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Author: John Williams, M.D., Ph.D., 2009

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M1 - GI Sequence

Intestines

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Winter, 2009

University of Michigan
Medical School

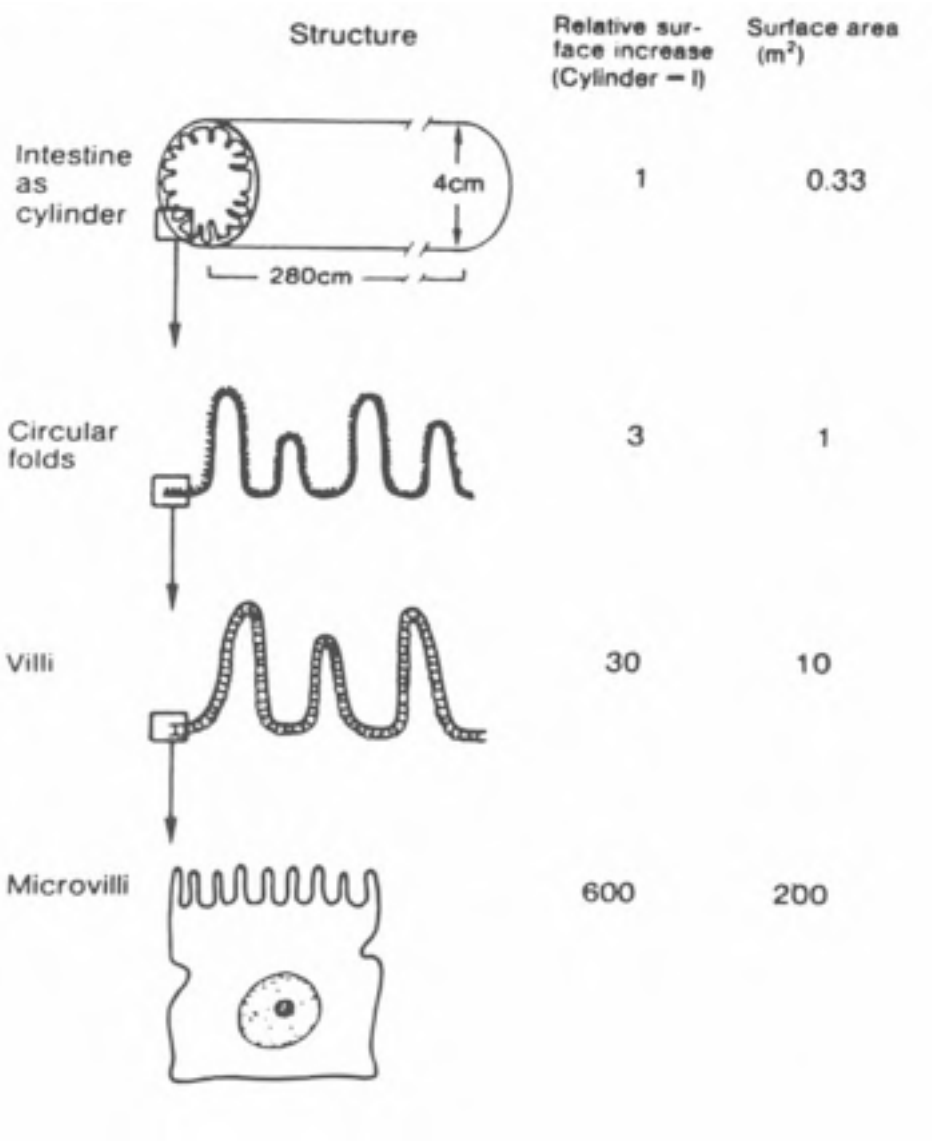
THE SMALL INTESTINE

Human small intestine 6-7 m long

Duodenum 20-30 cm
Jejunum 2.5 m
Ileum 3.5 m

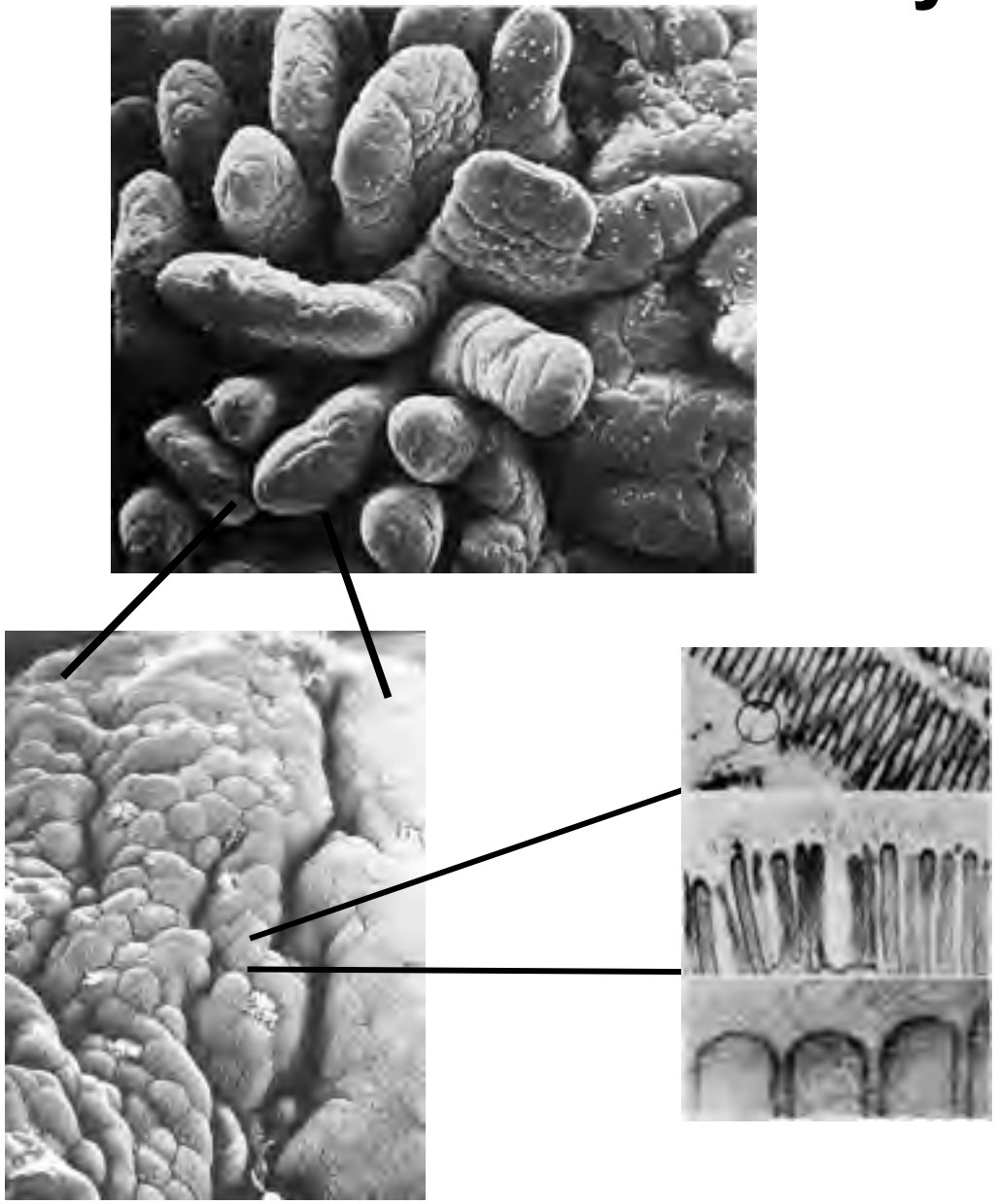
FUNCTIONS

Digestion
Absorption
Secretion
Motility



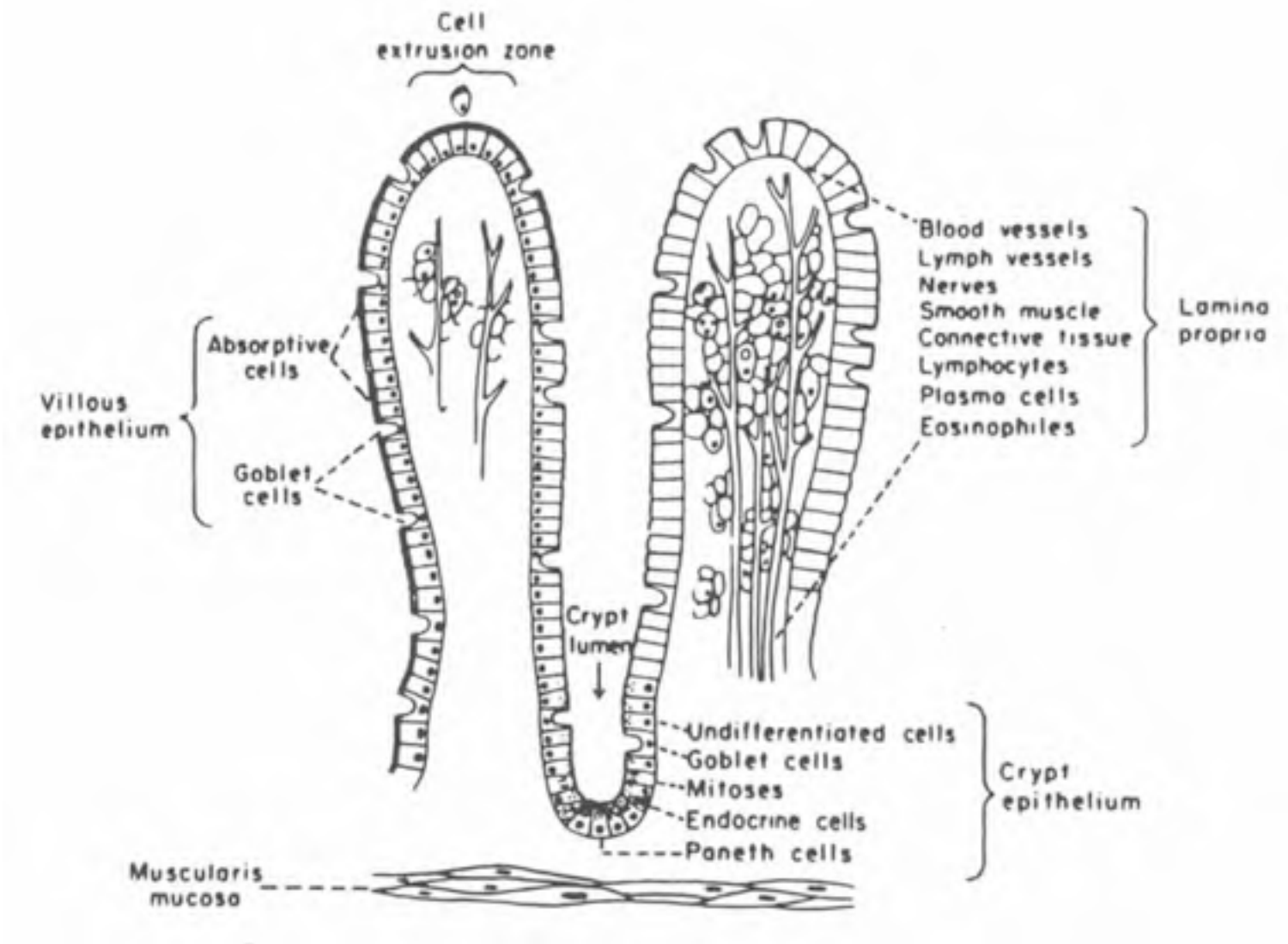
PD-INEL Fig. 7-2 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985: 144.

Small Intestine Anatomy



PD-INEL Sources Undetermined

Histologic organization of the small intestinal mucosa



PD-INEL Trier, JS, Modara, JL. “Functional morphology of the mucosa of the small intestine”. *In* Johnson, LR. *Physiology of the Gastrointestinal Tract*. Vol. II. Raven Press, New York, NY, 1981: 926.

DIETARY CARBOHYDRATES

POLYSACCHARIDES

1. STARCH
   - AMYLOSE
   - AMYLOPECTIN

60%

2. GLYCOGEN

DISACCHARIDES

30%

SUCROSE

LACTOSE

MONOSACCHARIDES

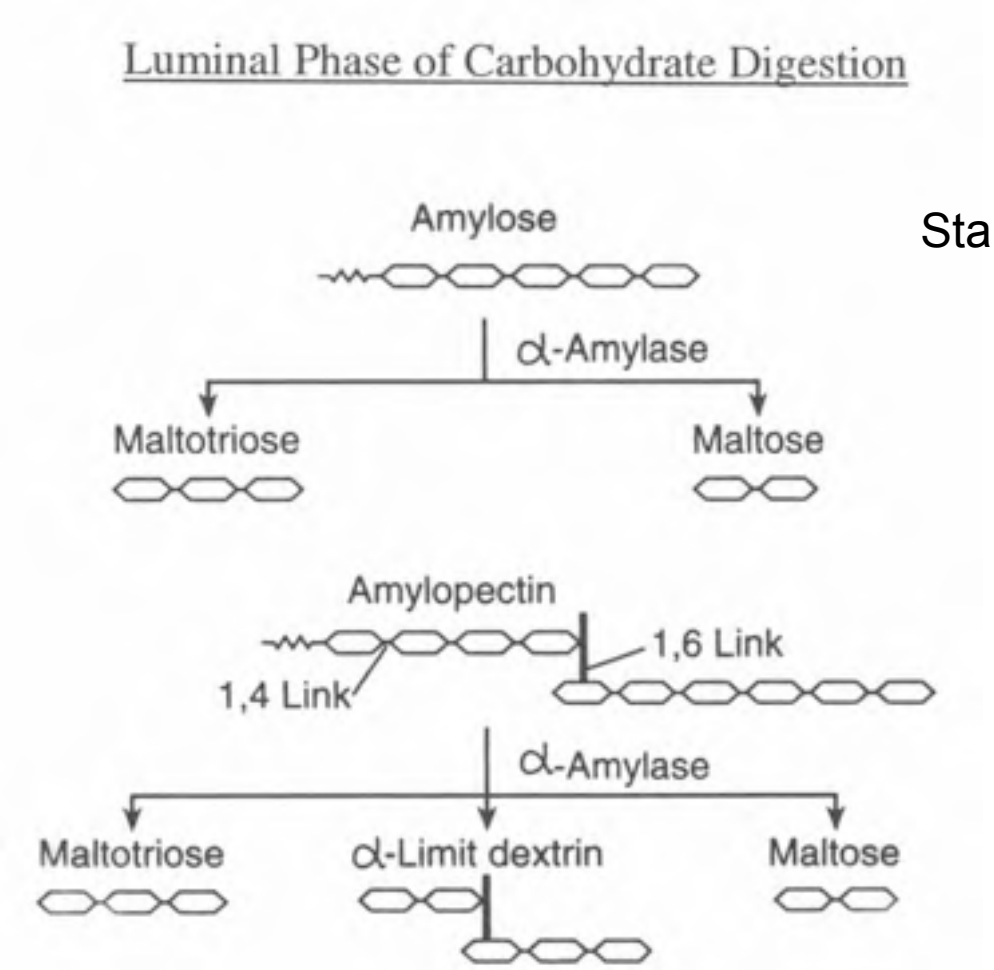
FRUCTOSE

GLUCOSE

INDIGESTIBLE CARBOHYDRATES

DIETARY CARBOHYDRATES (cont)

