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M1 - GI Sequence

Intestines and Colon

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Winter, 2009

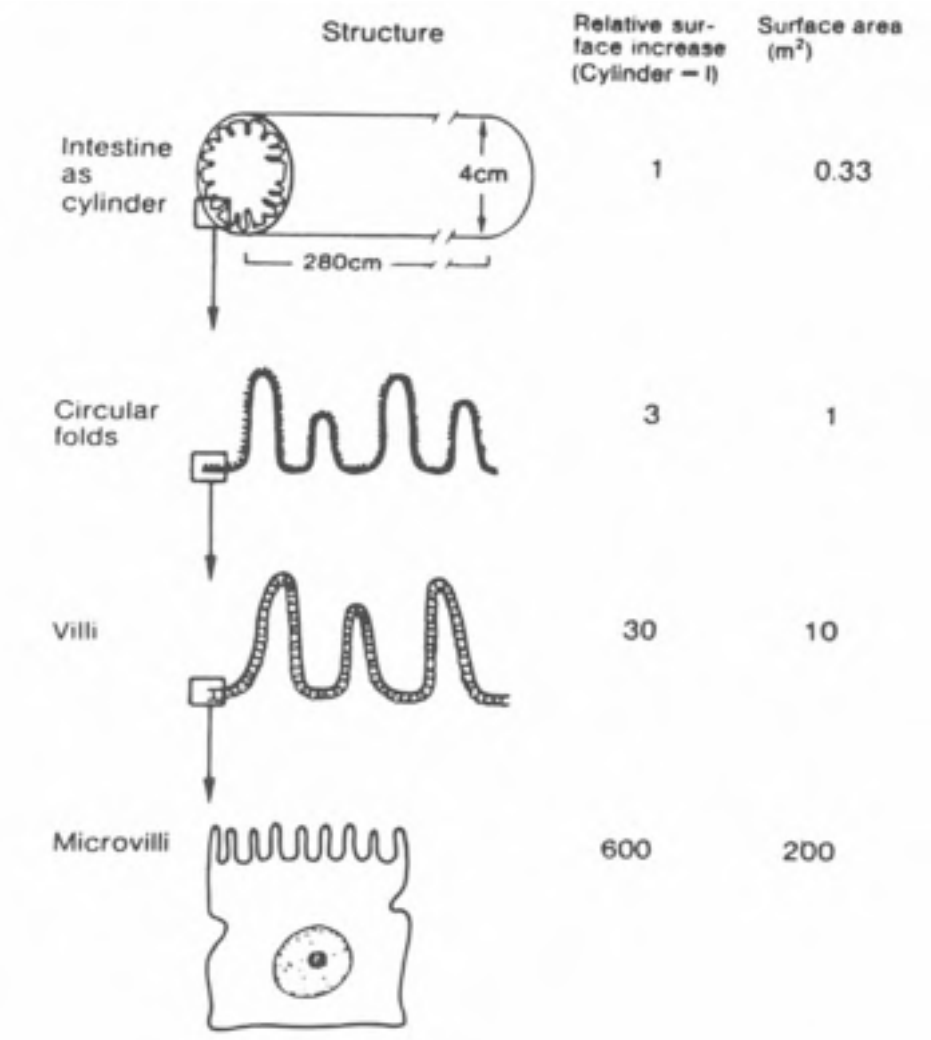
University of Michigan
Medical School

THE SMALL INTESTINE

Human small intestine 6-7 m long
Duodenum 20-30 cm
Jejunum 2.5 m
Ileum 3.5 m

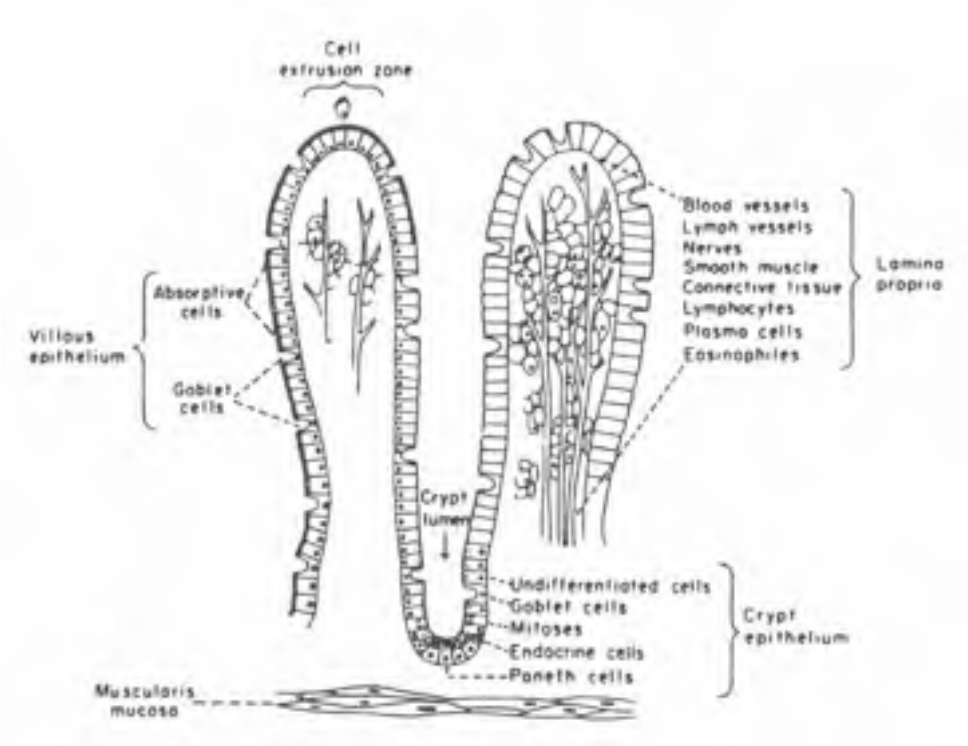
FUNCTIONS

Digestion
Absorption
Secretion
Motility



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

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.

DIGESTION

1. Mainly occurs in the upper part of small intestine

2. Intraluminal phase by secreted enzymes

3. Epithelial phase by brush border hydrolases or within enterocyte

DIETARY CARBOHYDRATES

POLYSACCHARIDES

1. STARCH
   AMYLOSE
   AMYLOPECTIN
2. GLYCOGEN

DISACCHARIDES

SUCROSE
LACTOSE

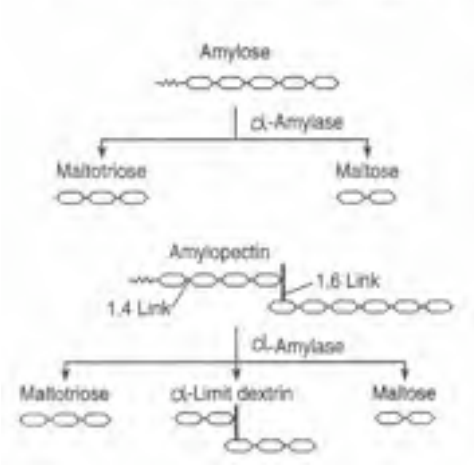
MONOSACCHARIDES

FRUCTOSE
GLUCOSE

INDIGESTIBLE CARBOHYDRATES

Dietary carbohydrates are made up of complex carbohydrates including starch and glycogen, simple sugars, and fiber. Carbohydrate intake normally totals 200-300g/ day and provides about 50% of the calories in an average American diet. It serves both as an energy and as a carbon source. Carbohydrate digestion includes a luminal phase with the enzymes (amylase) present in saliva and pancreatic juice and a brush border or membrane phase that takes place in the proximal small intestine. Only monosaccharides are appreciably absorbed and this is mediated by specific carriers in the small intestine mucosal cells.

