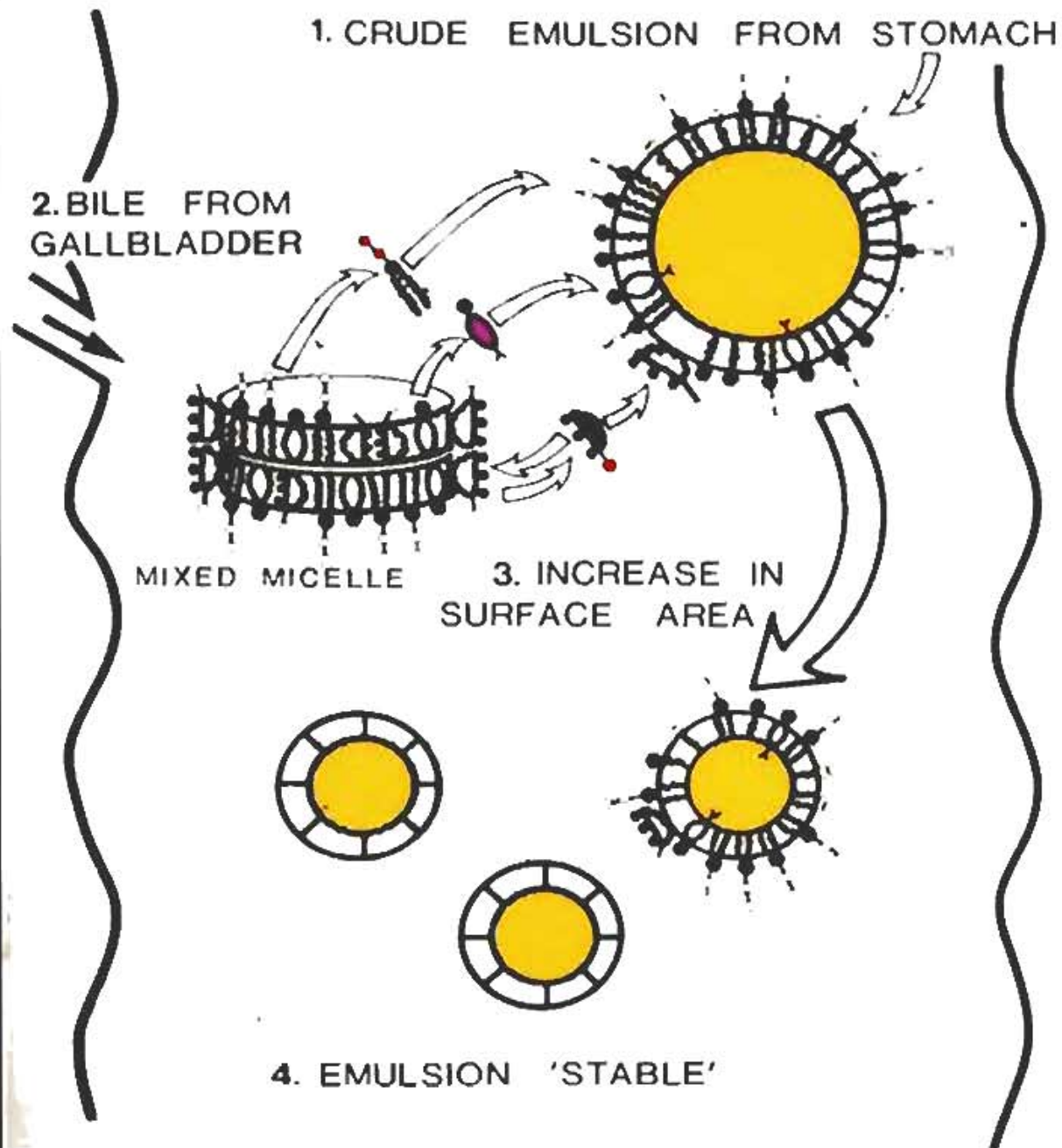
Ampulla of Vater

Pancreatic Duct

Lipases

# DUODENUM - JEJUNUM

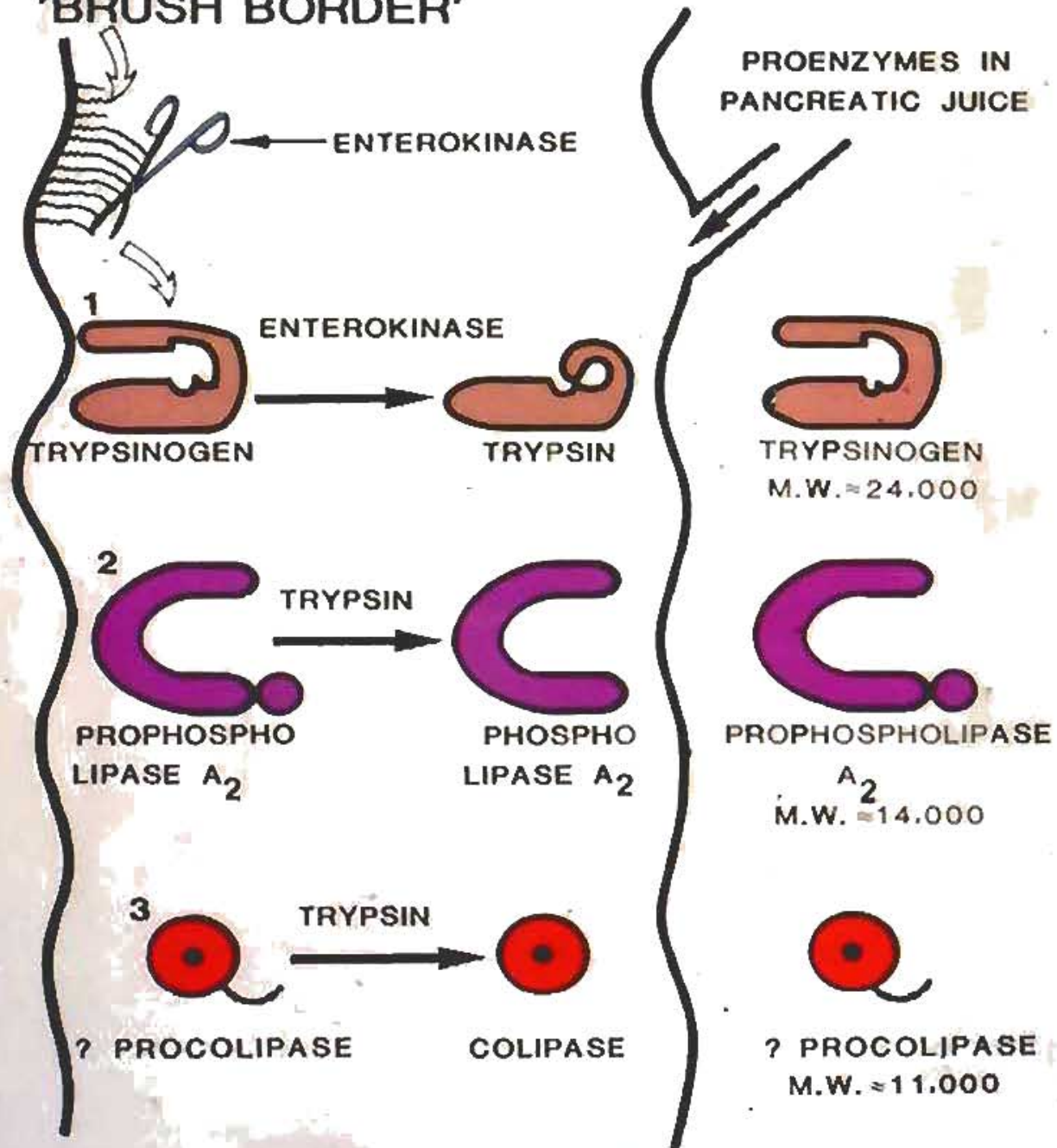