- Normal American diet contains 200-300 g (50% of caloric intake)
- Serves an energy and carbon source
- Digestion includes a luminal phase and a brush border phase
- Only monosaccharides are appreciably absorbed



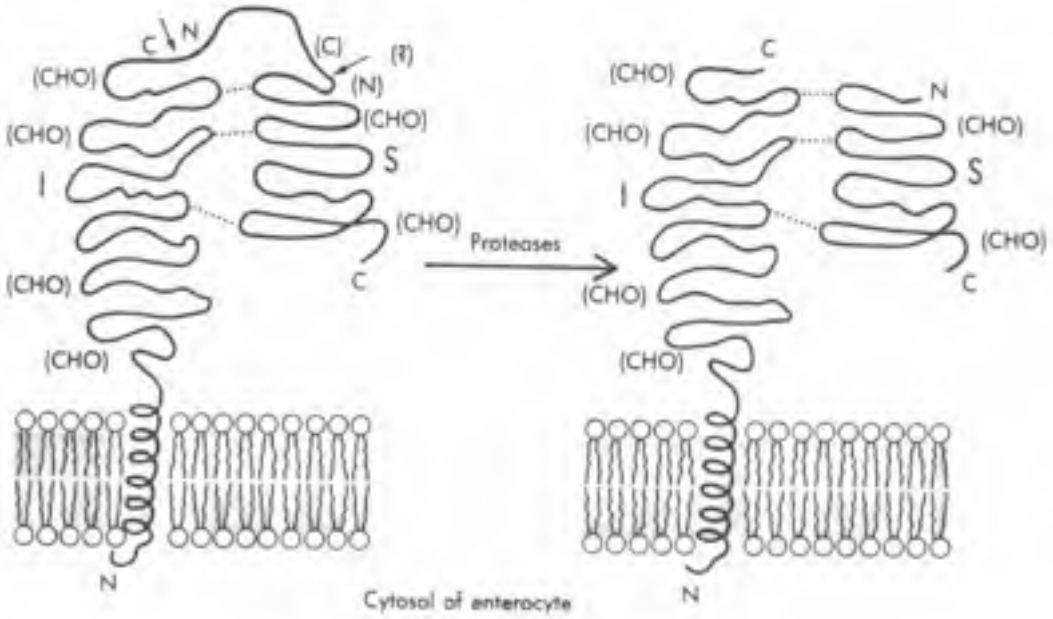
Starch= Amylose & Amylopectin

PD-INEL Source Undetermined

- Amylase (pH optima 7) cleaves interior α1-4 linkages but not α1-6
- Endproduct is a mixture of maltose, maltotriose and limit dextrans
- Acarbose – Amylase inhibitor

Intestinal Brush Border Phase of Carbohydrate Digestion

Structure of Sucrase-Isomaltase



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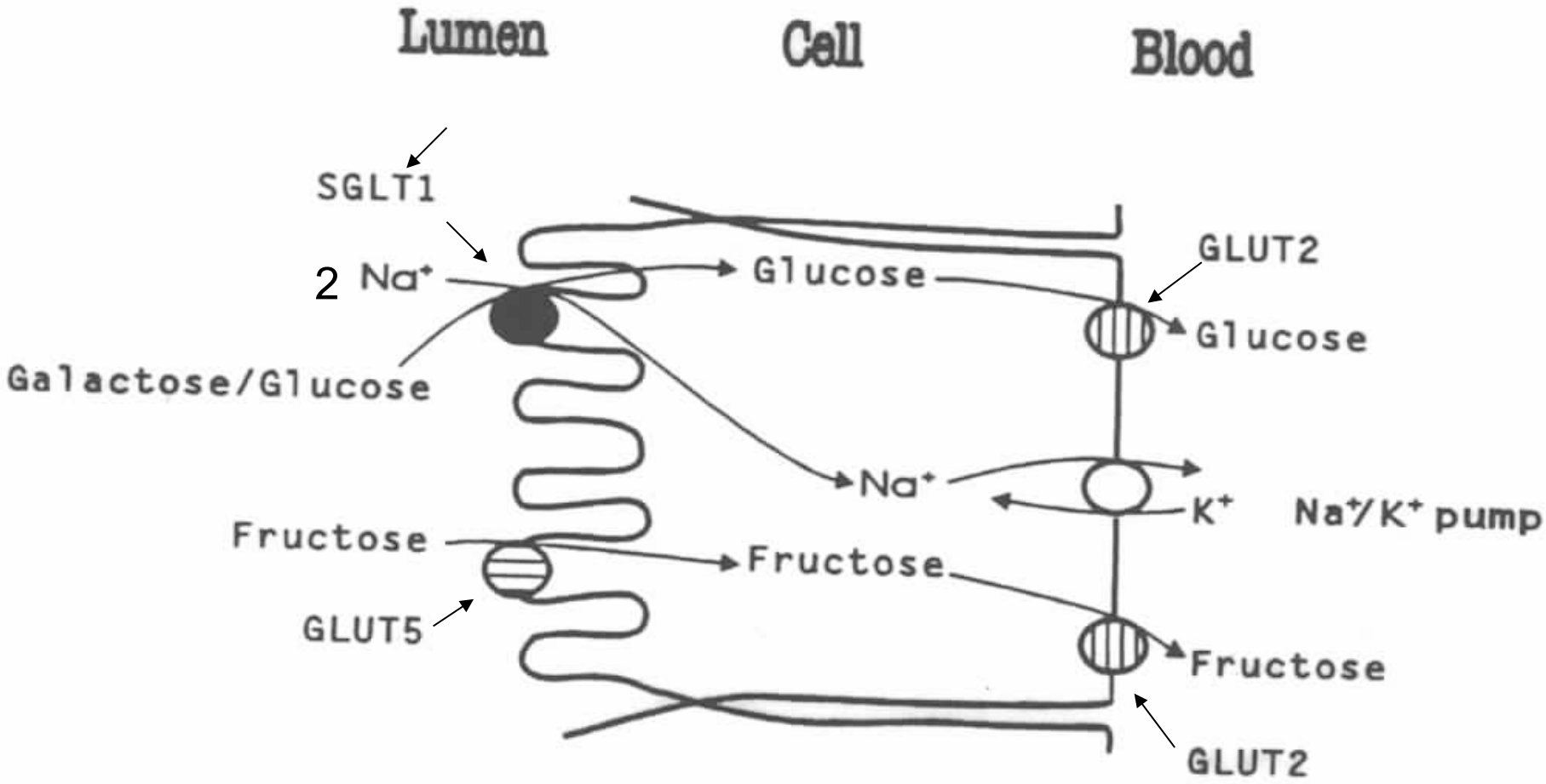
Intestinal Brush Border Hydrolysis of Oligosaccharides

Enzyme	Substrates	Molecular Site of Hydrolysis	Products
Maltase	Maltose, maltotriose	α-1,4 linkage	glucose
Sucrase*	Sucrose	α-1,4 linkage	glucose, fructose
Lactase	Lactose	β-1,4 linkage (but not of cellulose)	glucose, galactose
α-Dextrinase (isomaltase)	α-Limit dextrins	α-1,6 linkage	glucose, maltose, oligosaccharides

*Sucrase is also very active against maltose and maltotriose.

MECHANISM OF MONOSACCHARIDE ABSORPTION



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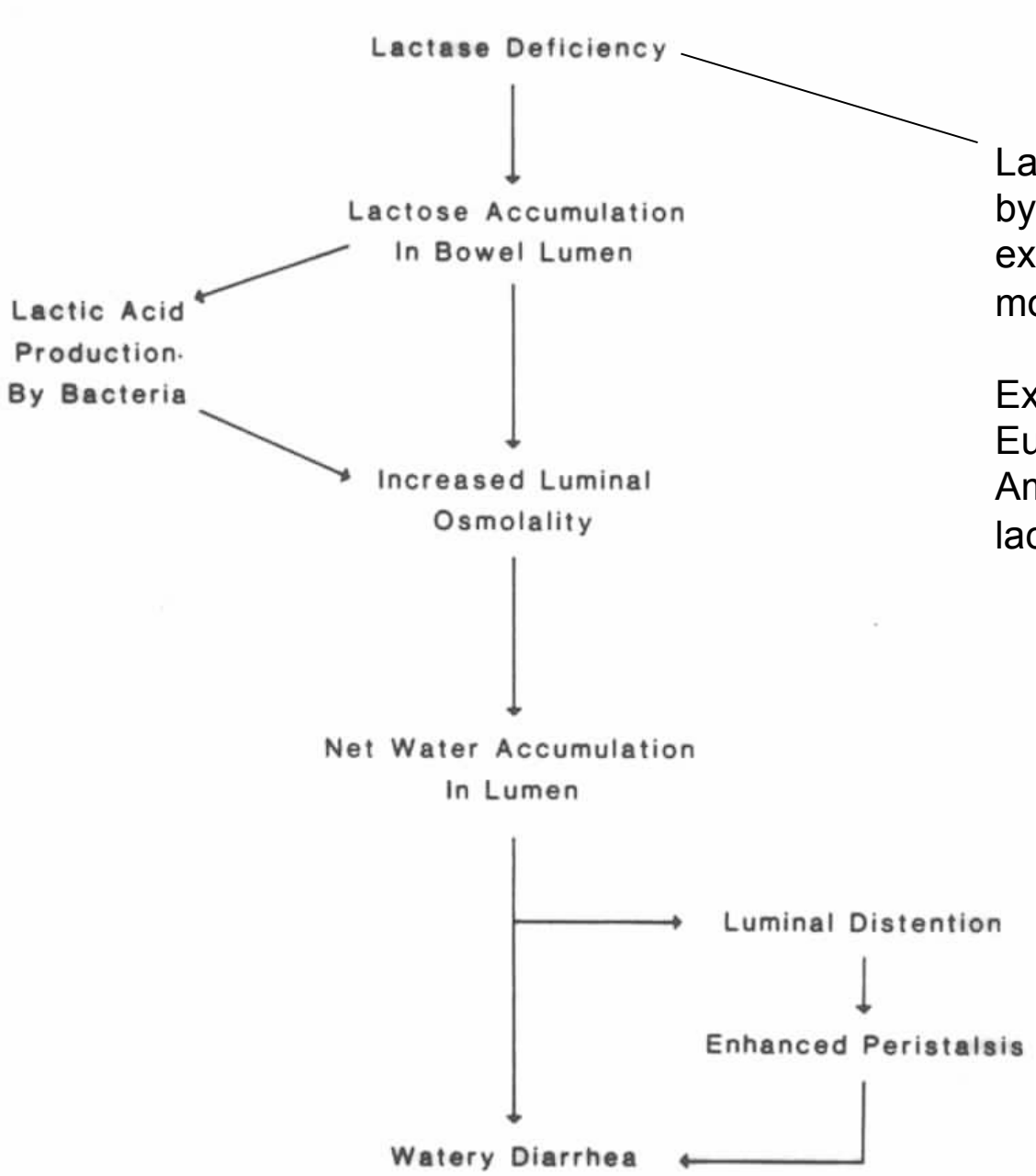


Lactase is present in infancy by disappears to a variable extent during childhood in most humans.

Exception is Northern Europeans and European Americans-commonly retain lactase into adulthood.

PD-INEL Fig. 7-15 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985: 169.

DIETARY PROTEIN

- Normal humans require about 0.75 g/kg body weight of high quality dietary protein daily

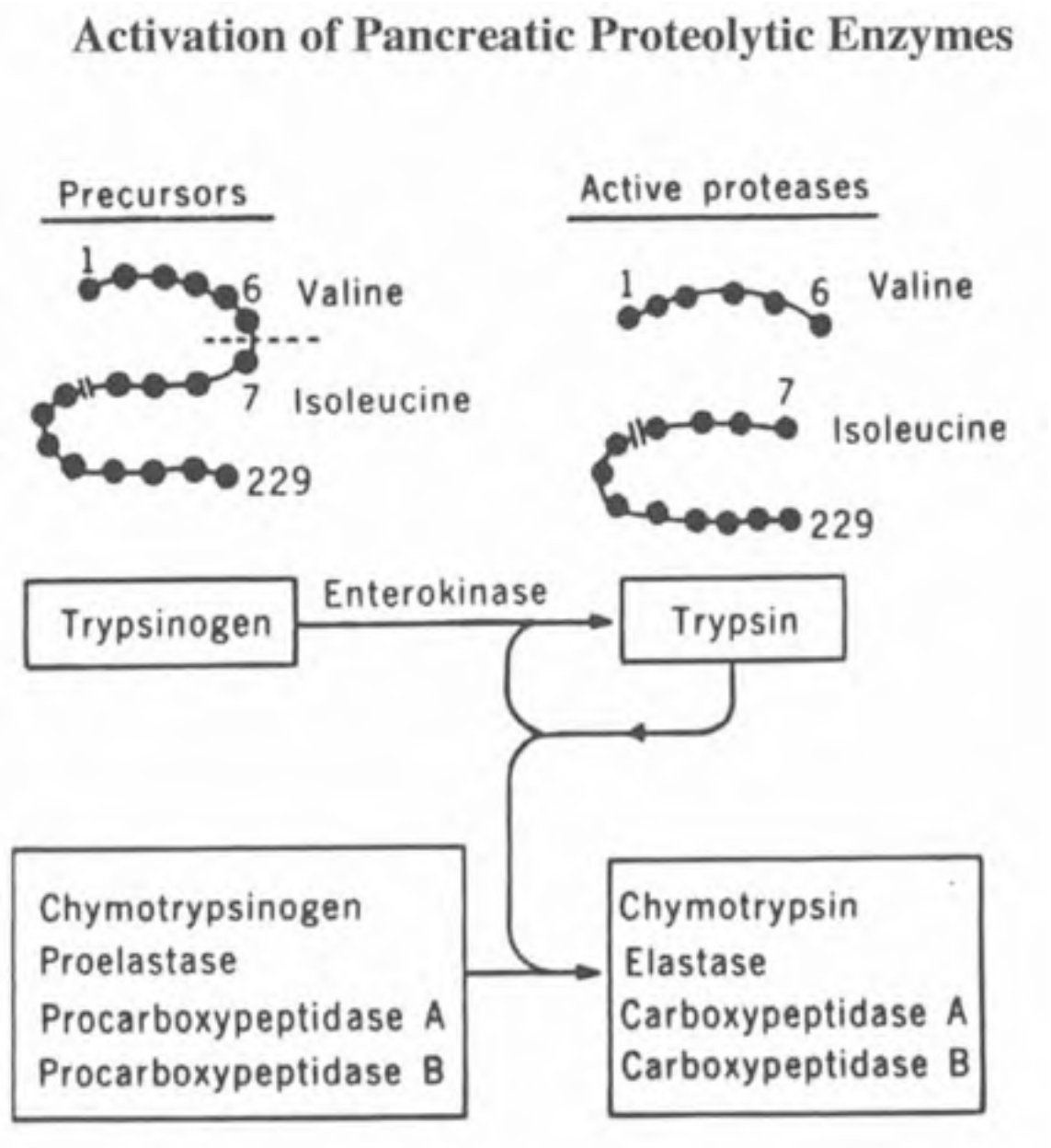
- Nine essential amino acids are not synthesized and must be obtained from diet