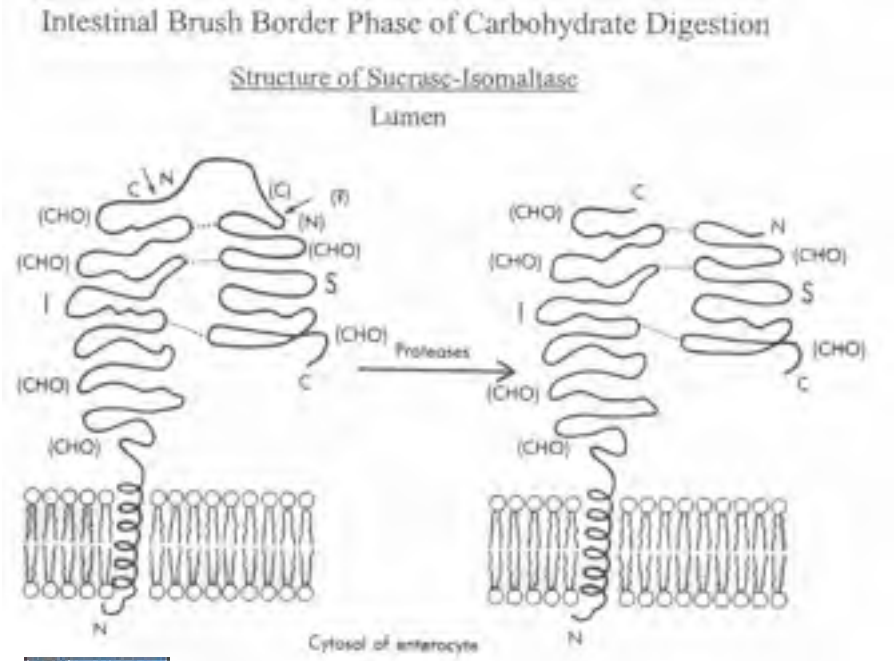
Luminal Phase of Carbohydrate Digestion



PD-INEL Source Undetermined

Pancreatic and salivary α-amylase have a pH optimum of 7.0. The digestion products of starch (a mixture of amylose and amylopectin) after exposure to α-amylase are shown in the figure. Glucose units are indicated by hexagons. Amylase cleaves interior α1-4 linkages but doesn't affect α1-6 linkages. The end product is a mixture of maltose, maltotriose, and small polymers of glucose some with branched chain structure (α-limit dextrin). Glycogen (animal starch) is made up of branched chairs of glucose and is broken down similar to amylopectin.

Acarbose – An amylase inhibitor used to delay glucose absorption.



PD-INEL Source Undetermined

The sucrase-isomaltase complex is inserted into the endoplasmic reticulum membrane as a single polypeptide chain. When endoplasmic reticulum vesicles fuse with the brush border membrane of small intestinal epithelial cells, pancreatic proteases cleave the protein into its sucrase (S) and isomaltase (I) polypeptides by acting at the sites shown by the arrows. CHO indicates the presence of carbohydrate side chains and the dotted lines represent noncovalent interactions between the S and I subunits.

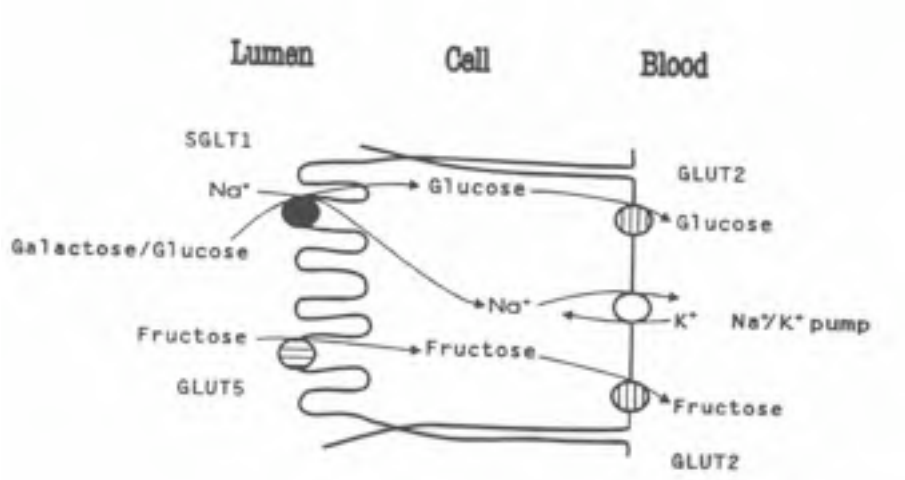
Intestinal Brush Border Hydrolysis of Oligosaccharides

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.

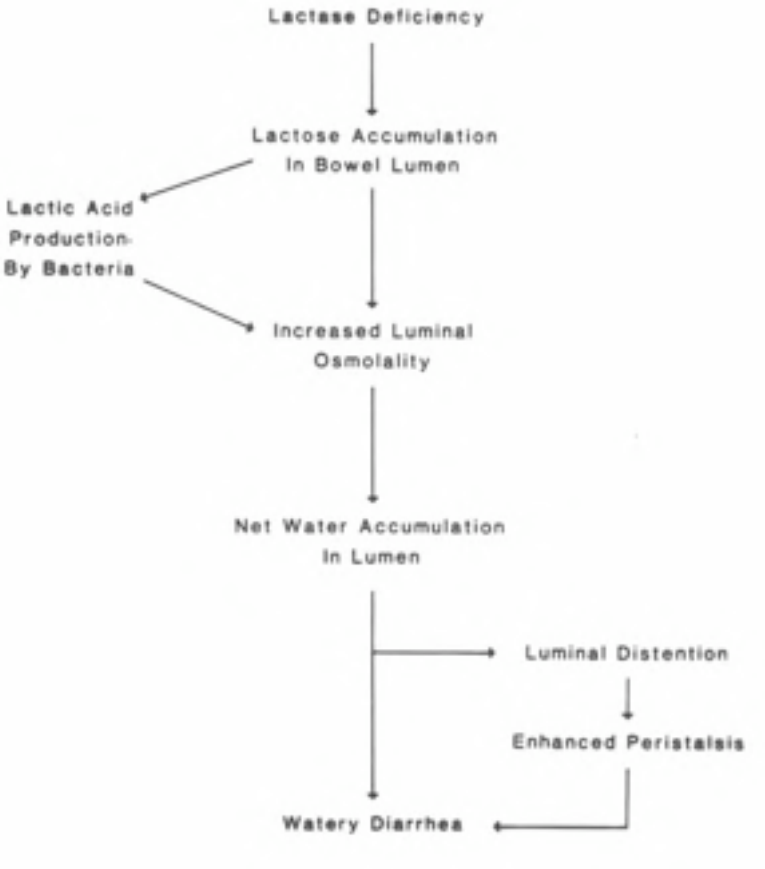
PD-INEL Source Undetermined

MECHANISM OF MONOSACCHARIDE ABSORPTION



PD-INEL John Williams

A model for glucose, galactose, and fructose transport across the intestinal epithelium. Glucose and galactose are transported into the enterocyte across the brush border membrane by the Na^+/glucose cotransporter (SGLT1), and then they are transported out across the basolateral membrane down their concentration gradients by the glucose transporter GLUT2. The low intracellular Na^+ driving uphill sugar transport across the brush border is maintained by the Na^+/K^+ pump on the basolateral membrane. Glucose and galactose therefore stimulate Na^+ absorption across the epithelium. Fructose is transported across the cell down its concentration gradient across the brush border and basolateral membranes. GLUT5 is the brush border fructose transporter, while GLUT2 handles fructose transport across the basolateral membrane. Both GLUT2 and GLUT5 are facilitated diffusion transporters. Glucose-galactose malabsorption manifest in newborn children can be due to mutations in SGLT1.

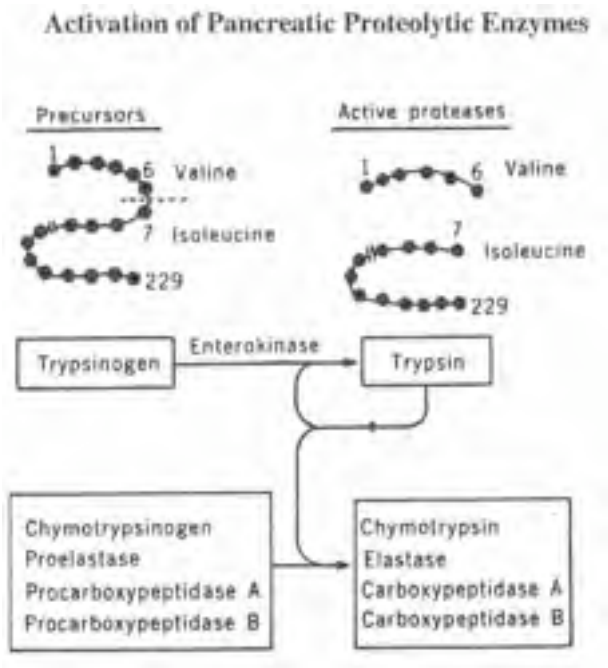


PD-INEL Fig. 7-15 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985: 169.