## ADSORPTION OF BILIARY LIPIDS TO EMULSION INTERFACE





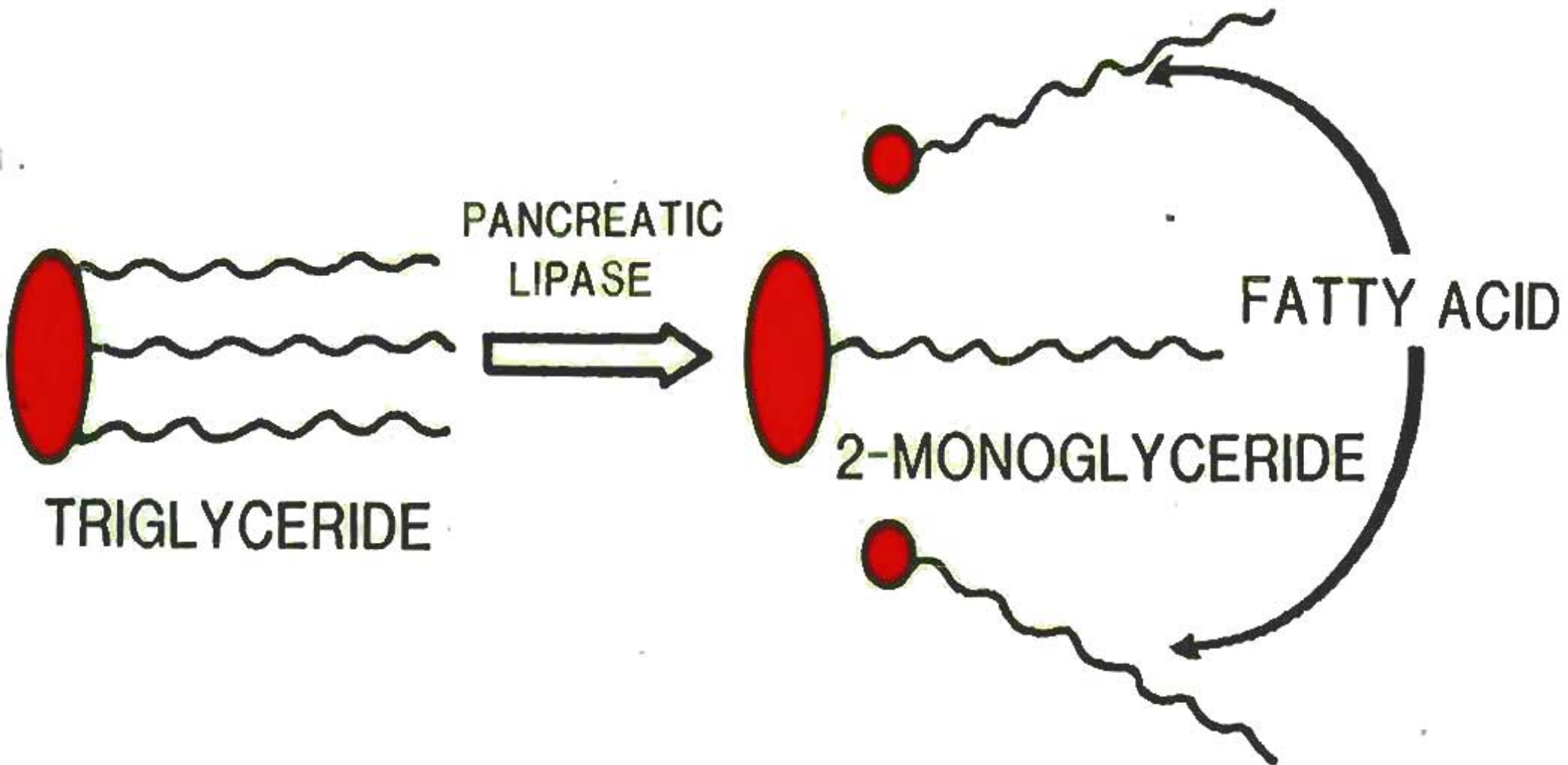
# DUODENUM - JEJUNUM

'BRUSH BORDER'