- Normal American diet contains 70-90 g/day

    Also endogenous protein in digestive secretions and shed epithelial cells

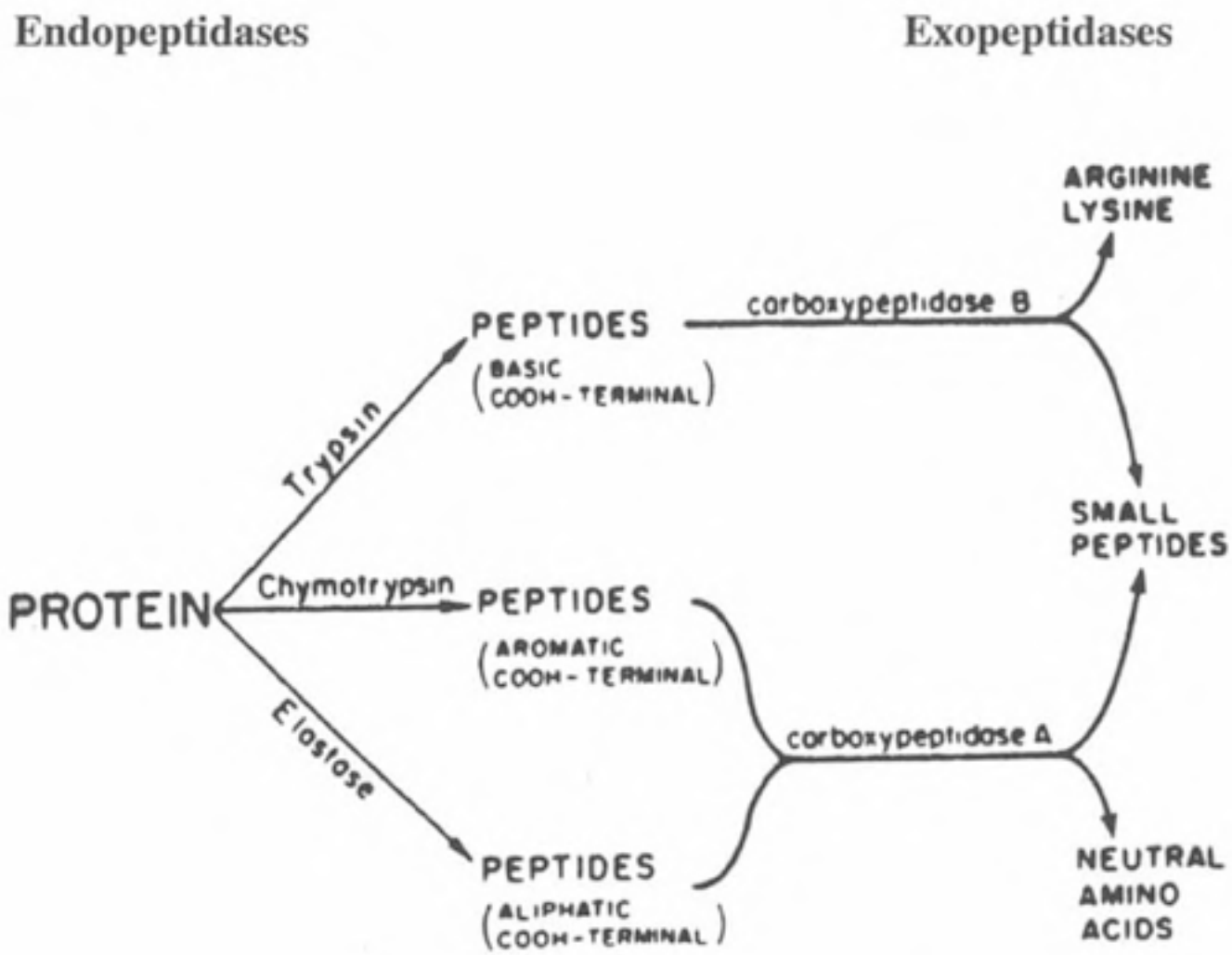
DIETARY PROTEIN (cont)

- Digestion includes a luminal and brush border phase
- Both amino acids and di- and tri-peptides absorbed
- Digestion normally quite complete



PD-INEL Fig. 11-8 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 114.

Luminal Phase of Protein Digestion

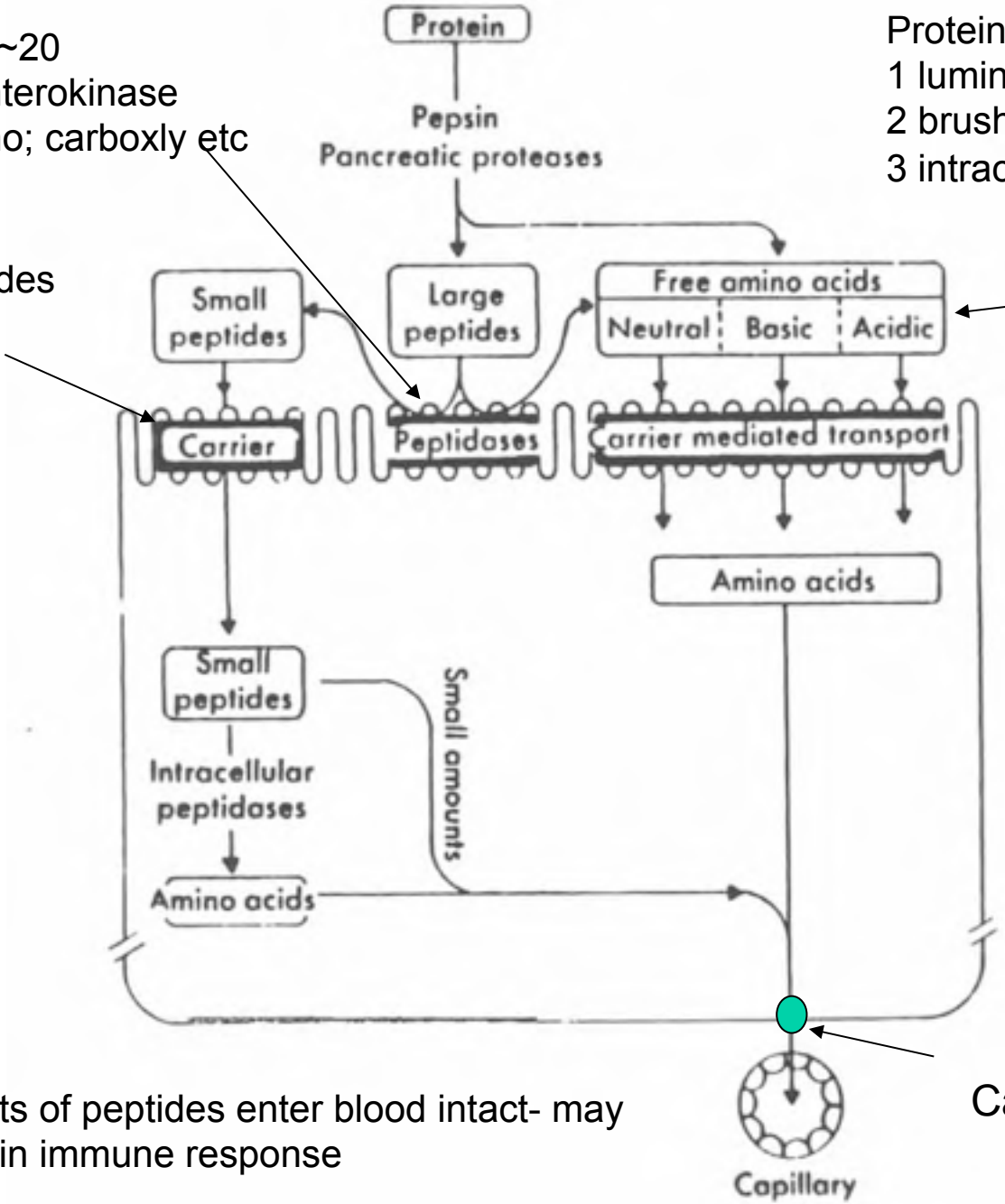


PD-INEL Fig 7-18 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985: 174.

Peptidases ~20
Including enterokinase
Endo-; amino; carboxly etc

Protein Digestion
1 luminal (stomach, pancreas)
2 brush border (enterocyte)
3 intracellular (enterocyte)

Di & tri Peptides
H+ coupled
PepT1



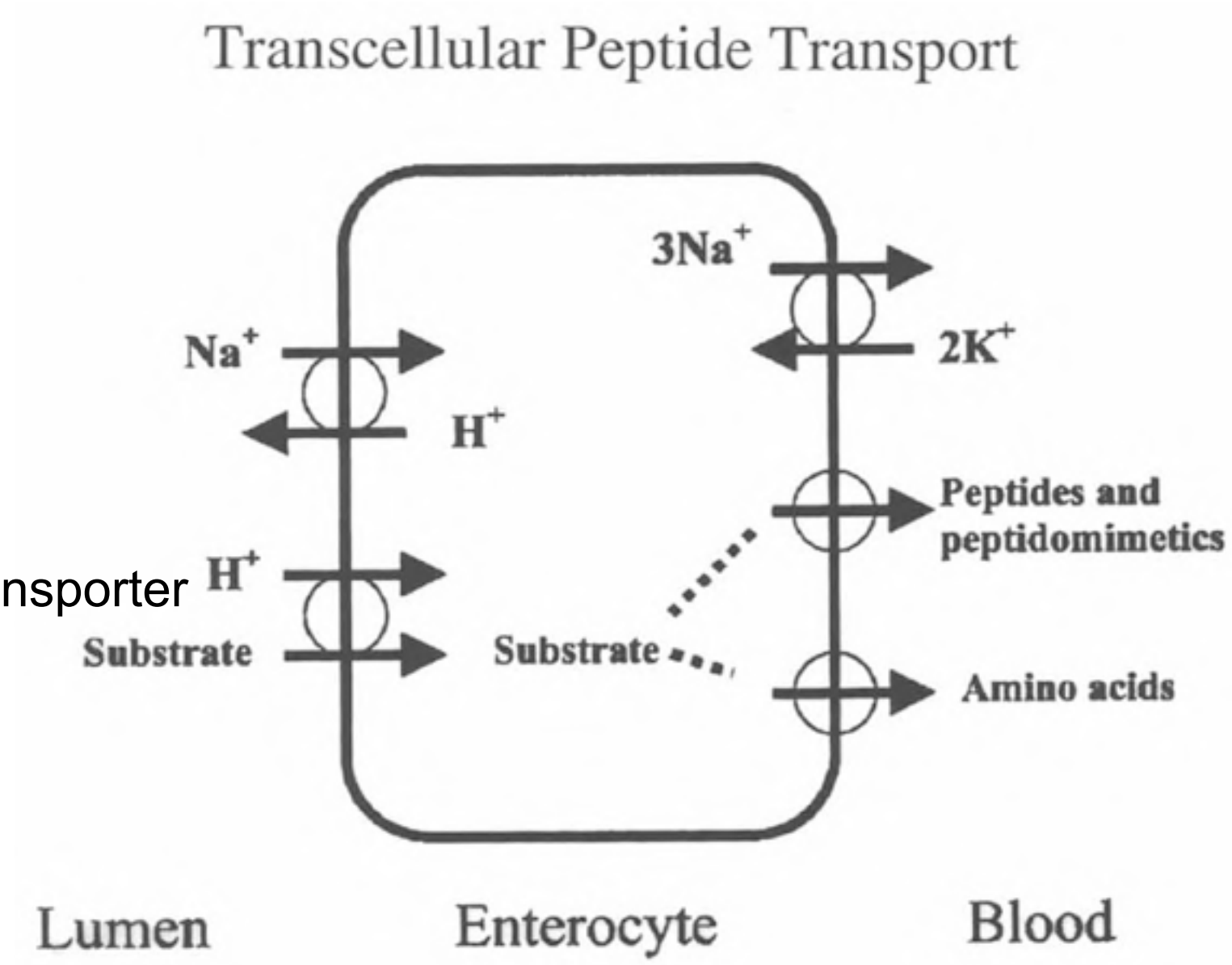
Na+ coupled

Small amounts of peptides enter blood intact- may be important in immune response

Carrier to exit cell

PD-INEL Source Undetermined

Apical transporter
PepT1



PD-INEL Source Undetermined

Defects in Absorption of Protein Digestion Products due to Altered Transport Systems in Gut and Kidney

- Cystinuria

  Autosomal Recessive
  Increased excretion in urine with renal stones

- Hartnup Disease

  Autosomal Recessive
  Impaired absorption of neutral amino acids
  Symptoms of Niacin deficiency (Pellagra)

Patients normally don't show protein malnutrition-
di and tri peptides sufficient

DIETARY LIPID

- Normal American diet about 100g/day primarily as triglyceride
- Long chain “essential” polyunsaturated fatty acids, cholesterol, and fat soluble vitamins also present
- Lipid digestion begins in stomach and is completed in upper intestine in the lumen
- Multiple lipase enzymes have pH optima between 6 and 7