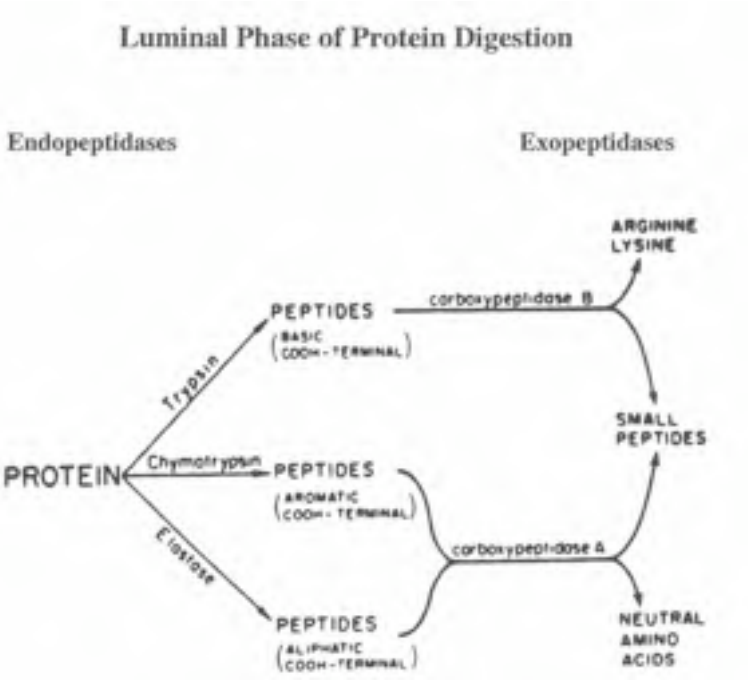
Mechanisms involved in excess water loss (diarrhea) produced by lactase deficiency (carbohydrate intolerance).

PROTEIN DIGESTION

Normal humans require about 0.75 g/kg body weight of high quality dietary protein to ensure nitrogen balance and adequate essential amino acids. The nine essential amino acids are not synthesized by mammals and must be obtained from dietary sources. A normal American diet includes 70-90 g protein/day. In addition, endogenous protein enters gut in digestive juices and desquamated epithelial cells. Overall protein digestion and absorption is quite efficient with only a small amount of fecal nitrogen. Protein digestion begins with luminal hydrolysis by gastric and pancreatic proteases and continues with a brush border phase that further digests larger peptides to amino acids and di- and tripeptides which are absorbed by specific carriers. There are more brush border enzymes and carriers for protein than carbohydrate due to the greater number of amino acids than simple sugars resulting in a greater array of bonds.



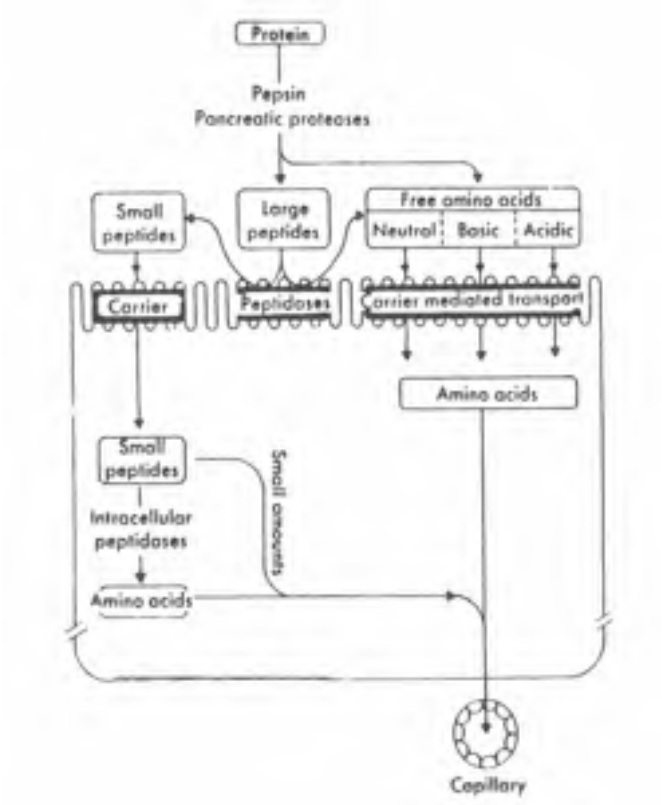
PD-INEL Fig. 11-8 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 114.



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

Intraluminal hydrolysis results in about 40% aminoacids and 60% small peptides.

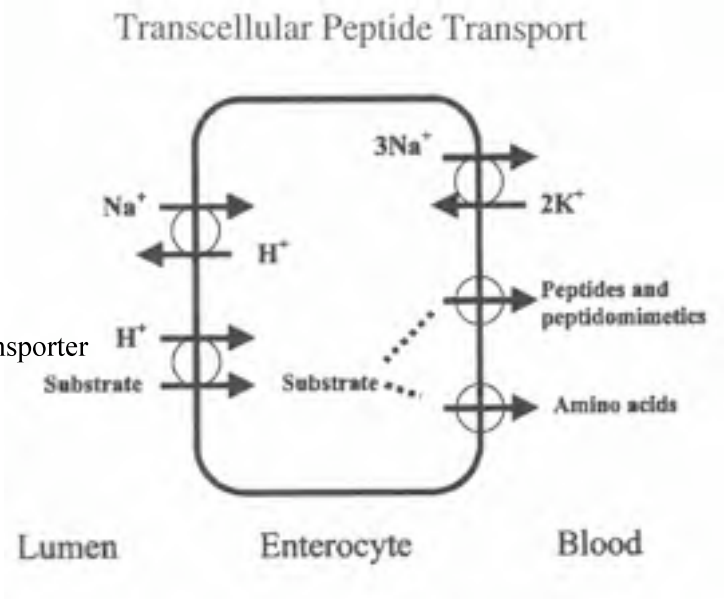
Summary of Digestion and Absorption of Dietary Protein



PD-INEL Source Undetermined

At the brush border there are about 20 different peptidases. Some are specific for distinct substrates such as enterokinase and folate conjugase while others are specific for different regions of peptides such as aminopeptidase and carboxypeptidase. These peptidases are glycoproteins anchored in the brush border similar to the oligosaccharidases such as sucrase-isomaltase. At least 7 different amino acid transporters are present some of which are Na^+ dependent. Specific transporters exist for neutral, cationic, and anionic amino acids as well as a separate transporter for proline are present in the gut and renal tubule brush border. The intestinal basolateral membrane possesses a different set of amino acid transporters which are similar to those present in all cells.

Small peptides of two or three amino acids are absorbed by a H^+ linked peptide transporter, PepT1, present in the brush border membrane. PepT1 operates as an electrogenic proton/ peptide cotransporter with ability to transport every possible di- and tri- peptide. Dietary peptides that are absorbed are broken down by intracellular peptidases and enter the the intracellular amino acid pool which exit across the basolateral membrane by amino acid transporters similar to those presented in most cells. A number of peptide-like drugs including β-lactam antibiotics and angiotensin converting enzyme (ACE) inhibitors are taken up by this transporter. These drugs or absorbed peptides must exit the cell via a basolateral peptide system.



Apical transporter PepT1

PD-INEL Source Undetermined

Defects in the absorption of protein digestion products can be caused by diseases due to altered expression and function of amino acid and peptide transport systems in the gut and kidney.

Cystinuria – autosomal recessive disease characterized by increased excretion of cationic amino acids and cystine. The primary clinical problem is renal stones enriched in cystine.

Hartnup disease – autosomal recessive disease of impaired absorption of neutral amino acids. Major symptoms are those of niacin deficiency (pellagra) as in humans significant niacin is synthesized from the neutral amino acid tryptophan.

These patients generally do not show symptoms of protein malnutrition due to absorption of di- and tri-peptides.

LIPID DIGESTION

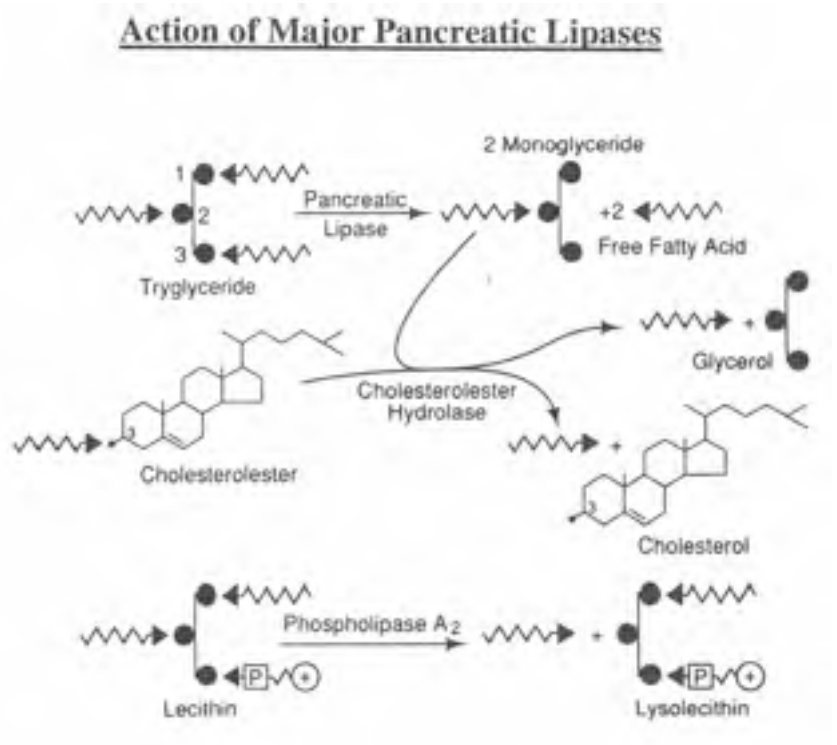
Usual dietary intake is about 100g/day primarily as triglyceride. Normally less than 5g/day is excreted in stool. Long chain "essential" polyunsaturated fatty acids, cholesterol and fat soluble vitamins are also present in dietary fat. Increased fat in the stool is termed steatorrhea.