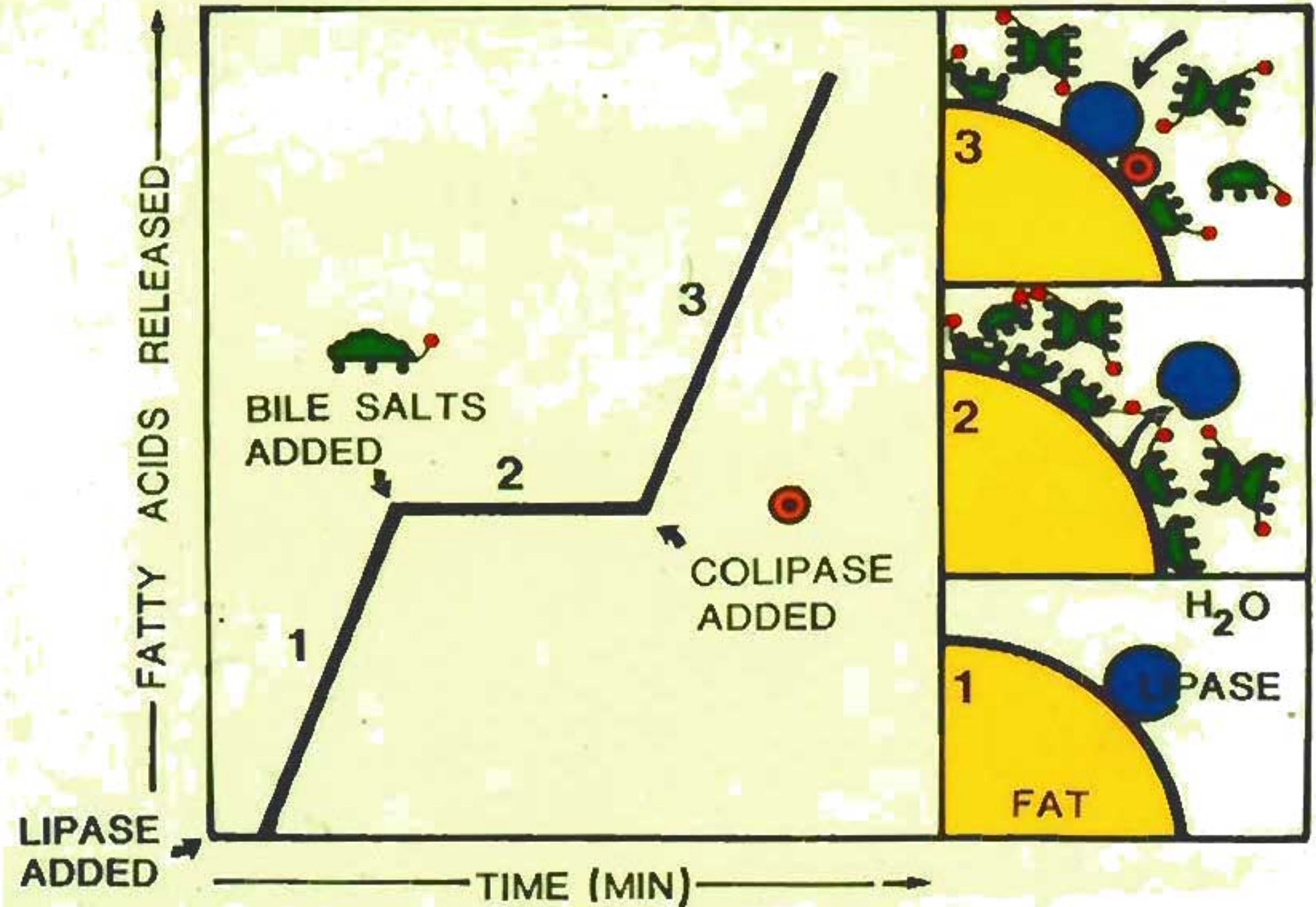




# POSITIONAL SPECIFICITY OF PANCREATIC LIPASE



# FAT (TRIGLYCERIDE) DIGESTION



# **Structure of the pancreatic lipase–procolipase complex**



Non-catalytic C terminus

Catalytic N terminus

Figure removed due to copyright reason. Please see:

van Tilbeurgh H., et al. "Structure of the pancreatic lipase-procolipase complex." *Nature* 359 (1992): 159-62.

van Tilbeurgh H., et al. "Interfacial activation of the lipase-procolipase complex by mixed micelles revealed by X-ray crystallography." *Nature* 362 (1993): 814-20.