STEPS IN LIPID DIGESTION

1. Emulsification
   physical process takes place in stomach
   phospholipids, proteins facilitate

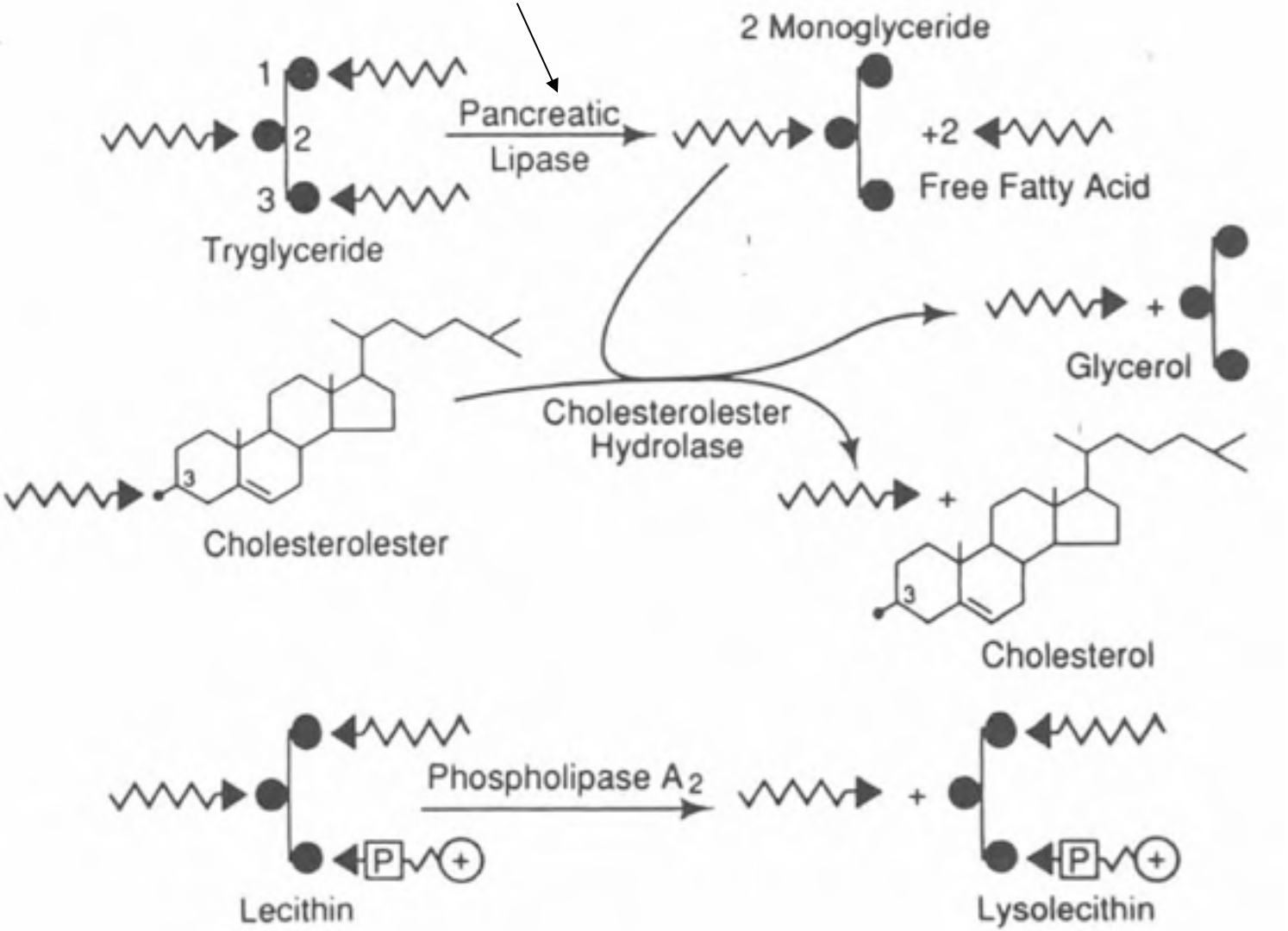
2. Digestion
   stomach and duodenum

3. Solubilization
   requires bile salts
   role of mixed micelles

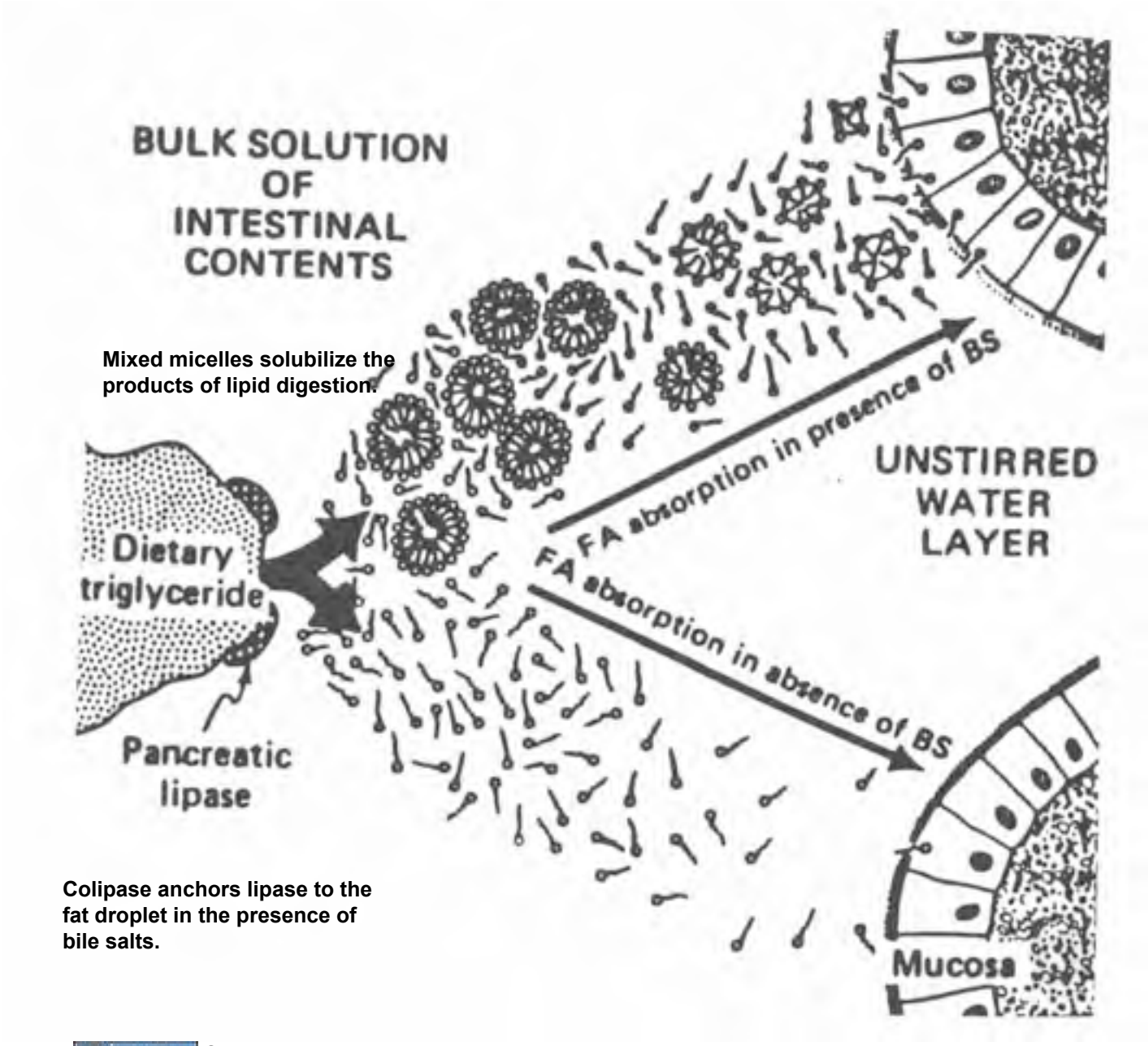
4. Absorption
   normally <5gm in stool- more is “steatorrhea”

Action of Major Pancreatic Lipases

- pH optimum 6-7
- in presence of bile salts acid inactivates



PD-INEL Fig. 8 Johnson, L. *Essential Medical Physiology* New York Raven Press 1992: 515.



PD-INEL Source Undetermined

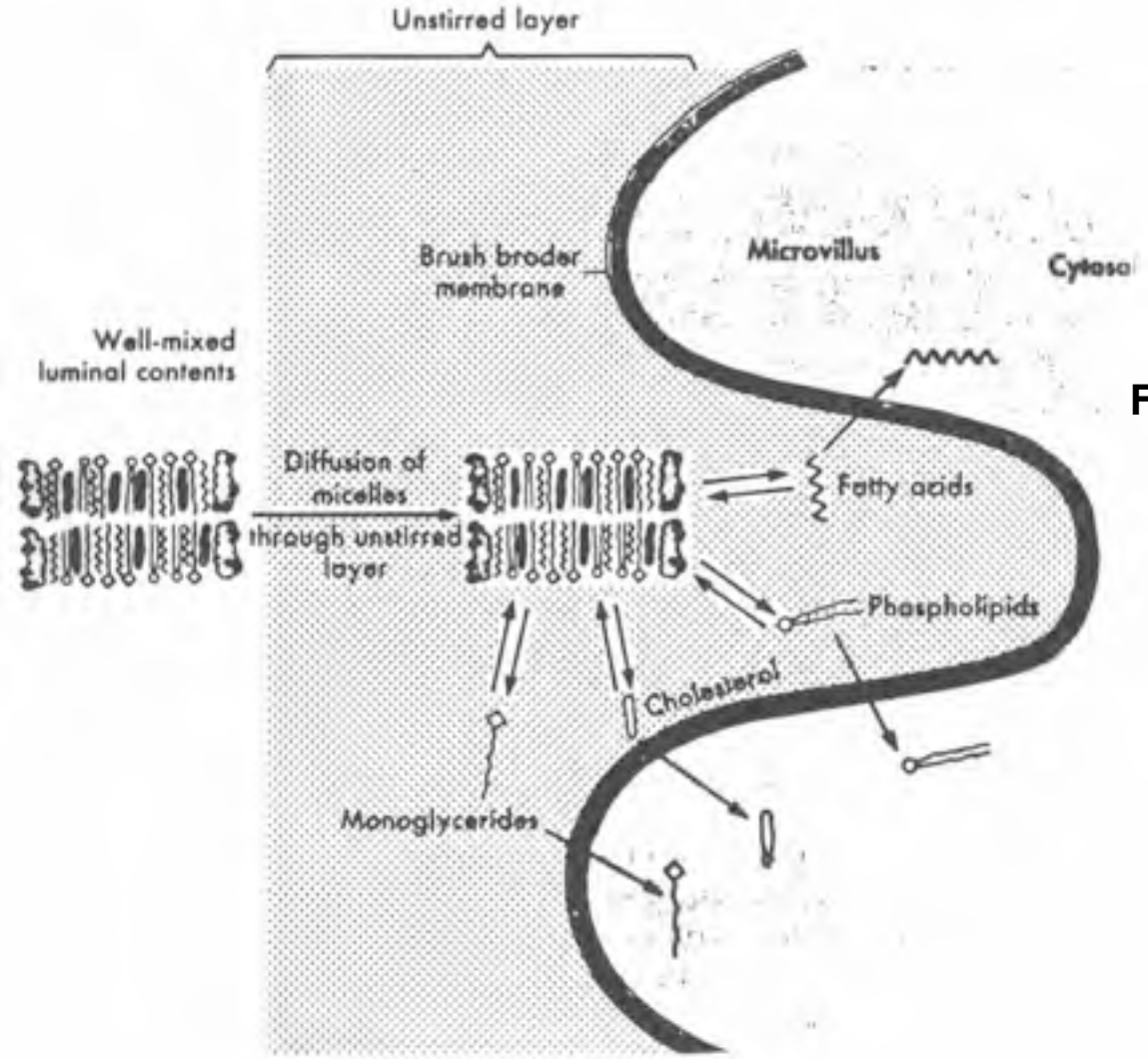
Ways to alter fat digestion and absorption

1. Olestra - Fake fat, can't be digested

2. Orlistat (Xenical) – Covalent Lipase inhibitor
   Now available OTC as Alli

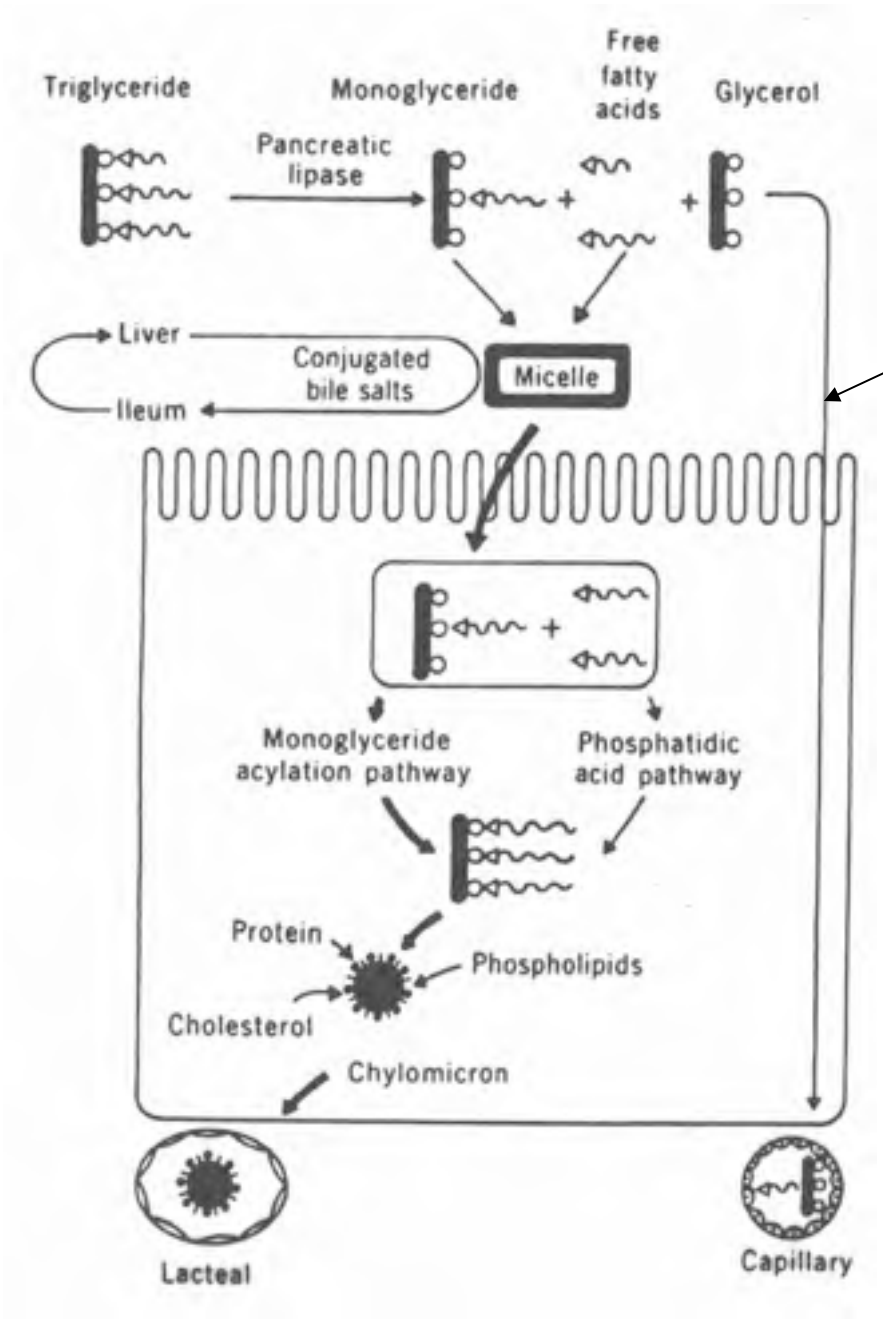
Side effect of both is malabsorption and diarrhea