Gastric Phase

Lipid digestion begins in the stomach with physical breakdown and emulsification to small lipid particles which can empty from the stomach. The major emulsifying factors are proteins and phospholipids. Gastric lipase which has a pH optima of 4-5 acts on triglycerides to produce diglyceride and free fatty acid (FFA). In newborns, lipase present in milk also works in the stomach. While in adults the gastric phase plays a minor role in fat digestion it plays a major role in newborns and can produce adequate lipolysis in some (but not all) patients with Cystic Fibrosis.

Intestinal Phase

Intestinal lipid digestion occurs almost exclusively in the lumen and involves three major pancreatic lipases and colipase which is not an enzyme but anchors lipase to the fat droplet preventing its displacement by bile salts. The three enzymes have distinct but overlapping substrate specificities. Pancreatic lipase is specific for the 1 and 3 position fatty acid in triglyceride. Cholesterol Esterase, also known as bile-salt dependent lipase, is activated by bile salts and is less specific cleaving a variety of ester bonds. An essentially similar form of bile-salt activated lipase is present in human breast milk. Phospholipase A2 cleaves lecithin to lysolecithin which is an especially good emulsifying agent. These lipases all have a pH optimum between 6 and 7 and therefore depend on neutralization of gastric acid to be effective.



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

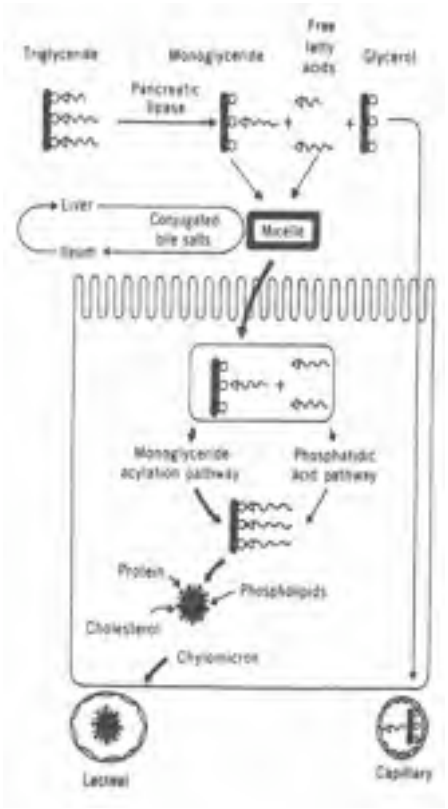
1. Olestra – Fake fat; can't be digested

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

Side effect of both is fat malabsorption and diarrhea if on Diet with significant fat.

PD-INEL Source Undetermined

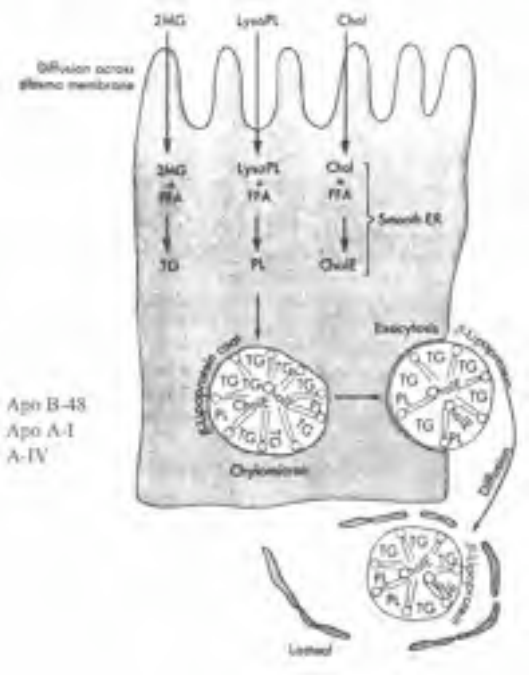
Mixed micelles of bile acids and lipid digestion products diffuse through the unstirred layer to reach the microvilli on the apical surface of the enterocyte. In the unstirred layer monomeric fatty acids are in equilibrium with micelles. Uptake of free fatty acids (FFA) and cholesterol has been traditionally held to be by diffusion but by recent evidence indicates a microvillus-membrane fatty acid transport protein. Once absorbed FFA are bound by intracellular fatty acid binding protein (FABP). As digestion products are absorbed from free solution by the enterocytes, more monomers shift out of the micelles. Bile salts are not absorbed simultaneously but must travel further down the intestine and are absorbed in the terminal ileum.



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.

Summary of the digestion and absorption of triglyceride. Monoglycerides and long-chain fatty acids enter the cells after first being incorporated into micelles. Glycerol and short-chain and medium-chain fatty acids, because of their solubility in the aqueous unstirred layer, enter without micelle solubilization. Resynthesis of triglycerides occurs in the enterocyte with packaging into chylomicrons which are released by exocytosis and due to their large size enter the lacteals, the terminal lymph vessels in the intestine.



PD-INEL Source Undetermined

Lipid resynthesis in the epithelial cells of the small intestine, chylomicron formation, and subsequent transport of chylomicrons. *FFA*, Free fatty acid; *2MG*, 2-monoglyceride; *TG*, triglyceride; *lysoPL*, lysophospholipid; *PL* phospholipid; *Chol*, cholesterol; *CholE*, cholesterol ester. In addition to β lipoprotein, other apolipoproteins including Apo B-48, Apo A-I, and Apo A-IV are constituents of triglyceride rich lipoproteins and play a role in their uptake and metabolism by peripheral tissues.

Cholesterol Absorption

For the average adult on a Western diet, about 1200-1700 mg of cholesterol enters the intestinal lumen daily. About 300-500 mg comes from the diet and the remainder largely from bile with a small amount from shed mucosal cells. A portion of dietary cholesterol is esterified and must be hydrolyzed by cholesterol esterase present in pancreatic juice. Biliary cholesterol is largely present in mixed micelles. Overall, about 50% of luminal cholesterol is normally absorbed.

The mechanism of cholesterol absorption across the brush border is poorly understood. The selectivity of cholesterol absorption versus plant sterols is now known to be due to two ABC transporters that pump these sterols back into the lumen. Mutations in ABC G5/8 protein underlie sitosterolemia (phytosterolemia), a disease in which these plant sterols accumulate in blood and body tissues. The novel cholesterol absorption blocker, Ezetimibe (Zetia), blocks the permease mechanism by which sterols enter the enterocyte. It is now in clinical use.

Cholesterol, which enters the enterocyte, moves to the ER and is esterified by acyl coenzyme A: cholesterol aceyltransferase (ACAT) and incorporated into chylomicrons which are exported into the lymphatic circulation. Following release of triglycerides in the periphery, chylomicron remnants are taken up by the liver and the cholesterol either secreted into the bile or secreted back into plasma as VLDLs or HDLs.

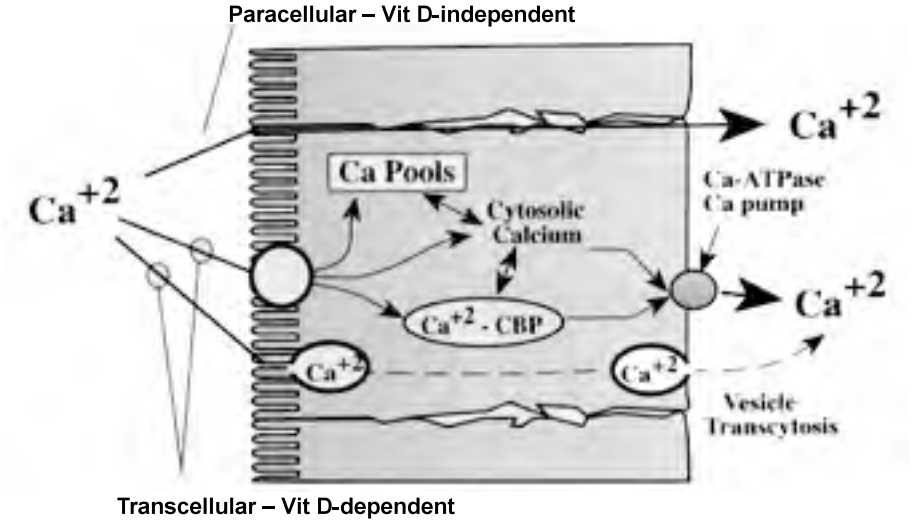
CALCIUM ABSORPTION

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

2. **Absorption is 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.