# Interfacial activation

Figure removed due to copyright reason. Please see:

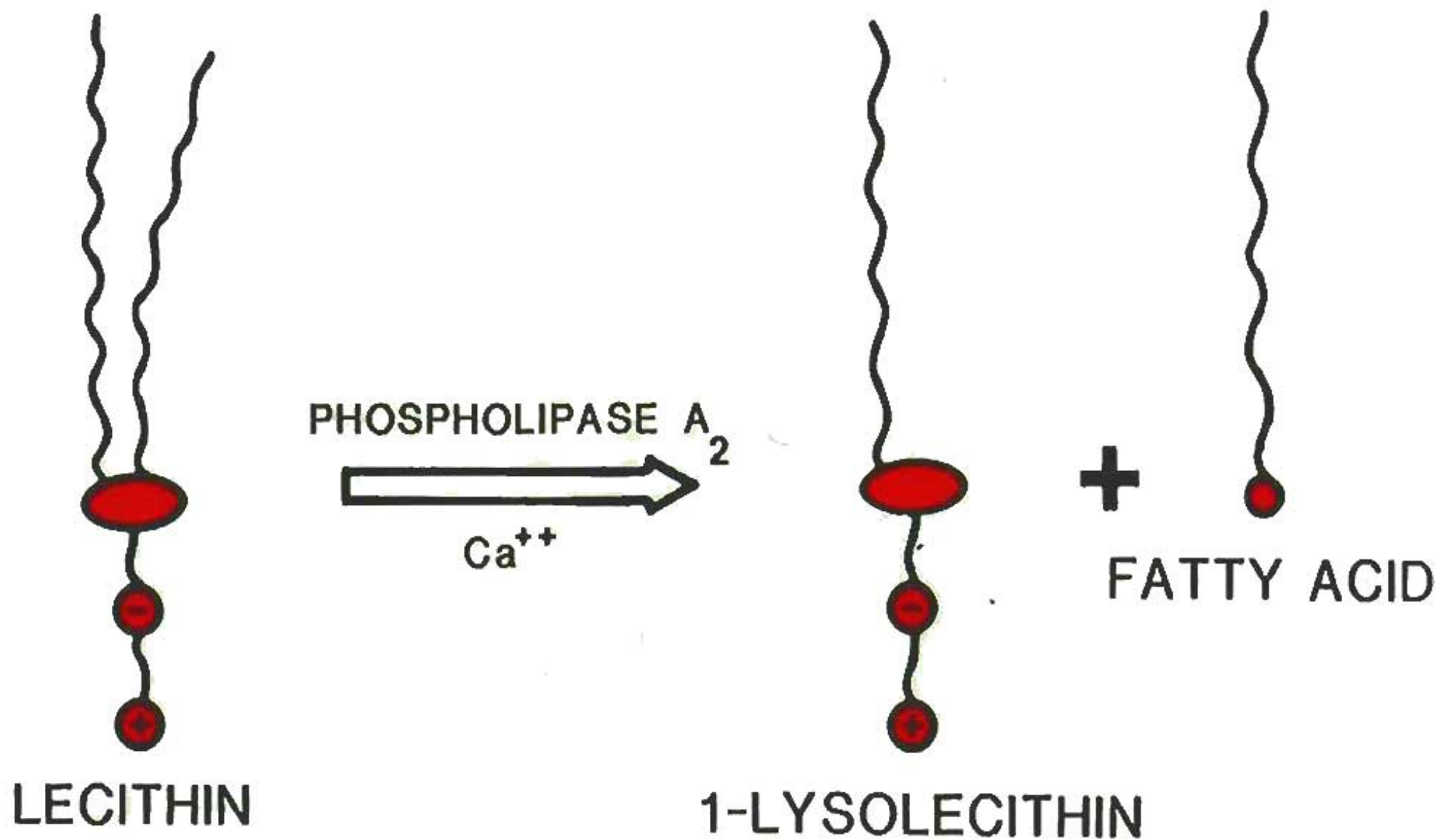
van Tilbeurgh H., et al. "Structure of the pancreatic lipase-procolipase complex." *Nature* 359 (1992): 159-62.

van Tilbeurgh H. et al. "Interfacial activation of the lipase-procolipase complex by mixed micelles revealed by X-ray crystallography." *Nature* 362 (1993): 814-20.