Lipid Absorption in the Small Intestine



FABP

PD-INEL Source Undetermined

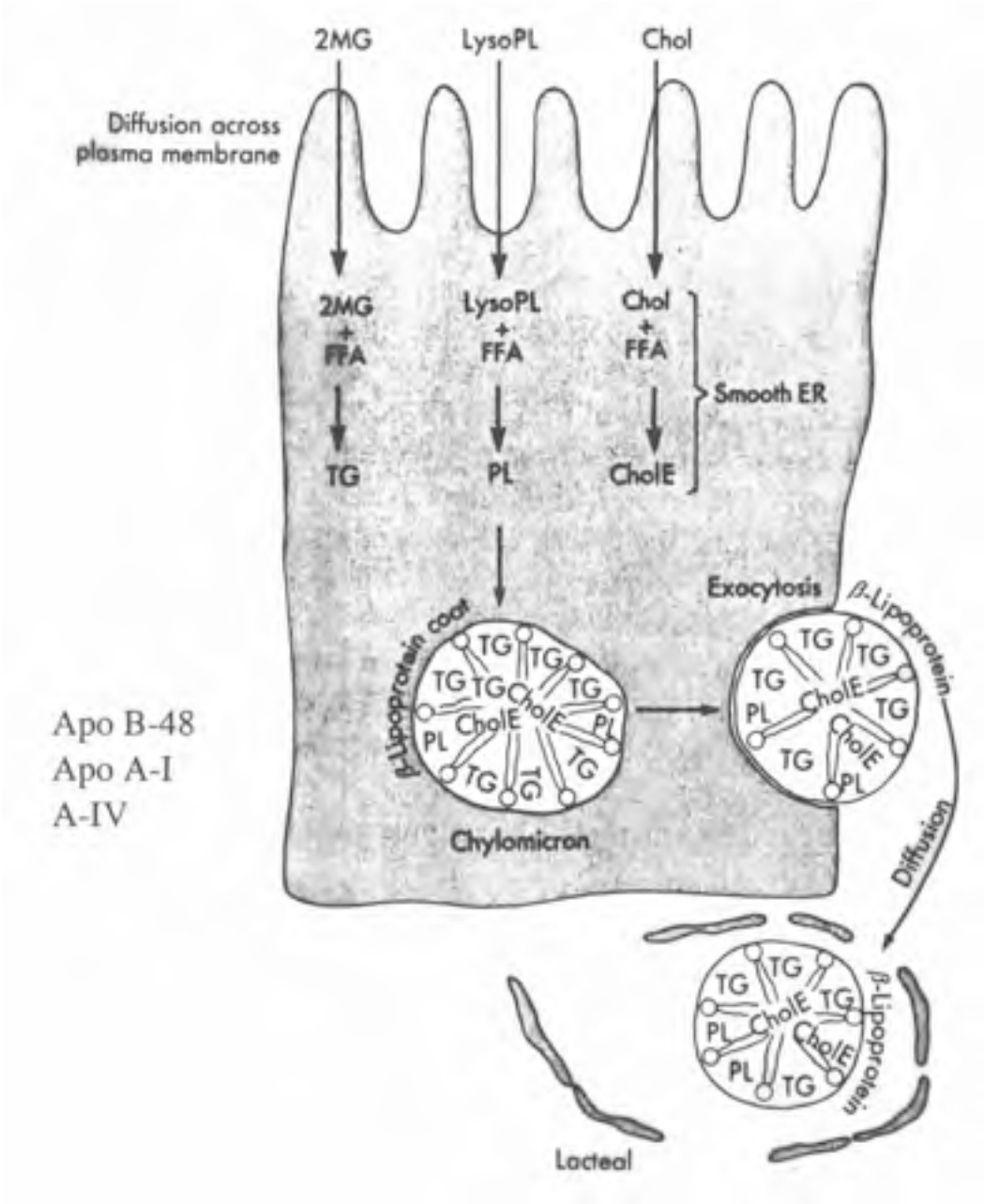


Short and medium chain fatty acids as well as glycerol

PD-INEL Fig. 11-14 Johnson, L. *Gastrointestinal Physiology*, 6th ed. Mosby Elsevier, St. Louis, MO; 2001: 136.

Medium Chain Triglycerides

1. Fatty acids are 6-12 carbons in chain length
2. Present in small amounts in normal diet
3. Can be digested and absorbed without bile salts due to increased water solubility
4. Fatty acids not reesterified but taken up into the portal vein



PD-INEL Source Undetermined

Cholesterol Absorption

- Luminal cholesterol comes largely from diet and bile; about 50% absorbed by intestine
- Cholesterol absorbed selectively as compared to plant sterols
- Absorbed cholesterol released in chylomicron and goes back to liver as chylomicron remnants
- Ezetimibe (Zetia) is a new drug that blocks cholesterol entry into the enterocyte

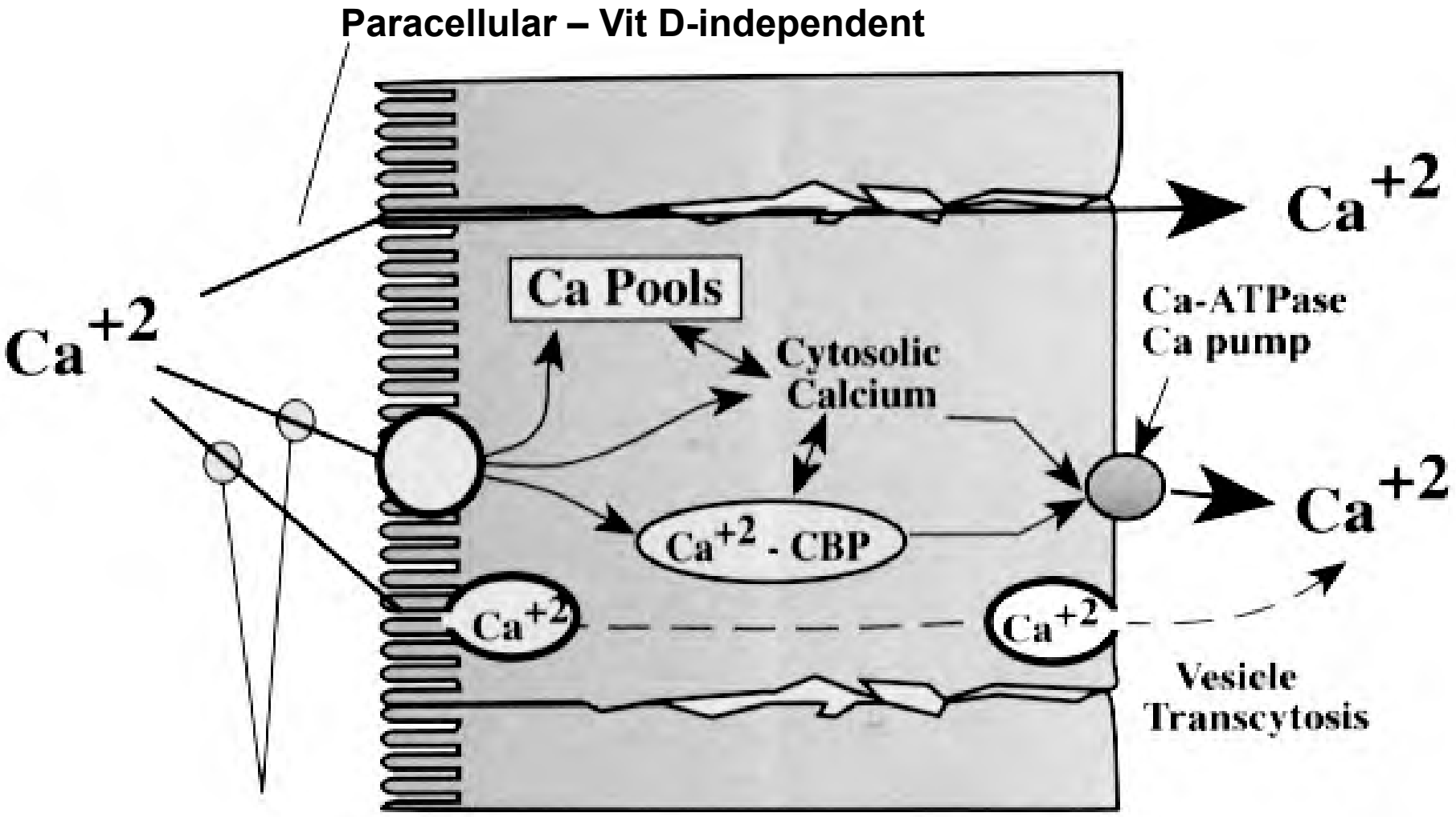
CALCIUM ABSORPTION

1. Dietary intake about 1000 mg/day with net absorption of about 100 mg/day

2. Most active in duodenum and involves an energy dependent, transcellular pathway

3. Regulated by active form of Vit D, $1,25(OH)_2$ Vit D, also known as $1,25(OH)_2$-cholecalciferol

Mechanism of Intestinal Calcium Absorption



PD-INEL Fig. 9 Chang, E, Sitrin, M, Black, D. *Gastrointestinal, Hepatobiliary, and Nutritional Physiology.* Lippincott – Raven, Philadelphia, PA; 1996: 204.

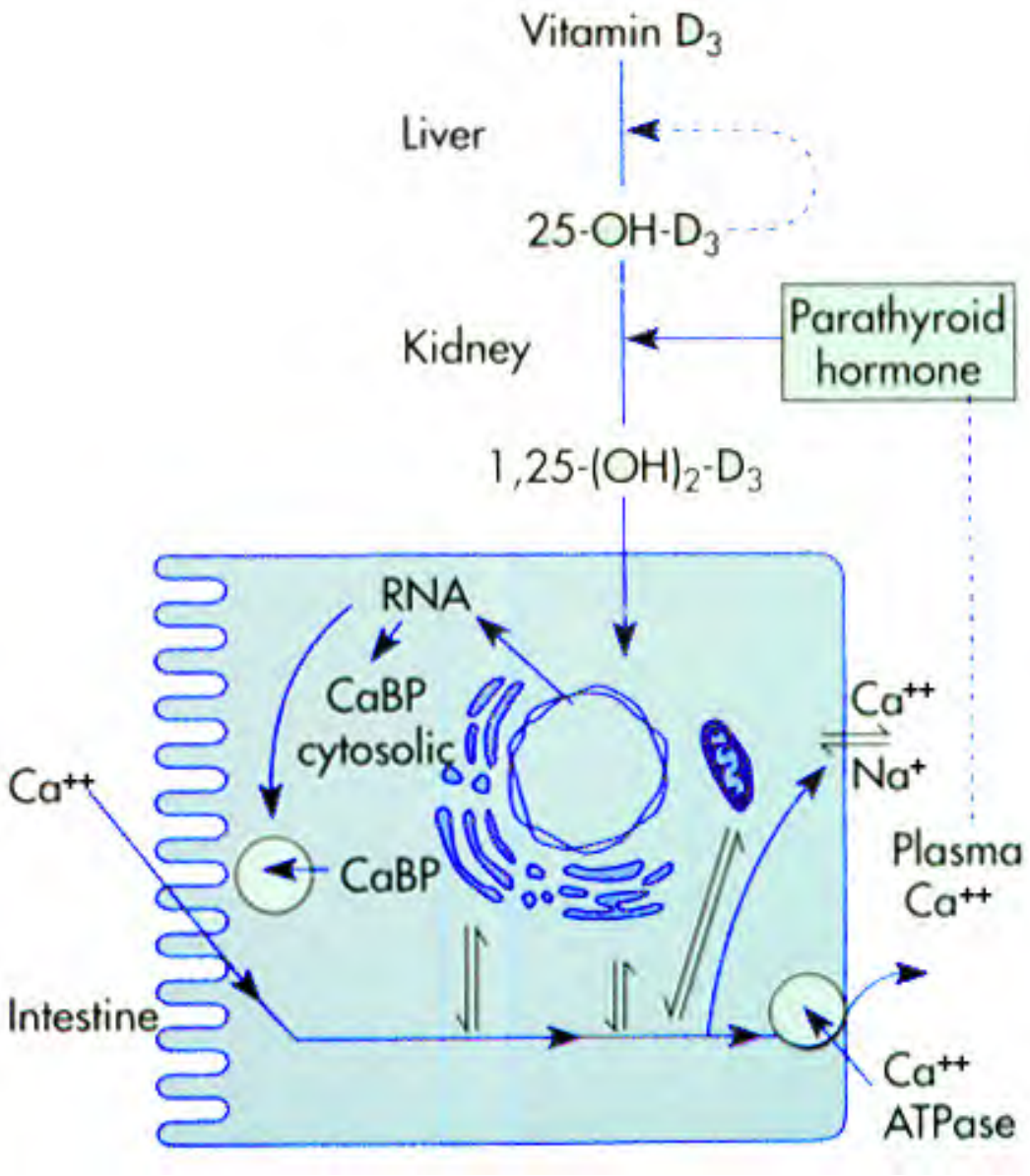
MOLECULAR COMPONENTS OF INTESTINAL CALCIUM ABSORPTION

1. Entry across the apical brush border is mediated by a specific Ca^{2+} entry channel known as CaT1

2. Within the enterocyte a calcium binding protein, calbindin binds and transports Ca^{2+}

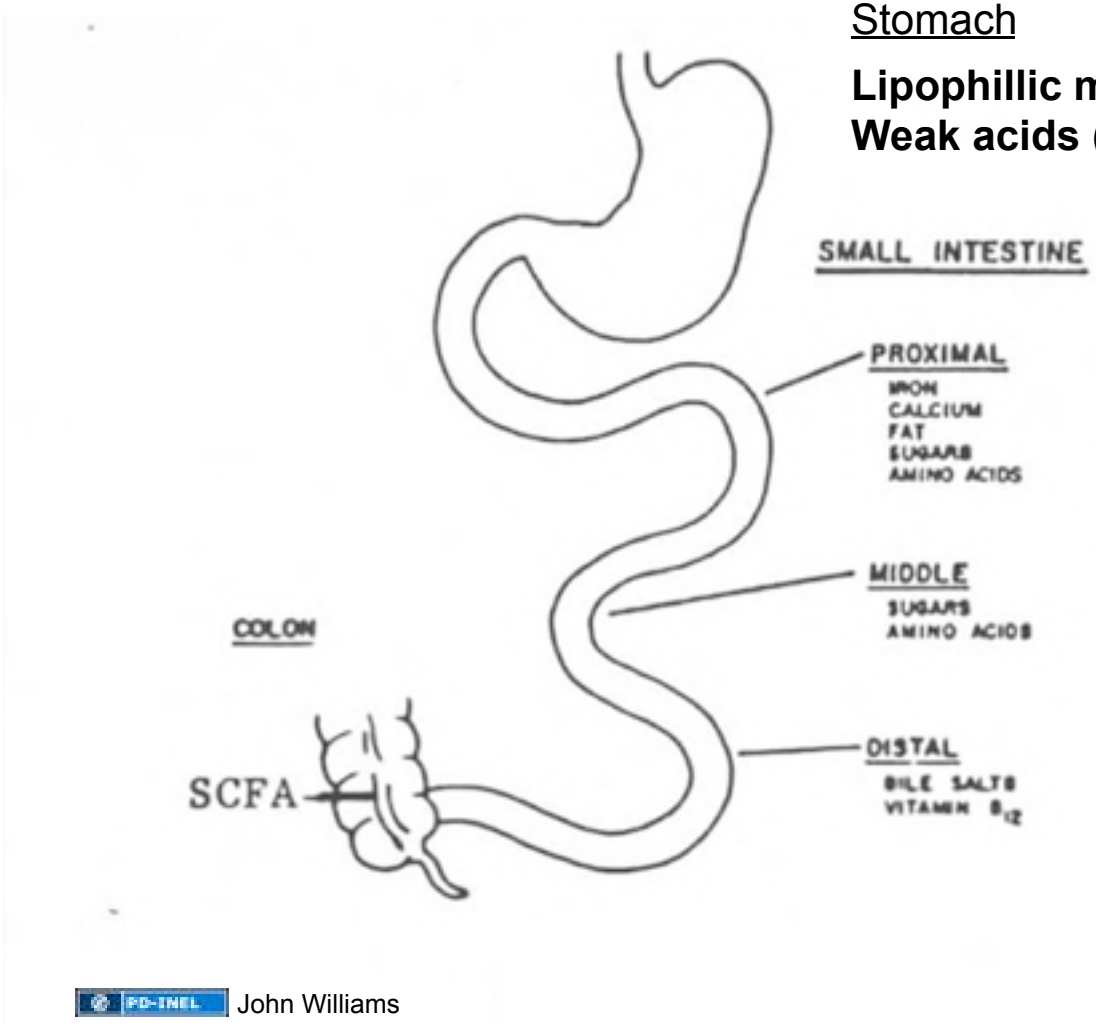
3. Ca^{2+} exit across the basolateral membrane is mediated by the plasma membrane Ca-$^{2+}$ATPase, PMCA1

Synthesis and Action of Vitamin D



PD-INEL Fig. 12-6 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 133.