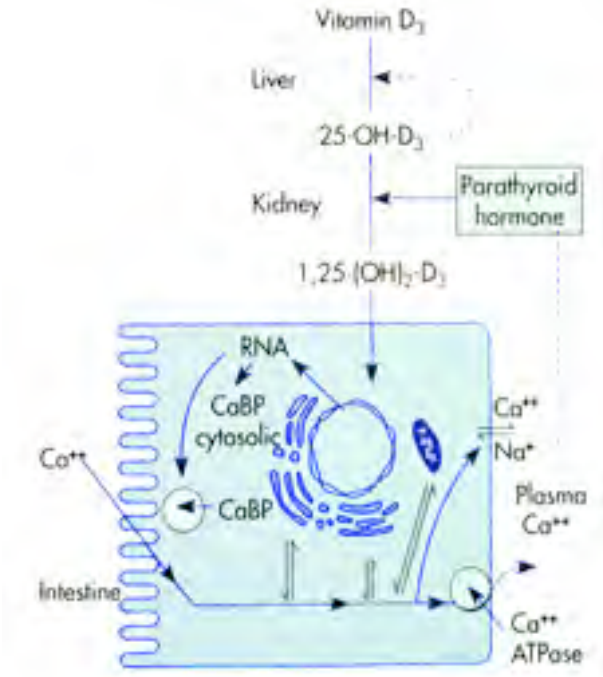
MOLECULAR COMPONENTS OF INTESTINAL CALCIUM ABSORPTION

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**

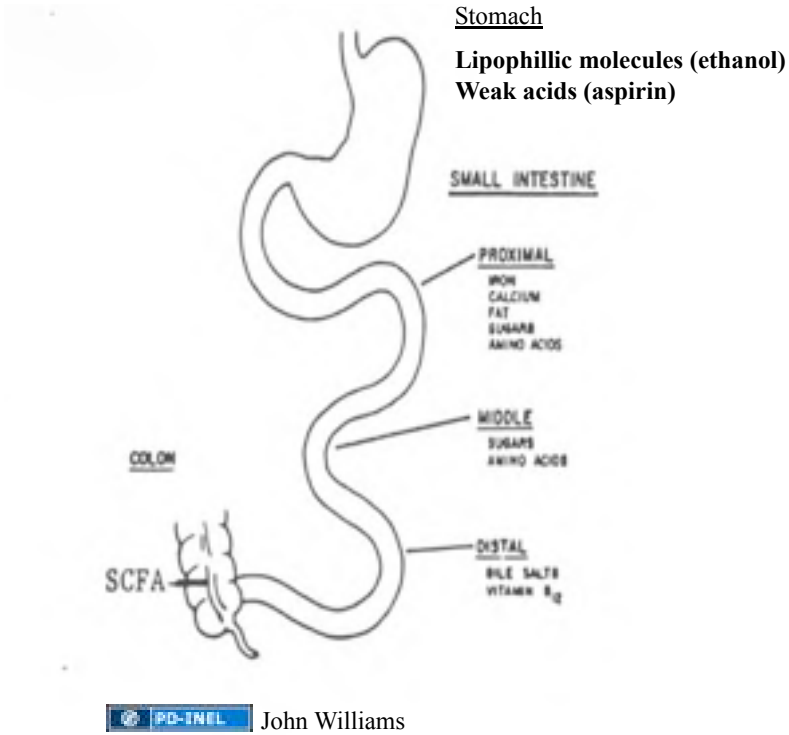
Synthesis and Action of Vitamin D



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

Vitamin D_3 is made in the skin by UV light acting on 7-dehydrocholesterol. It is then hydroxylated on the 25 position in the liver after which it is hydroxylated on the 1 position by the kidney with this last step regulated by parathyroid hormone. 1,25$(OH)_2$-D_3 binds to a nuclear Vit D receptor to regulate gene transcription.

Primary Sites of Nutrient Absorption



PD-INEL John Williams

SCFA = Short Chain Fatty Acids

Intestinal Water and Electrolyte Transport

Fluid dynamics in human GI tract include ingestion, equilibration, secretion, and absorption. Osmolar equilibration occurs in the duodenum where leaky tight junctions permit large one way water flux with equilibration occurring in a few minutes. Brunner's glands in the duodenum also secrete a bicarbonate rich fluid. The remainder of the small intestine secretes and absorbs fluid isotonically with a maximal absorptive capacity of about 15 l/day or about twice the amount normally absorbed. Less than 200 ml/day of water is normally excreted in the stool with excess water resulting in diarrhea.

Volumes and ionic composition of fluid in the human intestine.

Volumes and ionic composition of fluid entering the human intestine

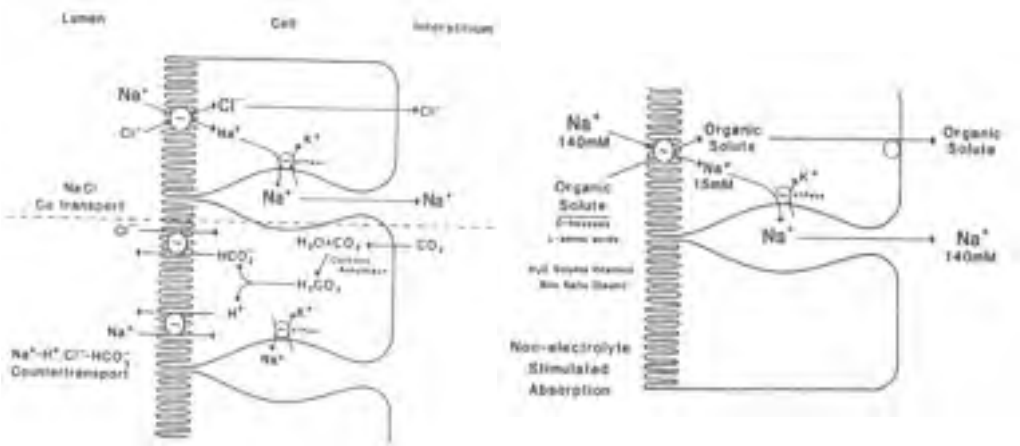
Segment	Per 24 hr			
	Vol (ml)	Na (mM)	K (mM)	Cl (mM)
Entering Duodenum				
Diet	2,000	150	50	200
Saliva	1,000	50	20	40
Gastric juice	2,000	100	15	280
Bile	1,000	200	5	40
Pancreatic juice	2,000	150	5	40
Small intestinal secretion	1,000	150	5	100
Total	9,000	800	100	700
Entering ileum	5,000	700	40	550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

PD-INEL Source Undetermined

DUODENAL FLUID DYNAMICS

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

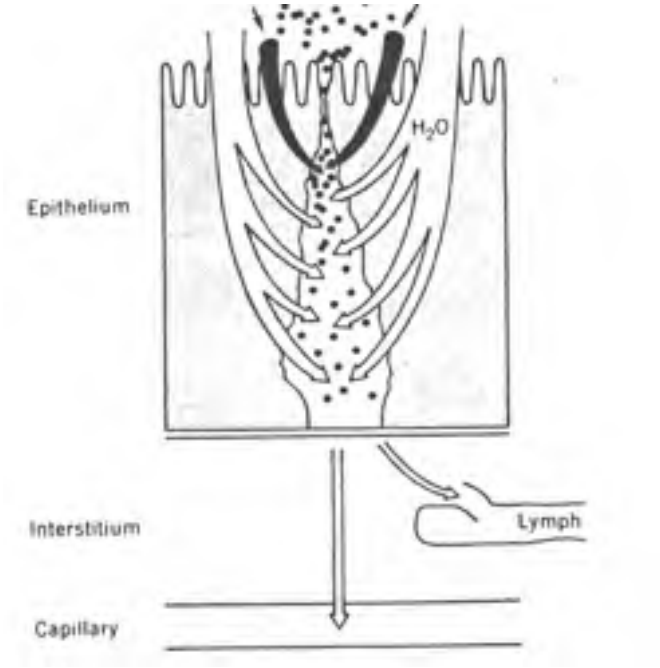
Cellular Models of Intestinal Sodium Absorption