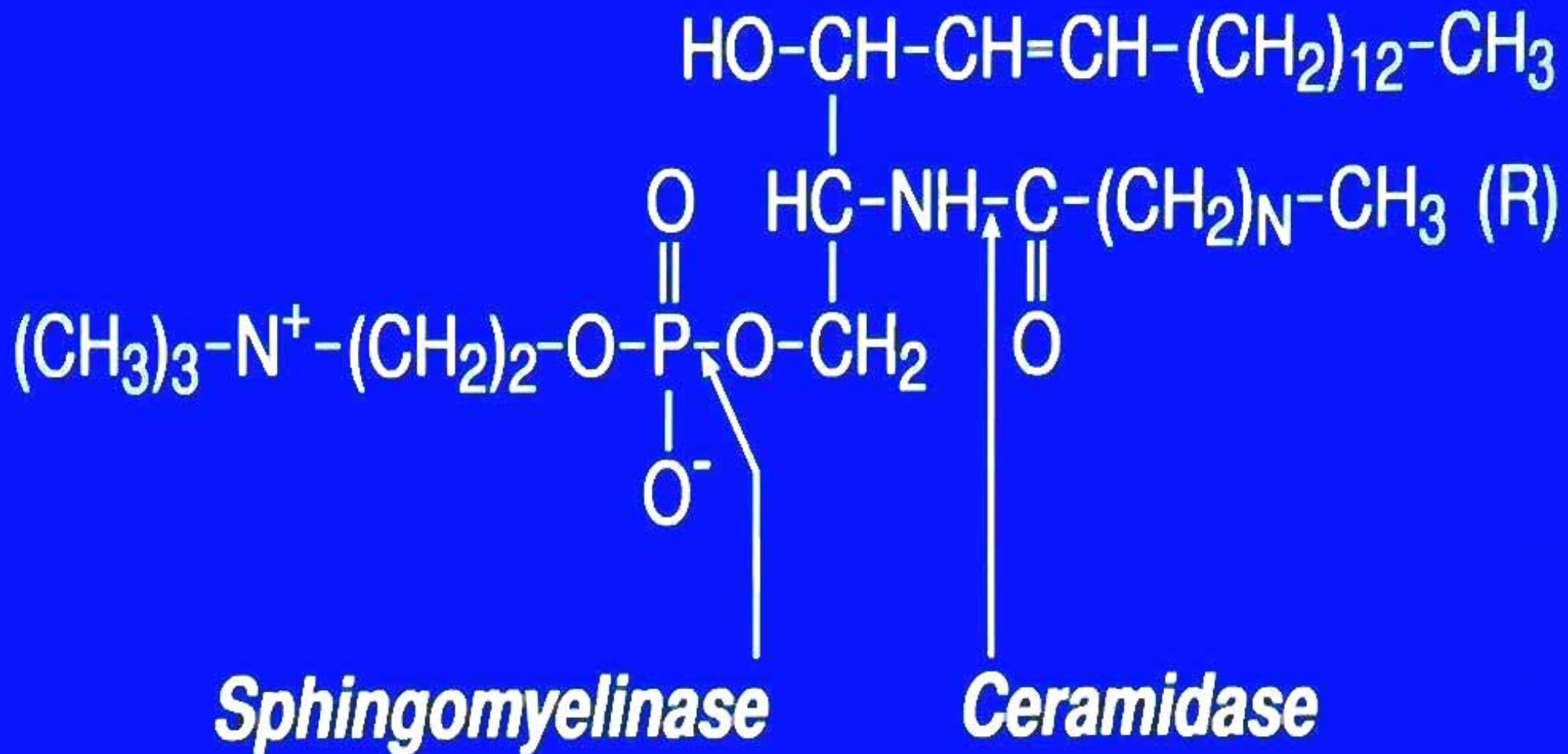
Figure removed due to copyright reason. Please see:

Figure 6 in Wang, X., et al. "The crystal structure of bovine bile salt activated lipase: insights into the bile salt activation mechanism." *Structure* 5 (1997): 1209-18

# POSITIONAL SPECIFICITY OF PANCREATIC PHOSPHOLIPASE A<sub>2</sub>: PARTIAL HYDROLYSIS



# SPHINGOMYELIN



R=Typical fatty acids are palmitic, stearic, behenic (22:0), nervonic (24:1) and lignoceric (24:0)



# PHYSICAL - CHEMISTRY OF FAT DIGESTION

Figure removed due to copyright reasons. Please see:

Figure 11 in Hernell, O., et al. "Physical-chemical behavior of dietary and biliary lipids during intestinal digestion and absorption. 2. Phase analysis and aggregation states of luminal lipids during duodenal fat digestion in healthy adult human beings." *Biochemistry* 29 (1990): 2041-2056.