Primary Sites of Nutrient Absorption



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INTESTINAL ELECTROLYTE ABSORBTION AND SECRETION

Volumes and ionic composition of fluid entering the human intestine

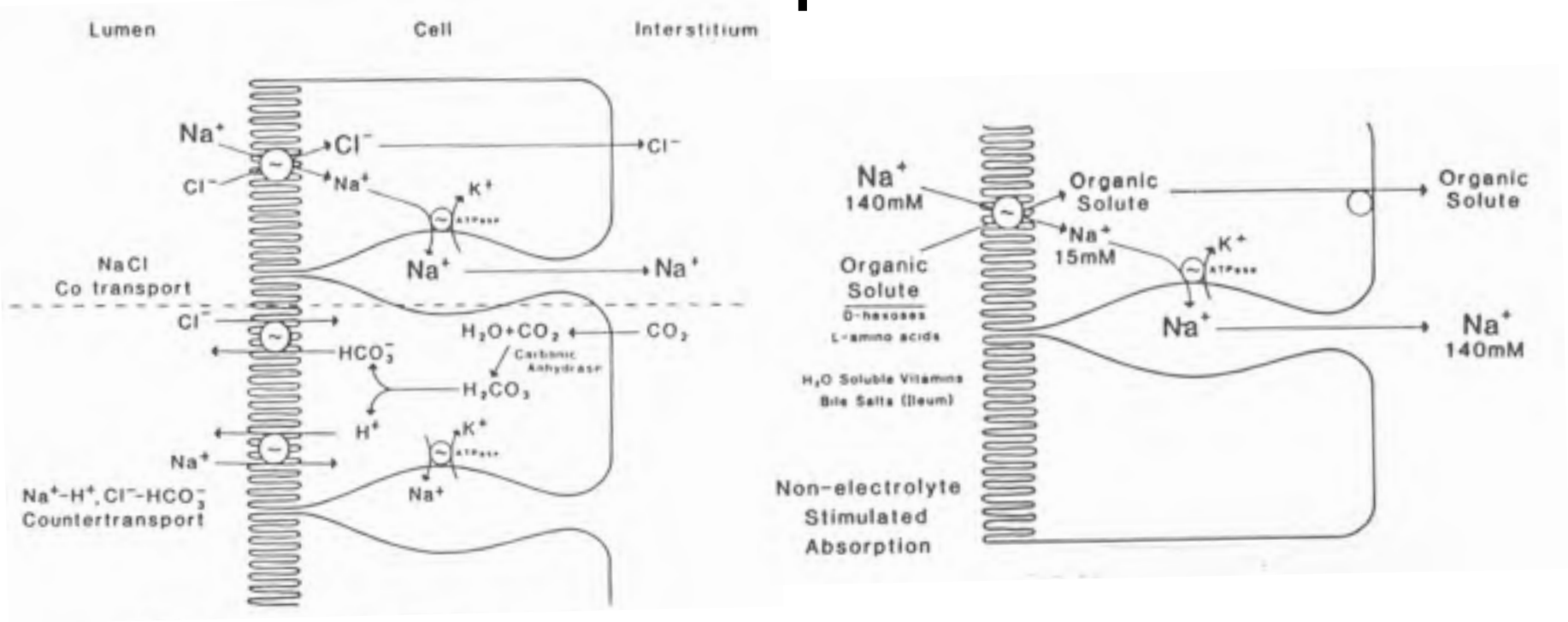
Segment	Vol (ml)	Per 24 hr Na (mM)	K (mM)	Cl (mM)
Entering Duodenum				
Diet	2,000	150	50	200
Saliva	1,000	50	20	40
Gastric juice	2,000	100	15	280
Bile	1,000	200	5	40
Pancreatic juice	2,000	150	5	40
Small intestinal secretion	1,000	150	5	100
Total	9,000	800	100	700
Entering ileum	5,000	700	40	550
Entering colon	1,500	200	10	100
Stool	100	3	8	2

PD-INEL Source Undetermined

DUODENAL FLUID DYNAMICS

- Mucosa is leaky allowing rapid osomotic equilibration of hypertonic and hypotonic meals
- Duodenal secretion of HCO_3^- from Brunner's glands
- Absorption by small intestine is then isotonic

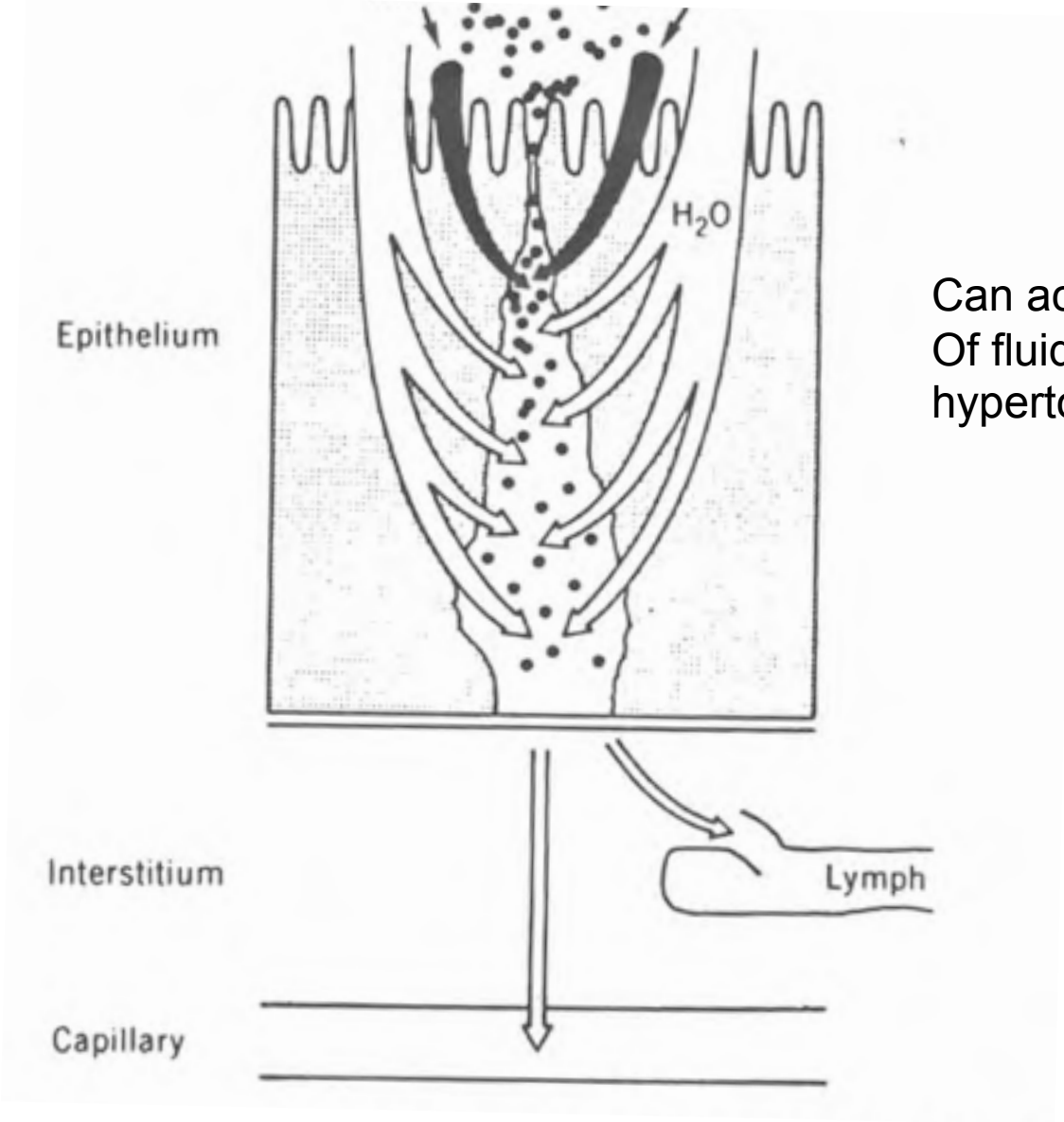
Cellular Models of Intestinal Sodium Absorption



Figs. 7-7 and 7-8 from Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Can be regulated by contents, neurotransmitterers, inflammatory mediators and systemic hormones particularly Angiotensin II

Fluid Absorption According to the Standing Osmotic Gradient Model

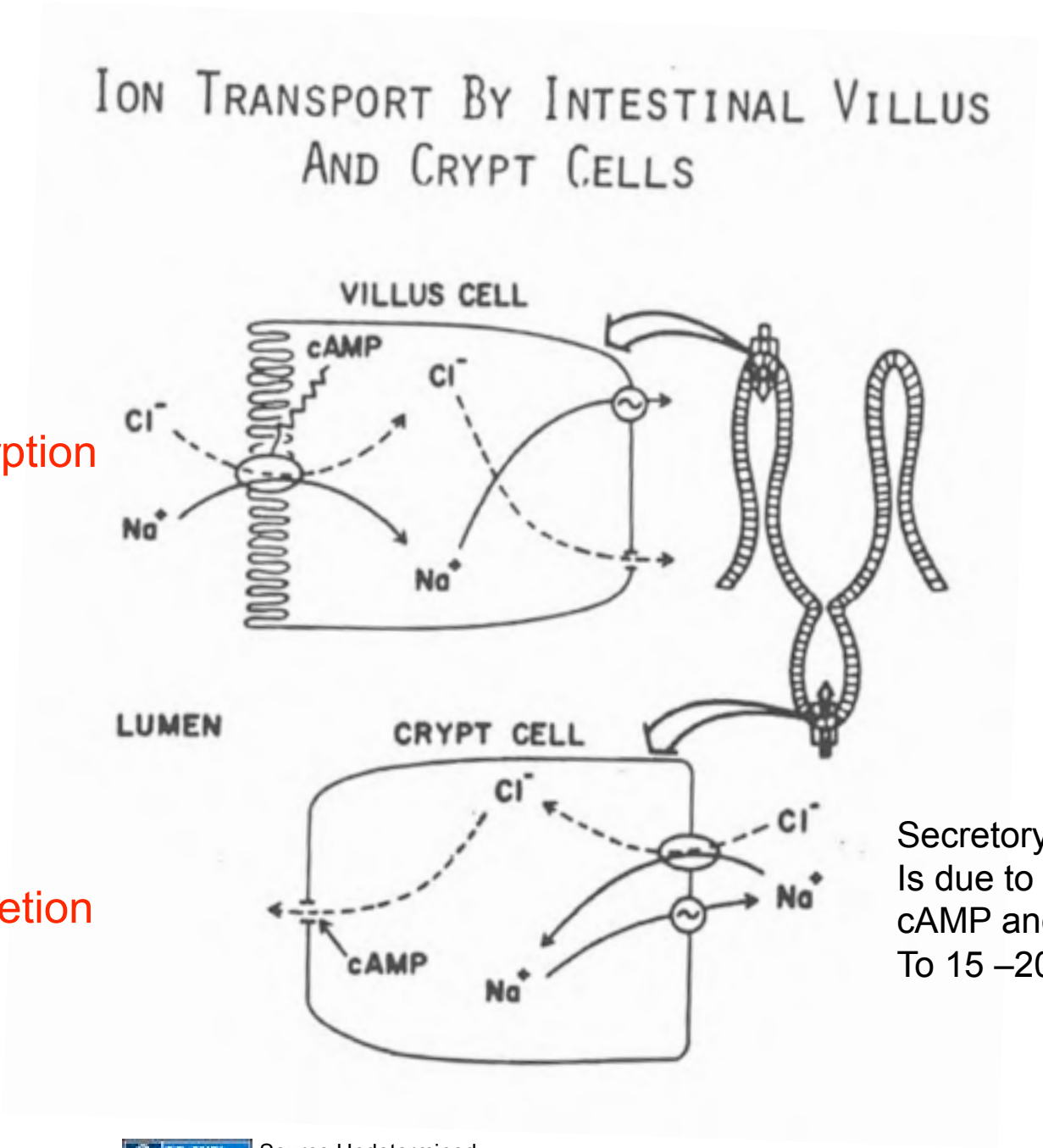


Can account for isotonic movement
Of fluid by use of localized
hypertonicity

PD-INEL Fig. 12-4 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007.