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

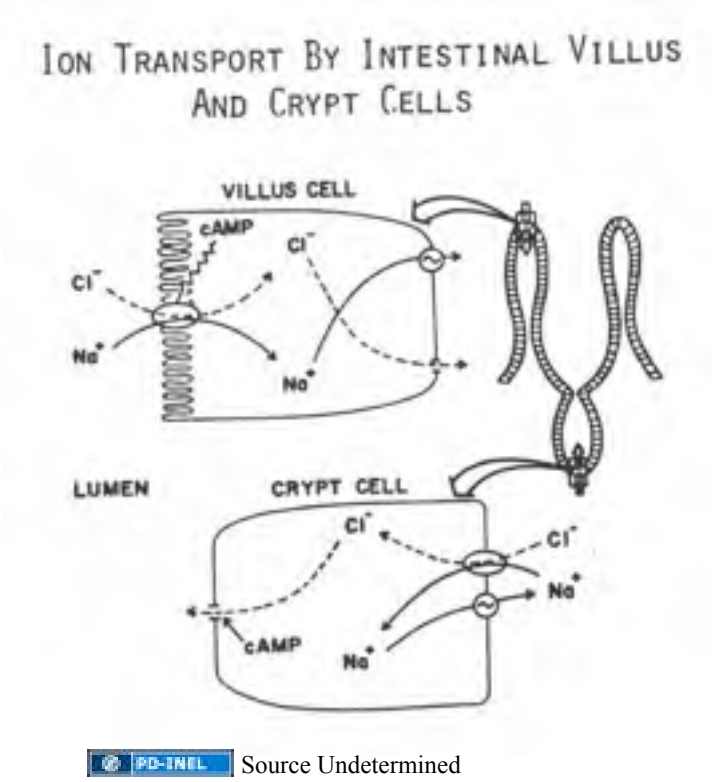
Of these on the left, the bottom coupled countertransporters are the primary ion uptake mechanism.

Fluid Absorption According to the Standing Osmotic Gradient Mode



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

This model can account for isotonic movement of fluid by use of localized hypertonicity. Water flows in to dilute the local hypertonic fluid but by the time fluid exits the lateral space it is isotonic.



PD-INEL Source Undetermined

The intestinal epithelium can both absorb salt and water and secrete fluid. Secretion is often local and in response to reflex stimulation prompted by distension or the presence of solid material. Absorption and secretion are believed to be topologically separated with secretion occurring primarily in the crypts. Secretion involves basal uptake of Na^+ and Cl^- and release of Cl^- across the apical membrane via the cyclic AMP regulated CFTR chloride channel. The secretory diarrhea of cholera is due to cholera toxin activating adenylcyclase and cAMP stimulating secretion to 15-20 liters per day.

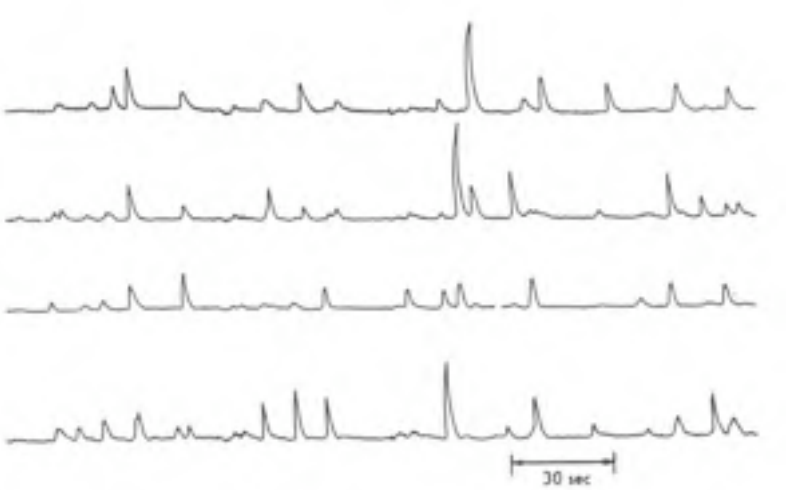
INDUCERS OF COLONIC AND SMALL INTESTINAL SECRETION

1. Bacterial Endotoxins (Cholera)
2. Certain Unsaturated Fatty Acids (Castor Oil)
3. Bile Acids
4. Anthrquinone Cathartics (Senna, Cascara)
5. Certain Hormones (VIP)

Functions of Intestinal Motility

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

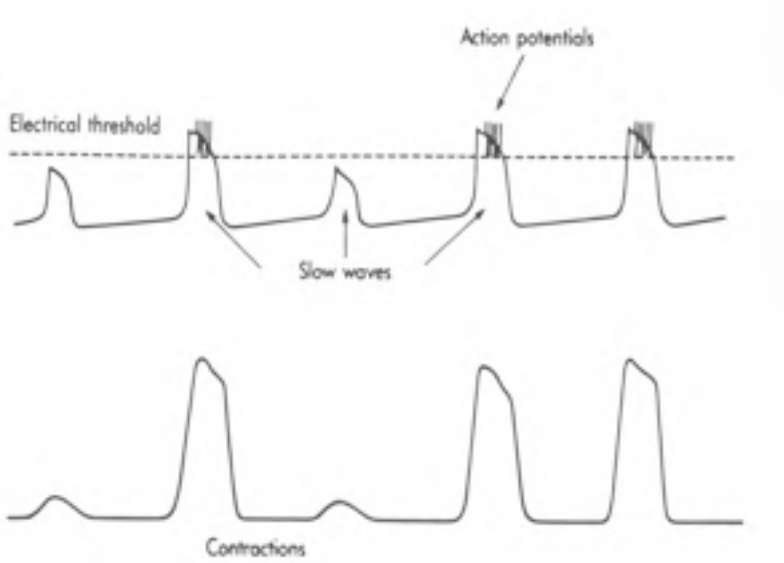
Intraluminal Pressure Changes in the Duodenum of a Concious Man



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

Intraluminal pressure changes recorded from the duodenum of a conscious man. Sensors were placed 1 cm apart. Note that the changes in pressure are phasic, lasting 4 to 5 seconds. Note also that a rather large contraction can take place at one site while nothing is recorded 1 cm away on either side.

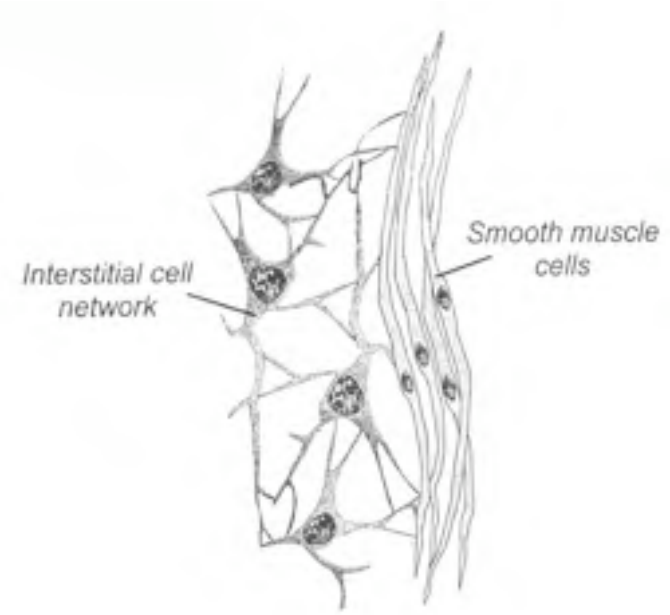
Slow Wave Electrical Changes Plus Action Potentials Control Contraction of Intestinal Muscle



PD-INEL Source Undetermined

In intestinal smooth muscle, slow waves occur with a frequency of 12/min in the duodenum decreasing to 9/min in the ileum. When the slow wave reaches the electrical threshold, trains of action potential spikes are generated. There are no action potentials on those slow waves that fail to reach the threshold. Slow wave amplitude is modulated by excitatory and inhibitory neurotransmitters. Contraction is driven primarily by action potentials.

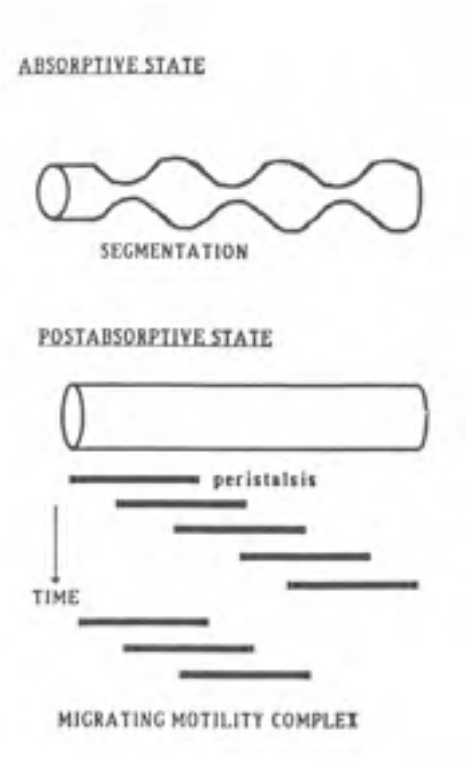
ICC Cells as Pacemaker for Slow Waves



PD-INEL Source Undetermined

Recent evidence indicates that slow waves in the intestine, as well as stomach and colon, have their origin in a network of non-neural cells termed interstitial cells of cajal (ICC cells). These cells, which show spontaneous electrical activity, form a network and couple to smooth muscle cells by gap junctions. They can be identified in the gut as the only cells bearing the c Kit receptor and mutations in this receptor or its ligand, stem cell factor (SCF) in mice leads to loss of intestinal slow waves.