# FATE OF FATTY ACIDS AND MONOGLYCERIDES IN ABSORPTIVE CELLS

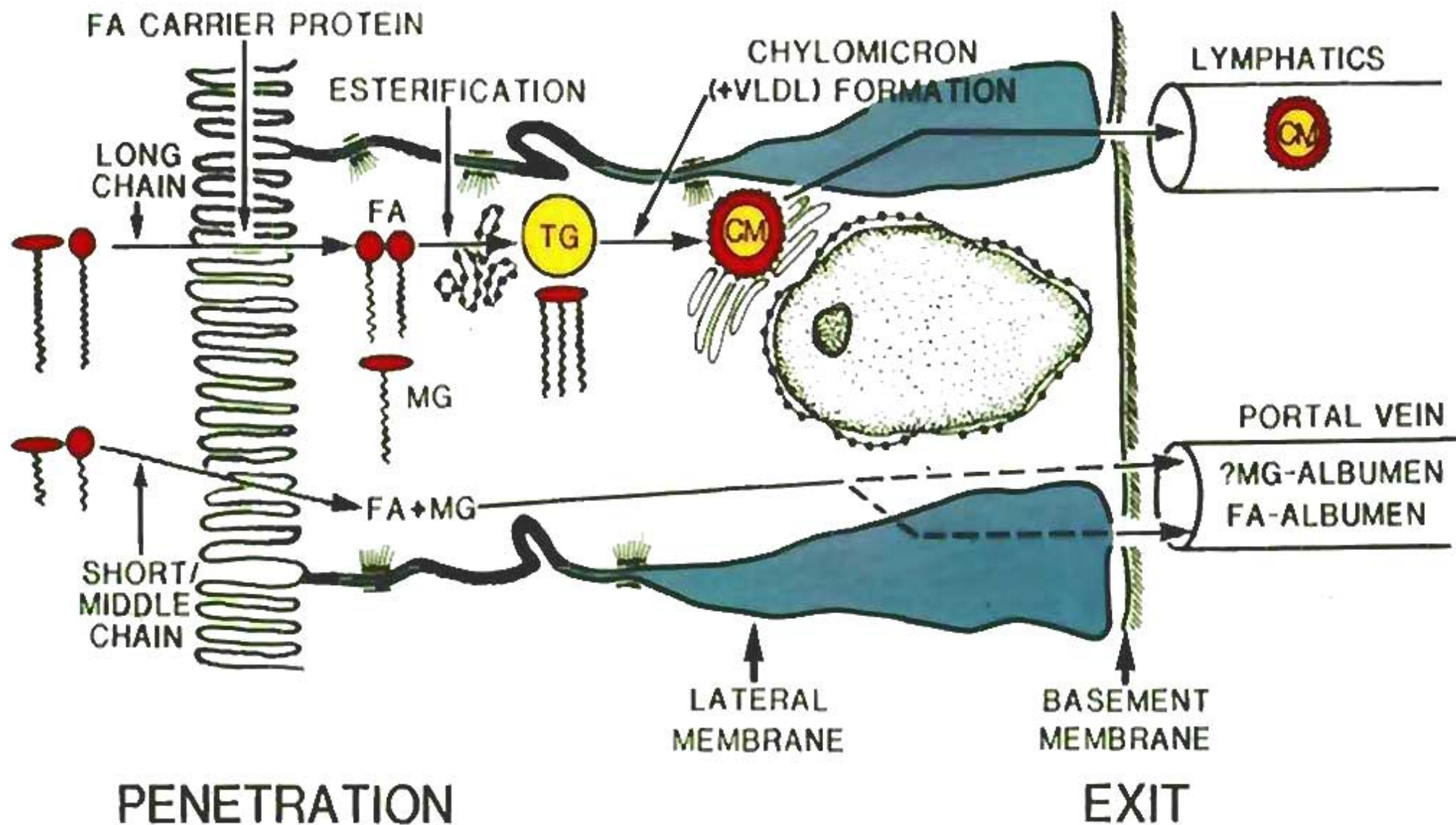
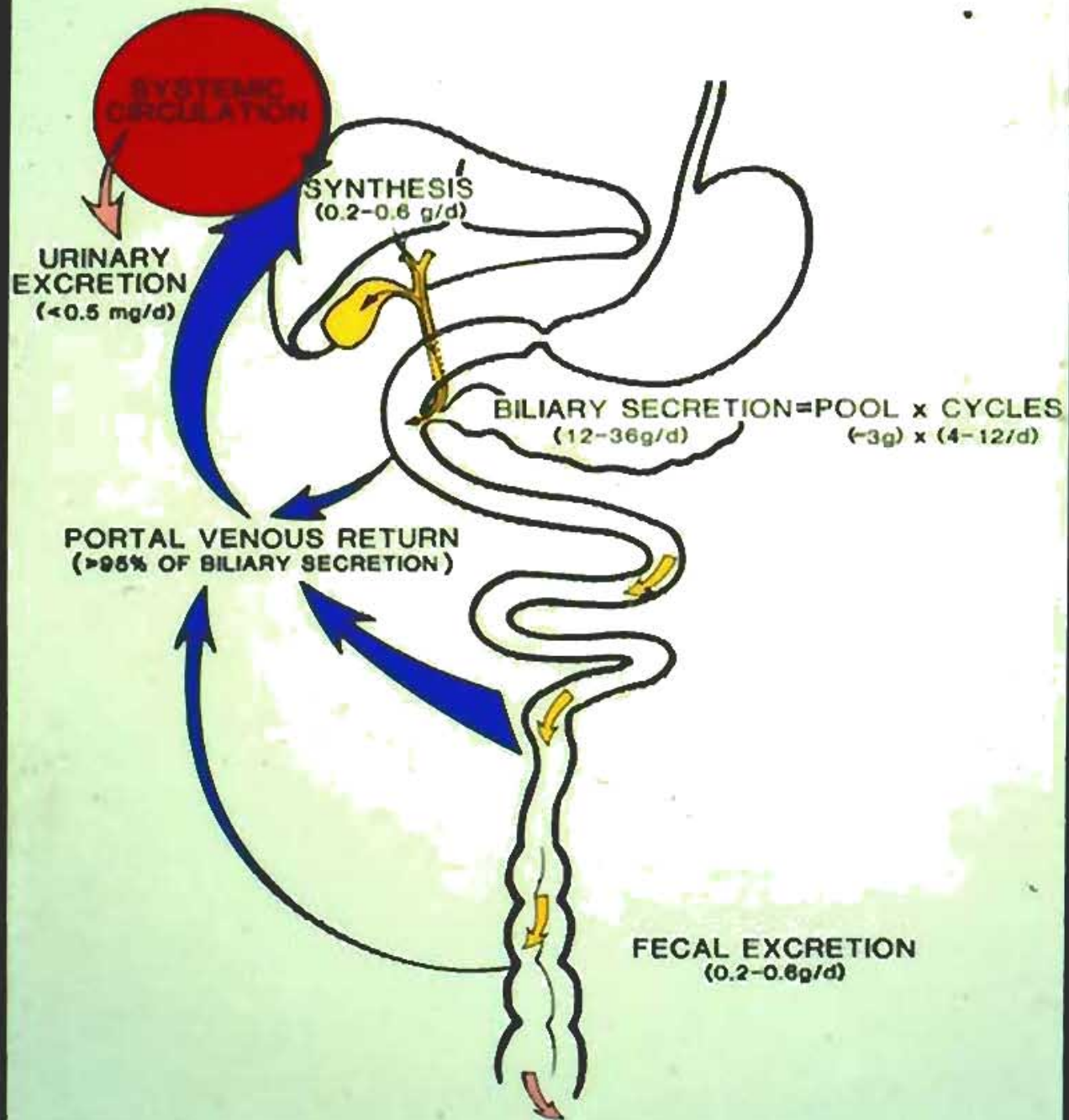