Absorption

Secretion



Secretory diarrhea of Cholera
Is due to Cholera Toxin activating
cAMP and stimulating secretion
To 15 –20 liters per day

PD-INEL Source Undetermined

INDUCERS OF COLONIC AND SMALL INTESTINAL SECRETION

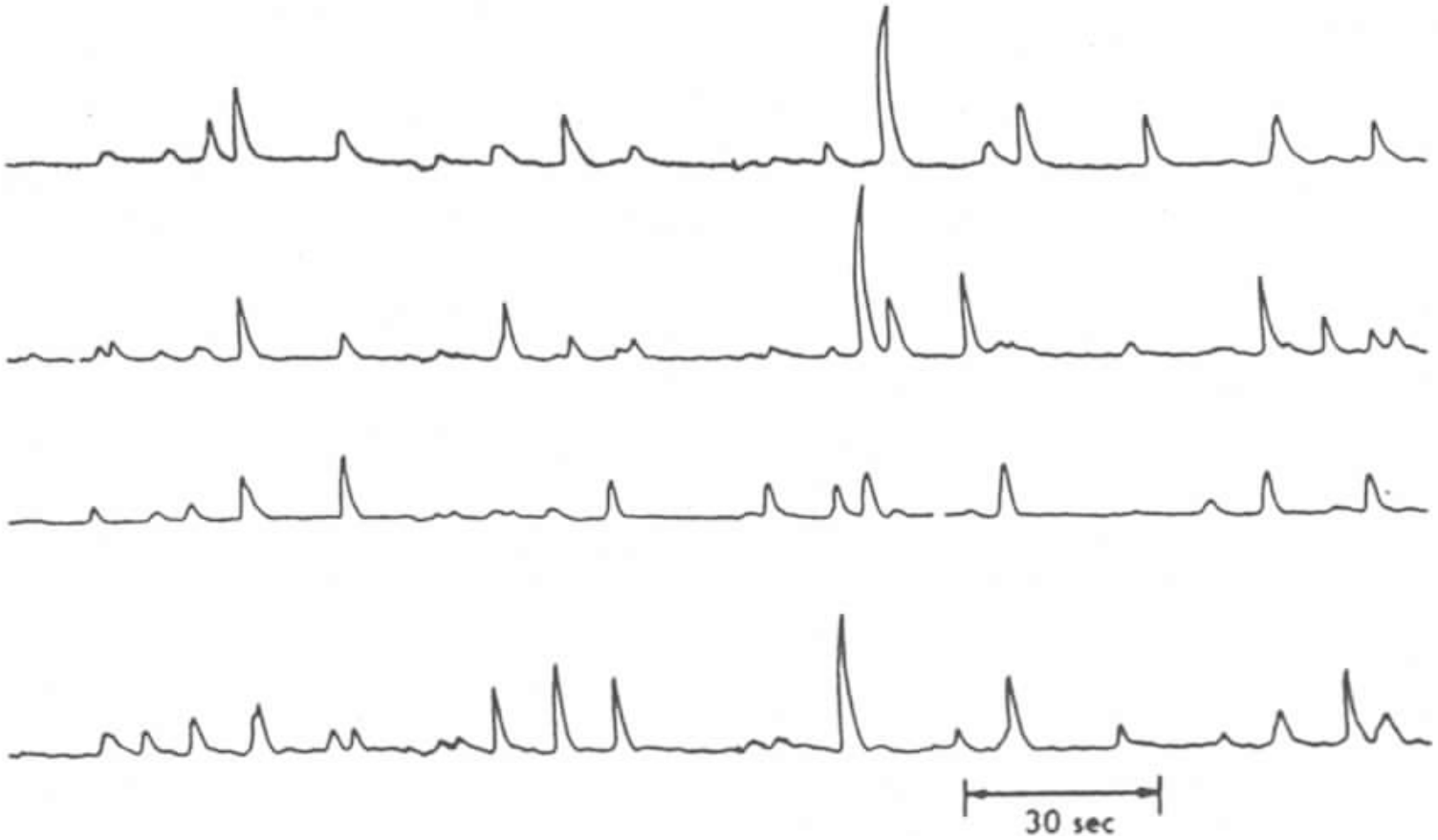
1. BACTERIAL ENDOTOXINS (CHOLERA)
2. CERTAIN UNSATURATED FATTY ACIDS (CASTOR OIL)
3. BILE ACIDS
4. ANTHROQUINONE CATHARTICS (SENNA. CASCARA)
5. CERTAIN HORMONES (VIP)

INTESTINAL MOTILITY

FUNCTIONS OF INTESTINAL MOTILITY

1. Mixing of foodstuffs, digestive secretions and enzymes
2. Facilitate contact of chyme with intestinal mucosa
3. Net propulsion in an aboral direction

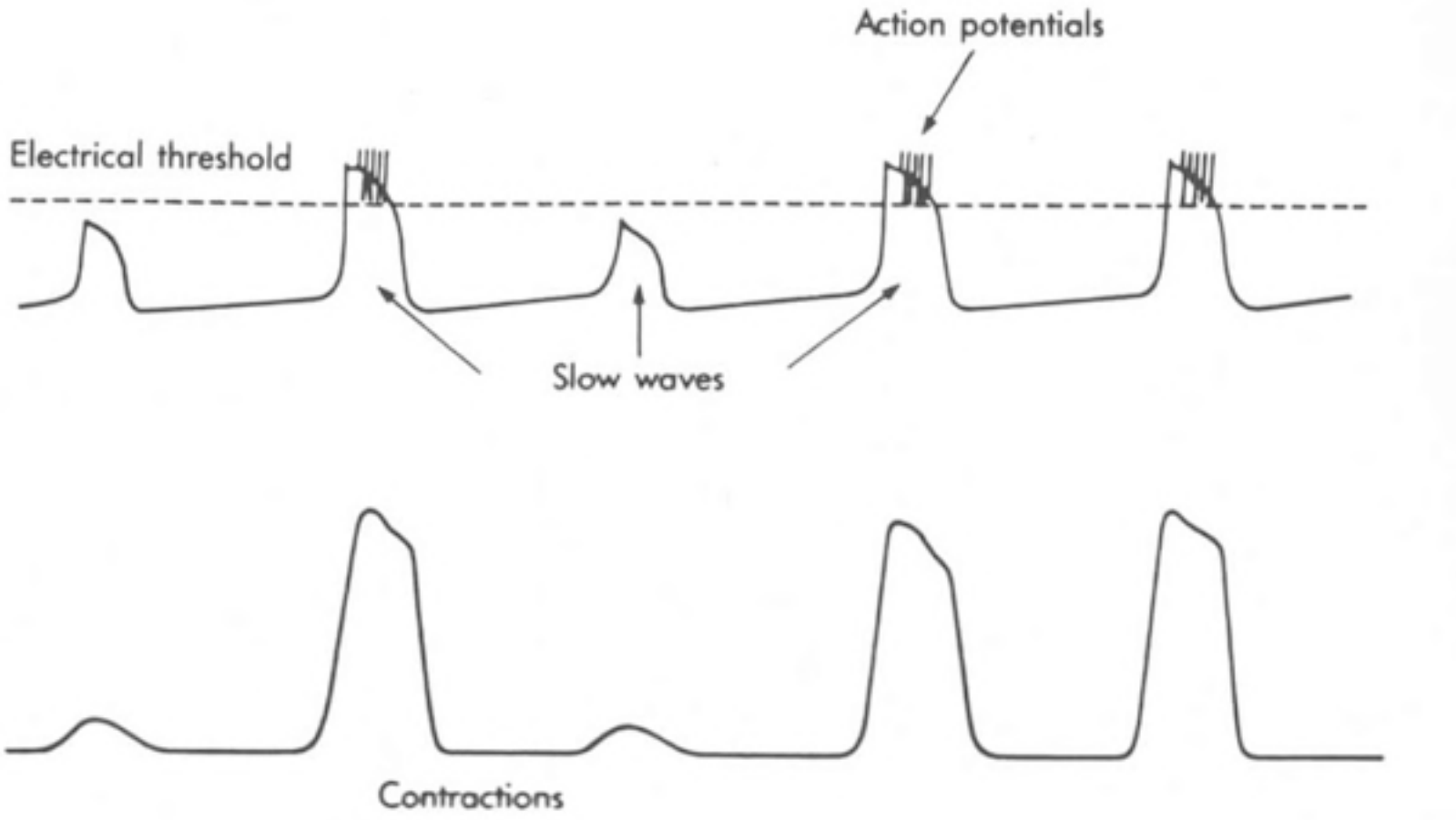
Intraluminal Pressure Changes in the Duodenum of a Concious Man



PD-INEL Fig. 5-1 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 42.

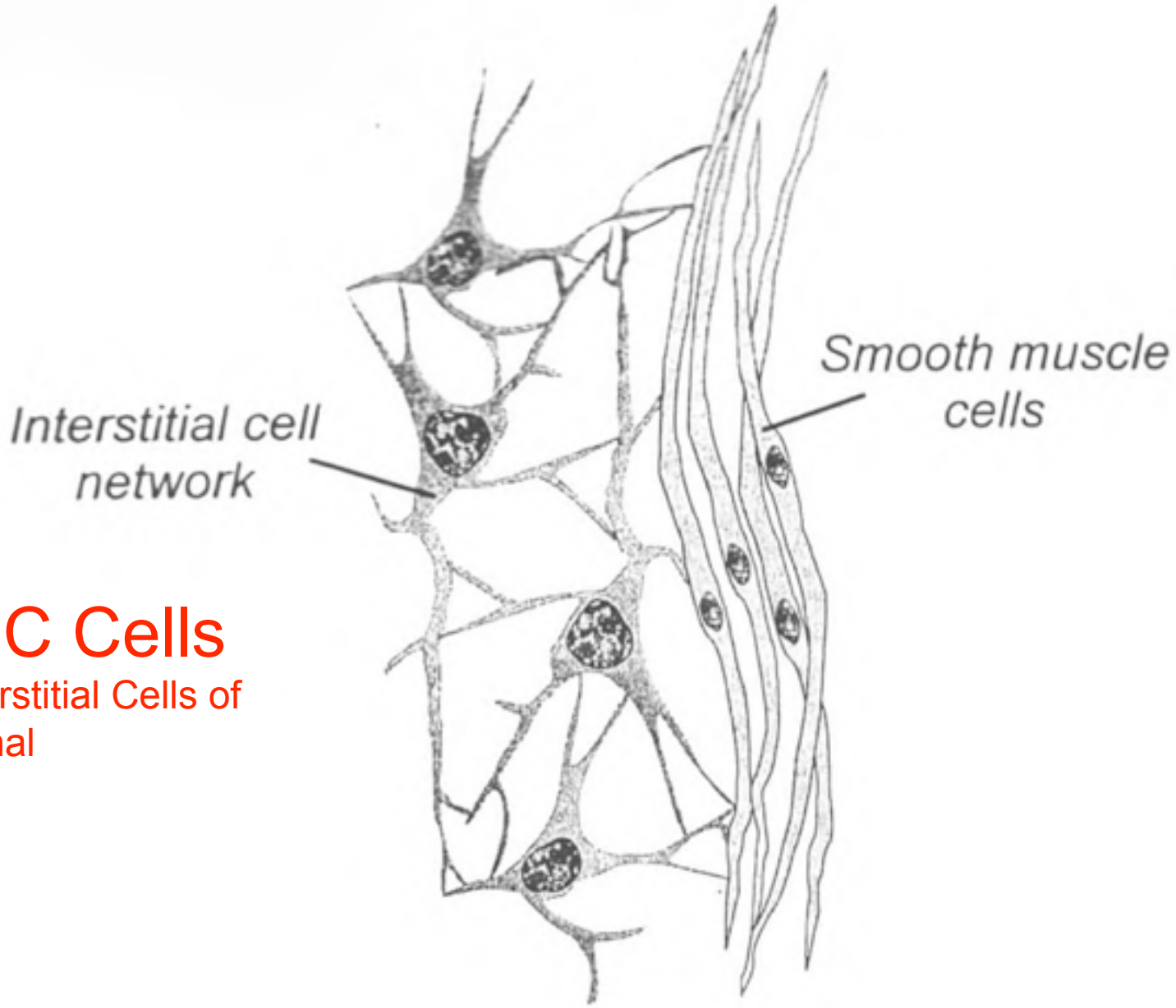
In duodenum contractions occur at intervals of 5 sec or multiples of 5

Electrical Threshold for Generation of Action Potentials



PD-INEL Source Undetermined

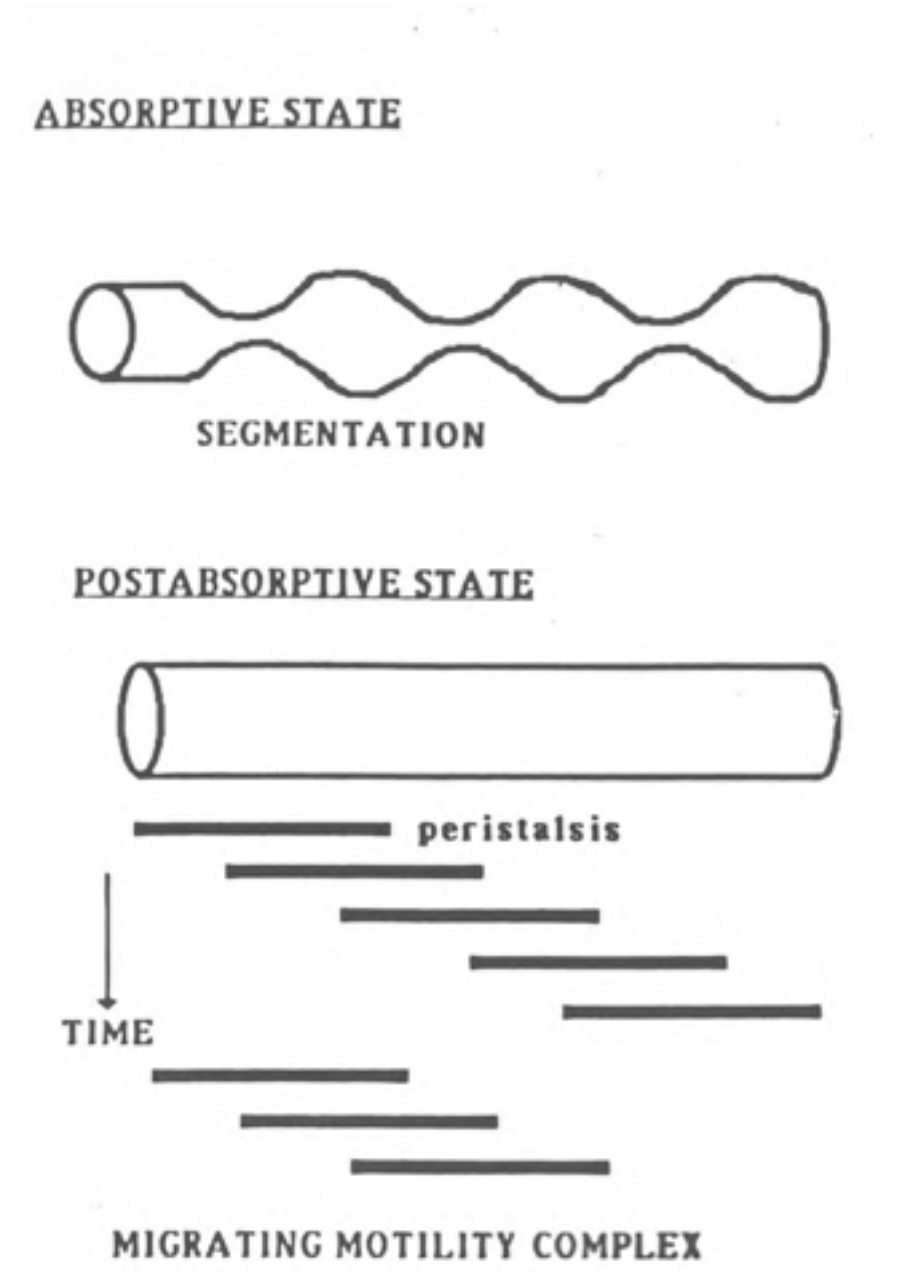
Frequency of slow waves is 12/min in duodenum and decreases to 9/min in The ileum. (Another site of pacemaker activity)