Motility Patterns in Absorptive and Postabsorptive State



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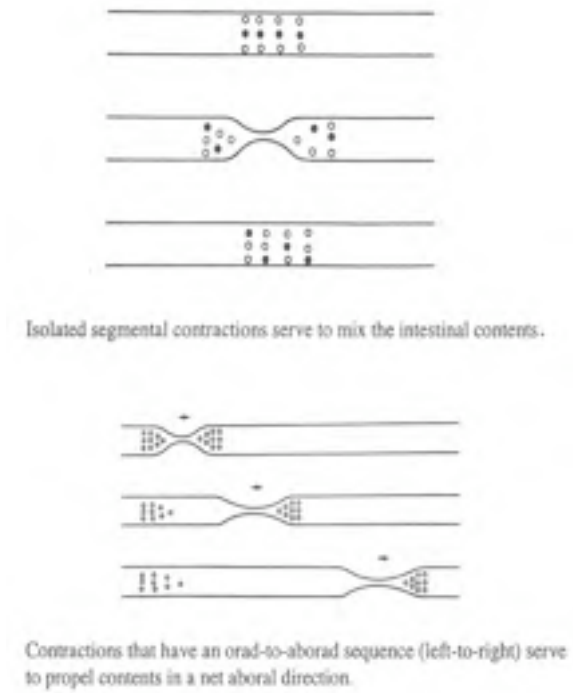
The absorptive state is defined as the time food (chyme) is present in the lumen of the small intestine. With each meal this usually lasts 4-6 hours.



Isolated segmental contractions serve to mix the intestinal contents.

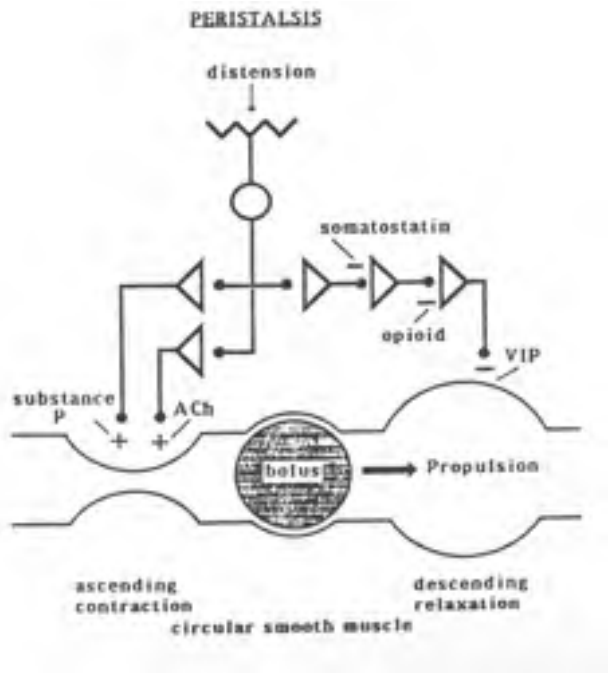
Contractions that have an orad-to-aborad sequence (left-to-right) serve to propel contents in a net aboral direction.

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

Segmental contractions (fed pattern of motility) are initiated by the presence of chyme in the intestine. However, contractions also occur in adjacent empty segments so neural reflexes or hormones are clearly involved. Segmental contractions serve to locally mix and circulate the intestinal content. In addition to segmental contractions, contractions of the muscularis mucosa alter intestinal folds. Rhythmic villar contractions occur after a meal and help mix the unstirred layer adjacent to the brush border and help compress and empty the lacteals.

Chyme moves through the small intestine and starts to exit in 2 hours. This is the result of a higher frequency of slow waves and contractions in the upper small intestine and the presence of short peristallic movements in the aboral direction. Movement needs to be slow enough for digestion and absorption to occur and some anti-diarrheal drugs act by inhibiting net intestinal transit.

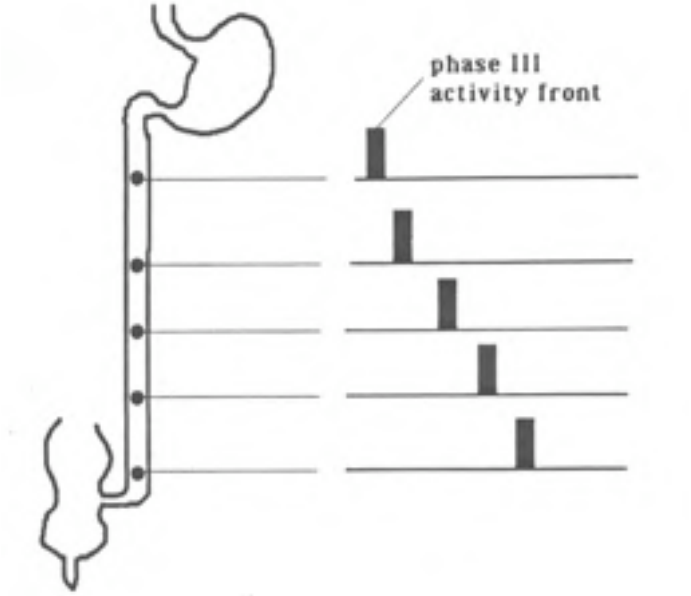
PERSISTALSIS



PD-INEL Jim Sherman

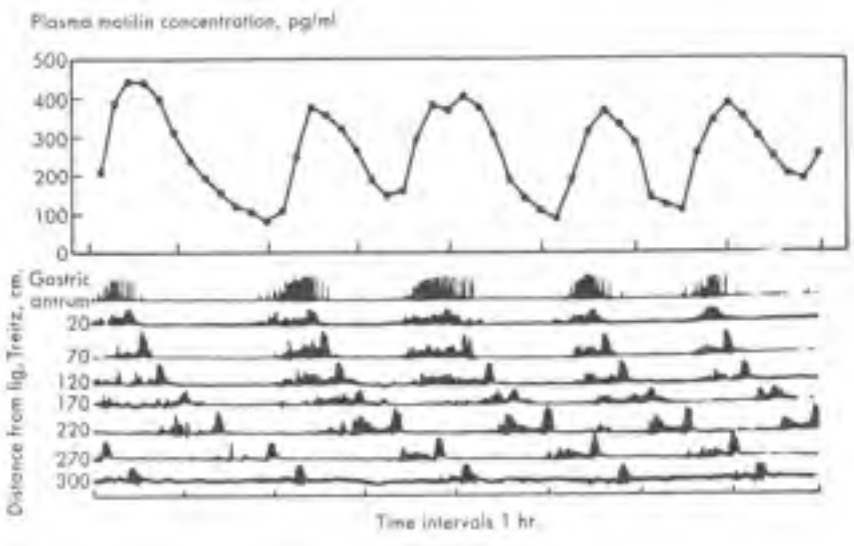
The predominant intestinal motor pattern in the interdigestive state is the migrating motility (motor) complex or MMC. It is initiated in the gastric antrum and sweeps down the small intestine taking about 90 min after which another wave starts. During passage out of the stomach the pylorus relaxes. It serves to sweep indigestible material and bacteria out of the intestine. The onset of each MMC coincides with a peak in plasma of the GI hormone motilin; motilin injection can initiate an MMC early. How motilin release is controlled is not well understood. There are motilin receptor agonists that act as prokinetic agents. Feeding inhibits the MMC when food enters the small intestine.