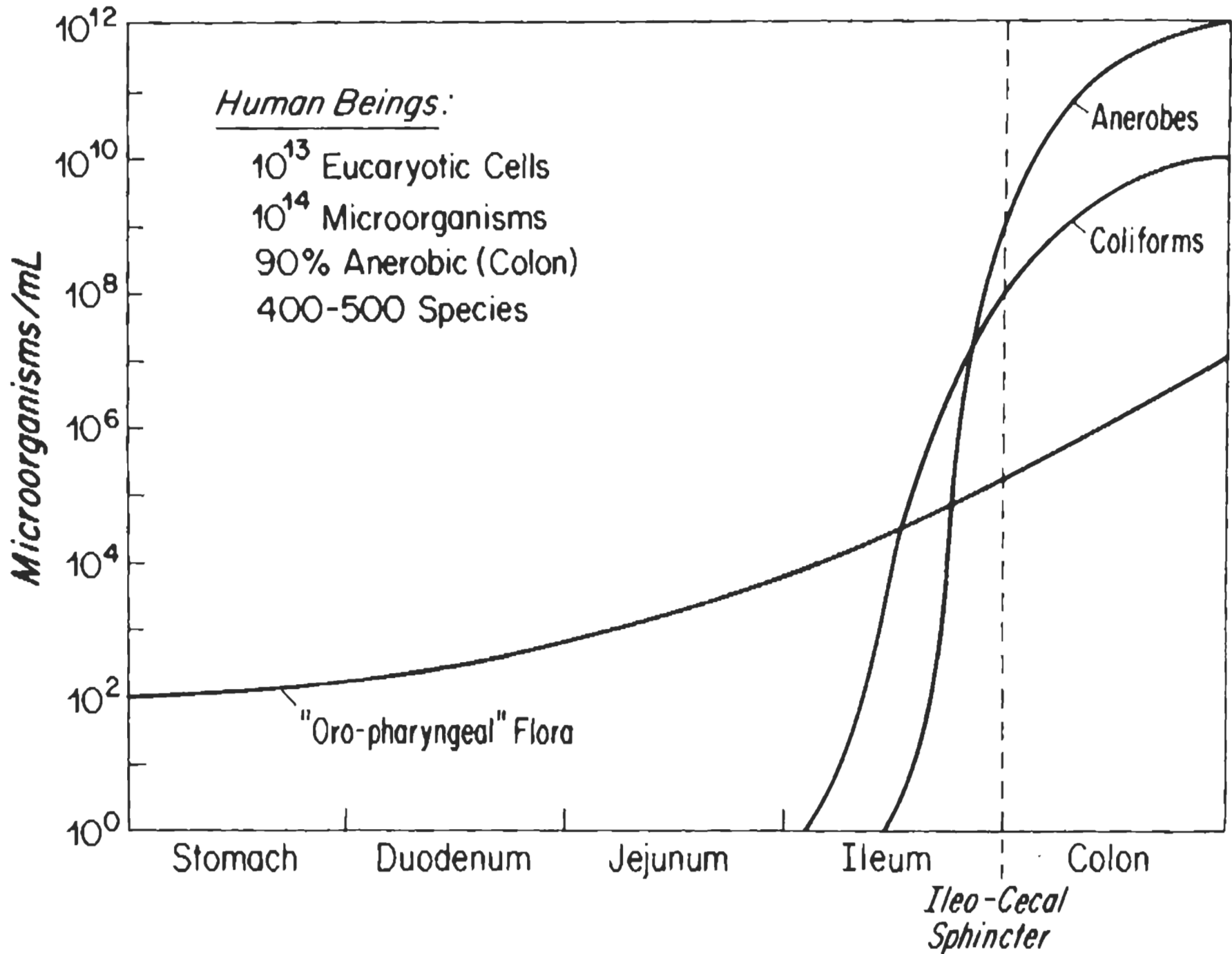
Figure removed due to copyright reasons. Please see:

Figure 1 in Lammert, F., and David Q.-H. Wang. "New Insights Into the Genetic Regulation of Intestinal Cholesterol Absorption." *Gastroenterology* 129 (2005): 718-34.

# ENTEROHEPATIC CIRCULATION OF BILE SALTS



# DISTRIBUTION OF MICROORGANISMS IN ALIMENTARY TRACT





# FATE OF FAT IN THE COLON

- TG  $\rightarrow$  3FA + Glycerol
- PL  $\rightarrow$  2FA + Glycerol + Phosphate + Choline
- CE  $\rightarrow$  1FA + Ch
- Reduction of FA double bonds to form saturated FA
- Oxidation of FA double bonds to form OH-FA (e.g., oleic acid  $\rightarrow$  9-hydroxy stearic acid: **potent cathartics**)
- Formation of  $\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$  (divalent) soaps
- Formation of  $\text{Na}^+$  and  $\text{K}^+$  (monovalent) soaps