ICC Cells

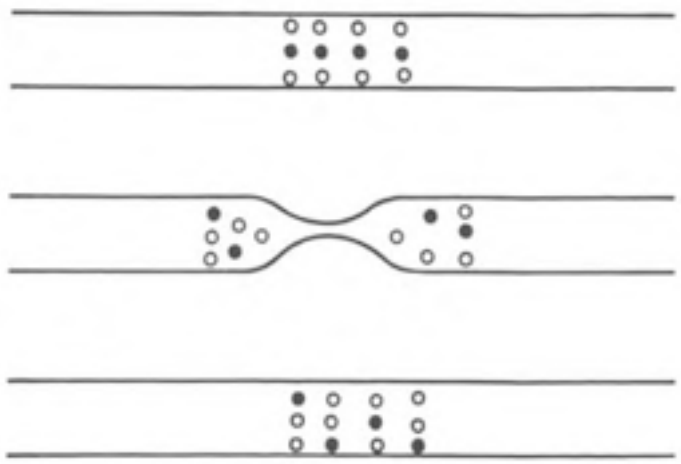
Interstitial Cells of Cahal

PD-INEL Source Undetermined



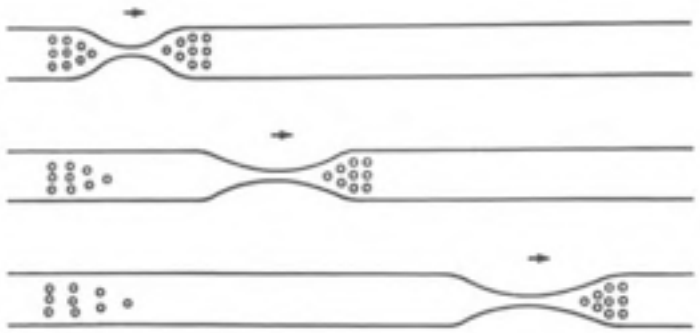
Fed pattern initiated by the Presence of chyme in the intestine

PD-INEL Source Undetermined



Isolated segmental contractions serve to mix the intestinal contents.

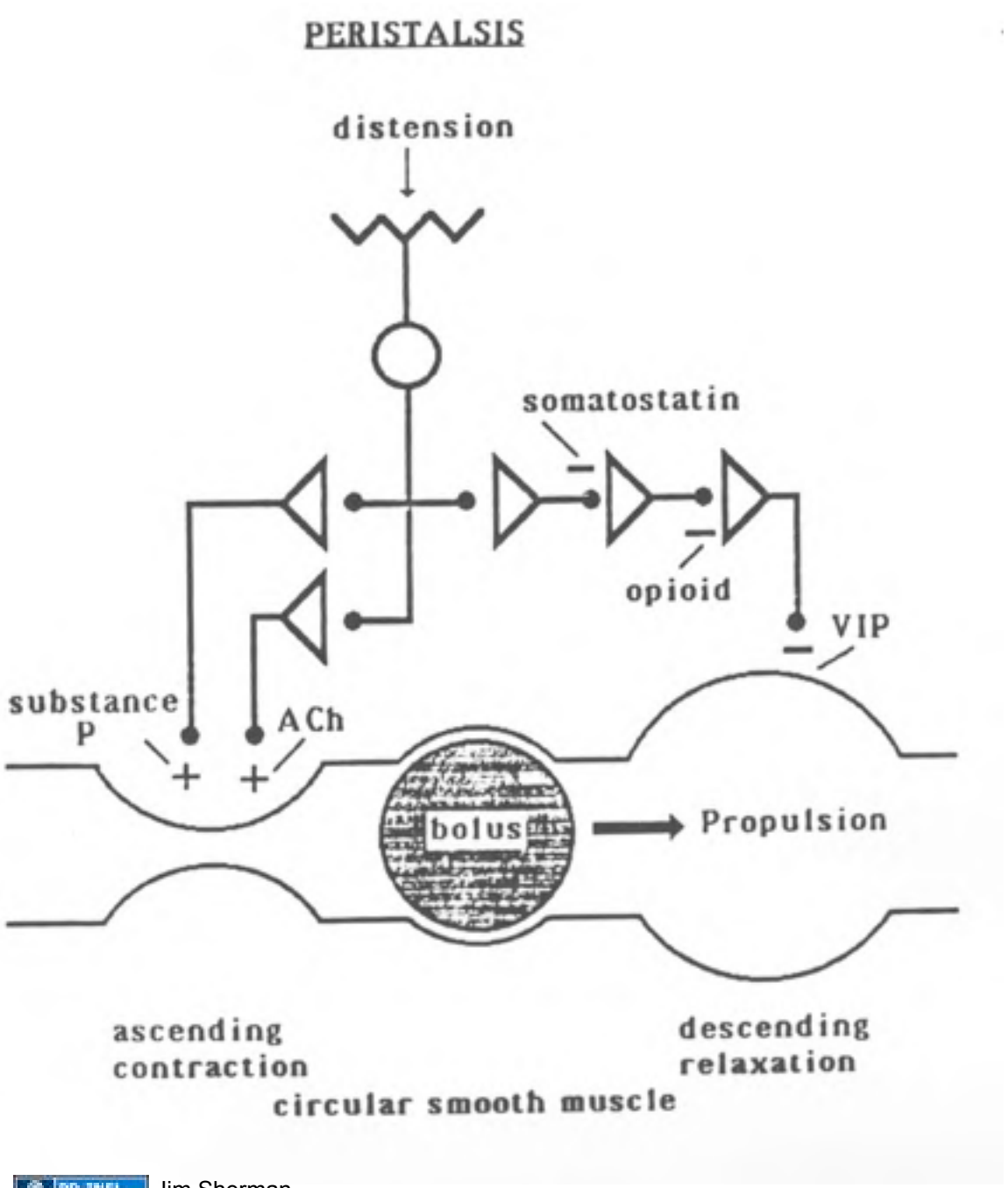
Villus contraction which increases after a meal also helps mix unstirred layer and compress the lacteal



Contractions that have an orad-to-aborad sequence (left-to-right) serve to propel contents in a net aboral direction.

Only very short peristaltic movements occur in the fed state

PD-INEL Fig. 5-3 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 44.



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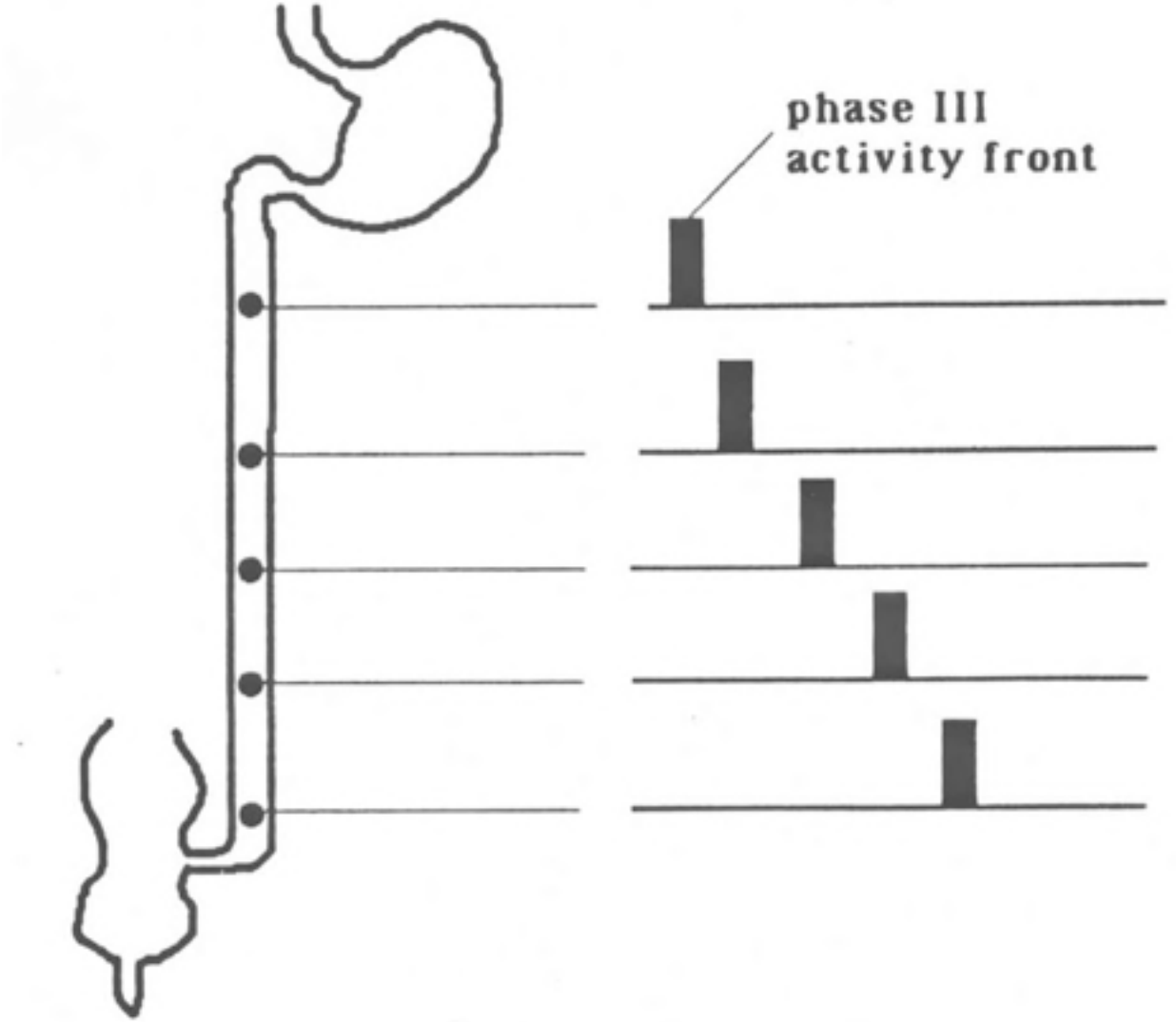
Migrating Motility Complex



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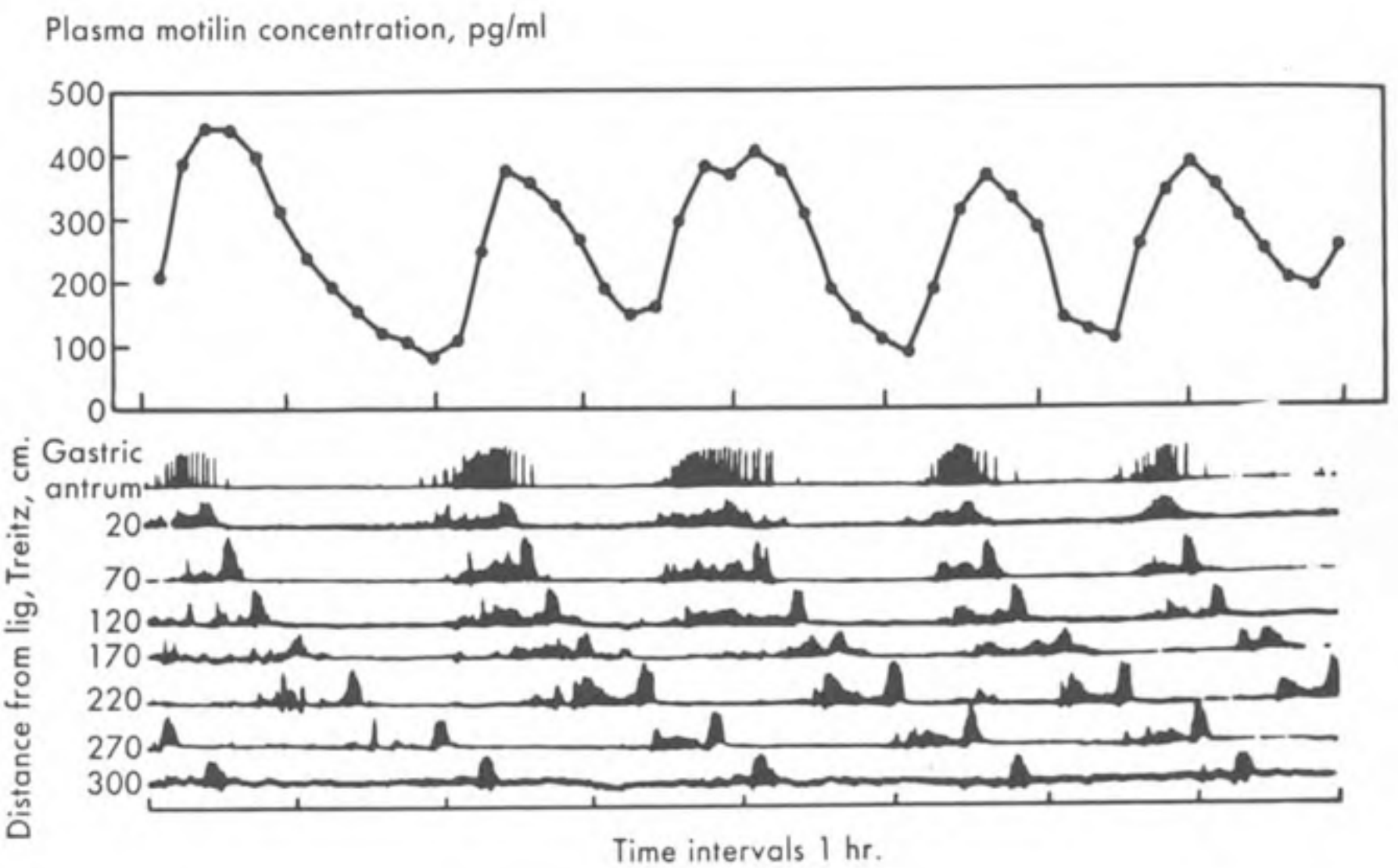
Relationship between Plasma Motilin and the MMC



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MINERAL ABSORPTION

ESSENTIAL MINERAL ELEMENTS

1. Required to maintain normal physiology and health

2. Occur in diet, sometimes as trace elements

3. Variable absorptions may be regulated

4. In steady state intestinal absorption equals body losses

Additional Source Information

for more information see: http://open.umich.edu/wiki/CitationPolicy

Slide 4 – Fig. 7-2 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985: 144.

Slide 5 – Source Undetermined

Slide 6 – Trier, JS, Modara, JL. "Functional morphology of the mucosa of the small intestine". *In* Johnson, LR. *Physiology of the Gastrointestinal Tract*. Vol. II. Raven Press, New York, NY, 1981: 926.

Slide 9 – Source Undetermined

Slide 10 – Source Undetermined

Slide 11 – John Williams

Slide 12 – Fig. 7-15 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985: 169.

Slide 15 – Fig. 11-8 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 114.

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