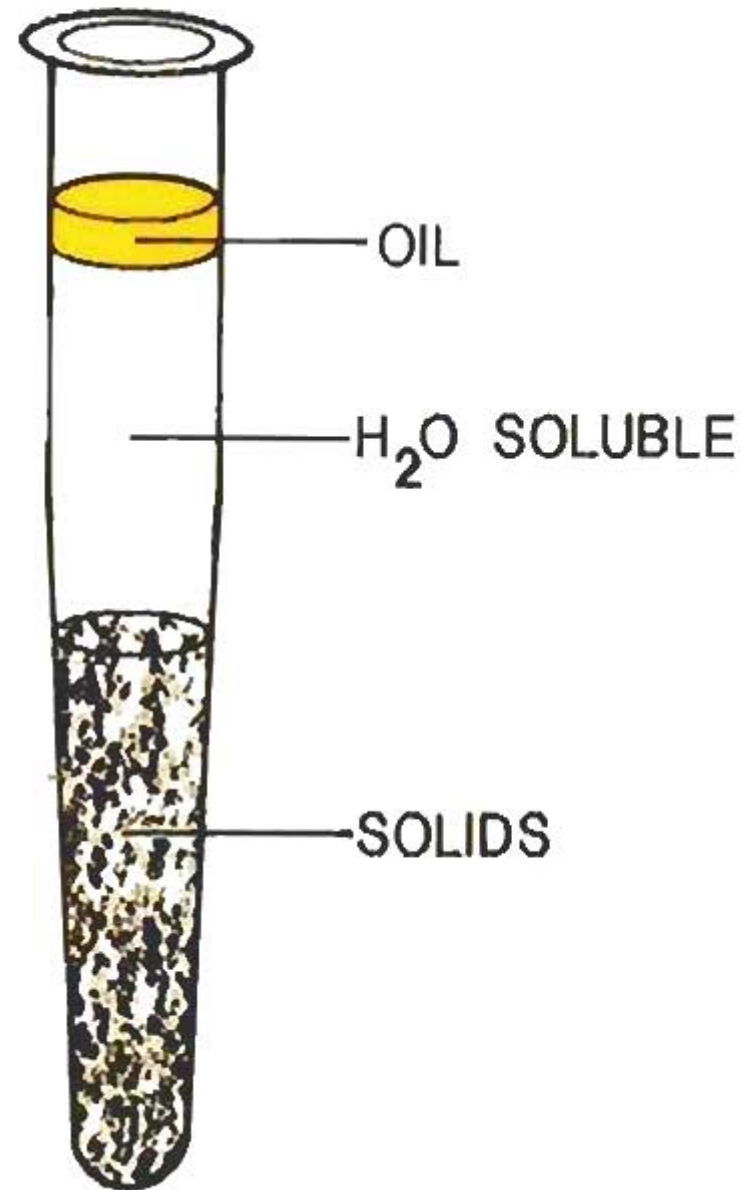
# 'NORMAL' FECAL FAT

2-5 g/day

DERIVED FROM

1. DIET
2. BILE
3. DESQUAMATED CELLS
4. BACTERIA

# PHYSICAL STATES OF FECAL FAT





# CHEMICAL AND PHYSICAL-CHEMICAL STATES OF NORMAL FECAL FAT (4-5g/24 hours)

CHEMICAL	PHASE	% TOTAL FAT
Fatty Acids (long-chain including OH-FA) Na <sup>+</sup> + K <sup>+</sup> Soaps	Oil or Solid	] 70
	Aqueous or Solid	
Ca <sup>2+</sup> + Mg <sup>2+</sup> Soaps	Crystalline Solids	10
Glycerides (TG, DG, MG)	Oil	0
Steroids ┌ Neutral (Ch) └ Acidic (Bile Acids)	Solid	] 15
	Aqueous or Solid	
Other (Bacterial PL)	Oil or Solid	5

# Classification of Malabsorption Syndromes

- **F**aulty Digestion (Intraluminal)
- **F**aulty Dispersion (Intraluminal)
- **F**aulty Absorption (Mucosal)
- **F**aulty Transport (Lamina Propria, Lymphatics)

# Work-up of Fat Malabsorption

- **Suspect**
- **Prove presence of malabsorption:  
Steatorrhea**
- **Distinguish faulty digestion/dispersion  
from faulty absorption/transport**
- **Confirm specific diagnosis**
- **Initiate specific treatment**



# DIAGNOSTIC PROFILE

Faulty  
Digestion/Dispersion

Faulty  
Absorption/Transport

Fecal Fat



Chemistry of  
Fecal Fat

FA Soaps  
(TG, DG, MG; only if massive)

FA Soaps

D-xylose

Normal



Small Bowel  
X-ray

±

Abnormal

Jejunal Biopsy

Normal

Abnormal

	Faulty Digestion/Dispersion	Faulty Absorption/Transport
Fecal Fat	↑	↑
Chemistry of Fecal Fat	FA Soaps (TG, DG, MG; only if massive)	FA Soaps
D-xylose	Normal	↓
Small Bowel X-ray	±	Abnormal
Jejunal Biopsy	Normal	Abnormal

# MIXED PATHOPHYSIOLOGIES IN FAT MALABSORPTION

DISEASE	MAJOR	MINOR	CAUSE
Celiac Sprue Whipple's Disease	Faulty Absorption/ Transport	Faulty Digestion/ Dispersion	Gut enteropathy <b>and</b> endocrinopathy
Pancreatic Insufficiency	Faulty Digestion	Faulty Dispersion	(Phospho)lipase/ colipase <b>and</b> bile salt deficiency
'Blind-Loop' Syndrome	Faulty Dispersion	Faulty Absorption	Bile salt deficiency <b>and</b> gut enteropathy

# **Hormonal Control of Appetite and Weight (I)**

**Rapidly acting (via vagal afferents to the arcuate and other nuclei of hypothalamus)**

- a) GHRELIN: from gastric endocrine cells when stomach is empty; stimulates appetite**
  
- b) CHOLECYSTOKININ (CCK): from endocrine cells in duodenum-jejunum; promotes satiety**

# Hormonal Control of Appetite and Weight (II)

**Long-term regulators (via blood to specific cells in hypothalamus, generally in proportion to body fat, and *exerting sustained inhibitive effects on food intake* while increasing energy expenditure)**

- a) INSULIN:** from  $\beta$ -cells of pancreas; augmented by VIP and in proportion to dietary intake of fat and sugars;
- b) LEPTIN:** from adipocytes in proportion to body stores of fat;
- c) PYY3-36:** from Neuropeptide Y endocrine cells in distal ileum and colon; blood levels increase several hours after ingestion of a meal.