Migrating Motility Complex



PD-INEL Jim Sherman

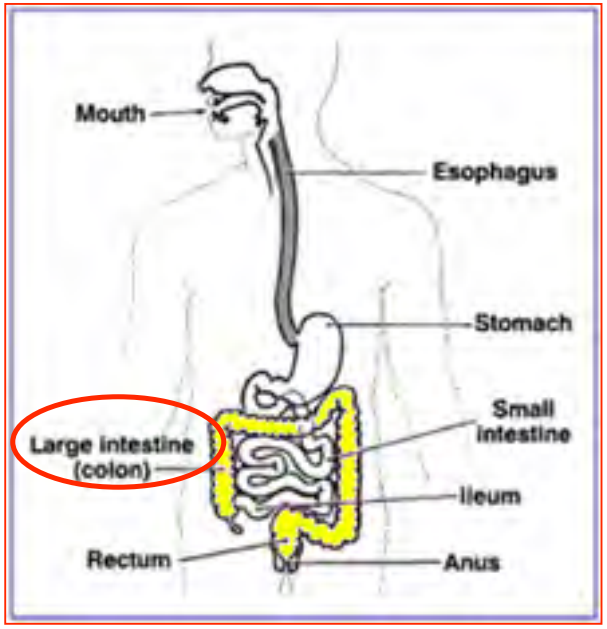
Relationship between plasma motilin and the MMC



PD-INEL Source Undetermined

The relationship between plasma levels of motilin (*upper tracing)* and the occurrence of migrating myoelectric complexes in the dog stomach and small intestine (*lower records).*

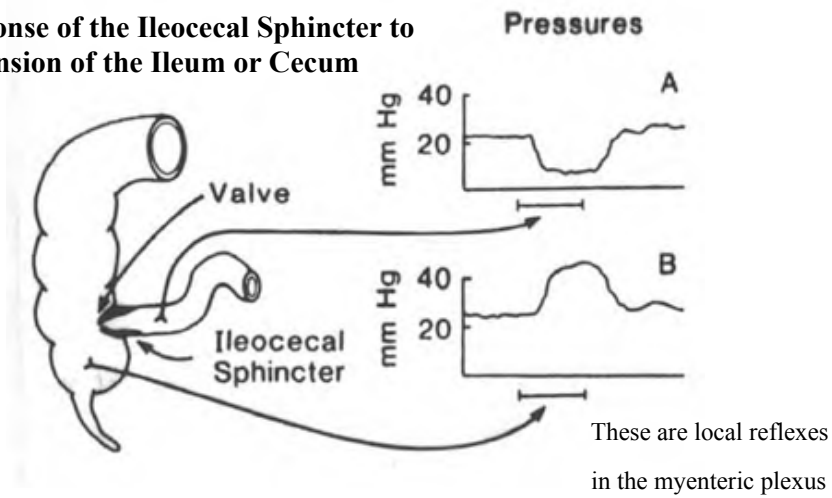
THE HUMAN COLON



Functions
1. Storage
2. Absorption of salt and water
3. Digestion and Absorption

PD-GOV National Digestive Diseases Information Clearinghouse

Response of the Ileocecal Sphincter to Distension of the Ileum or Cecum

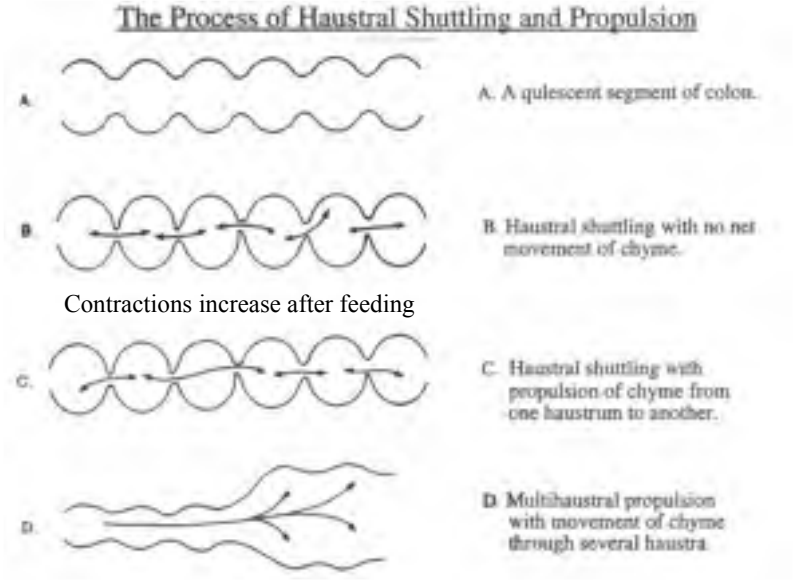


These are local reflexes in the myenteric plexus

PD-INEL Fig 7-30 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Colonic Motility

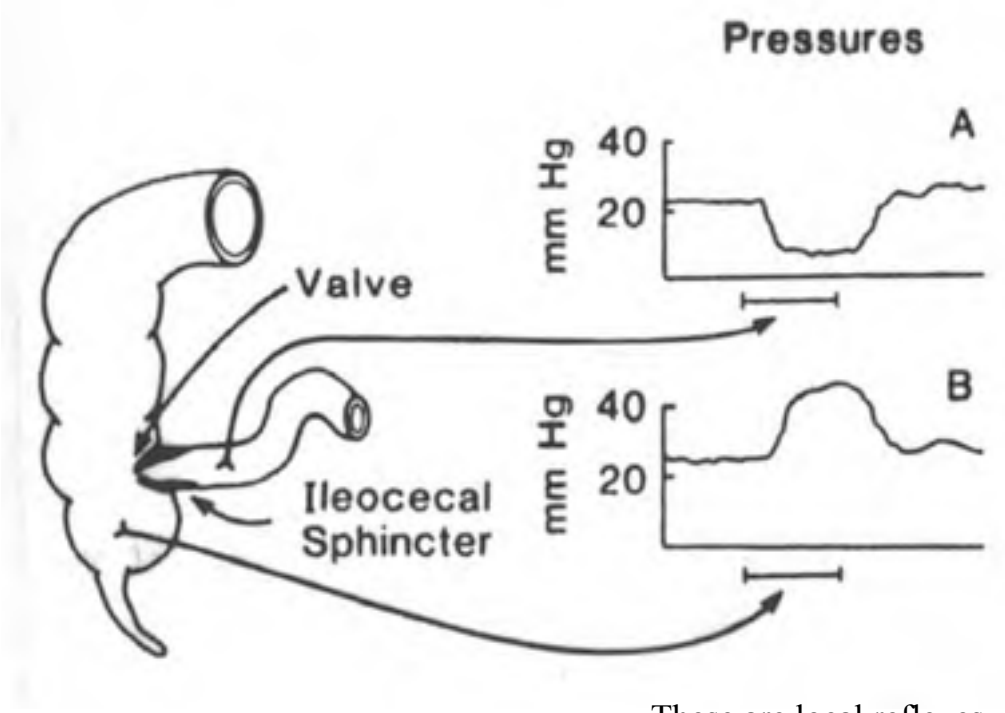
1. Slow wave frequency variable but highest in transverse colon and the rectum (11/min)
2. Contractions increase after feeding
3. Mass Peristalsis after a meal termed the "Gastro-Colic reflex



Contractions increase after feeding

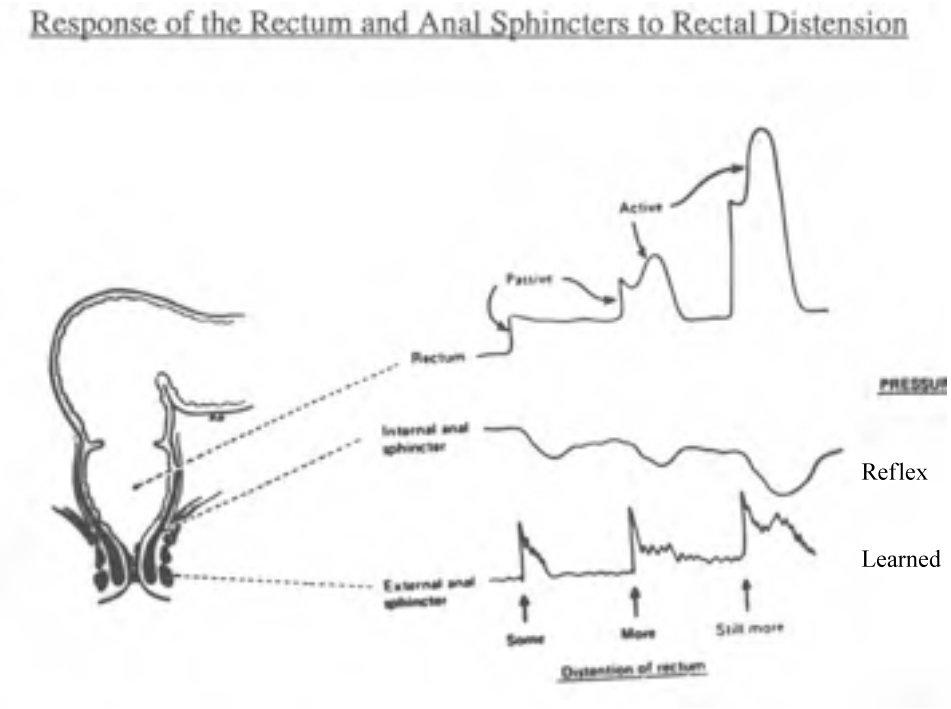
PD-INEL Fig. 8-6 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Response of the Ilecocecal Sphincter to Distension of the Ileum or Cecum



These are local reflexes
in the myenteric plexus

 Fig 7-30 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.



PD-INEL Fig. 8-9 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

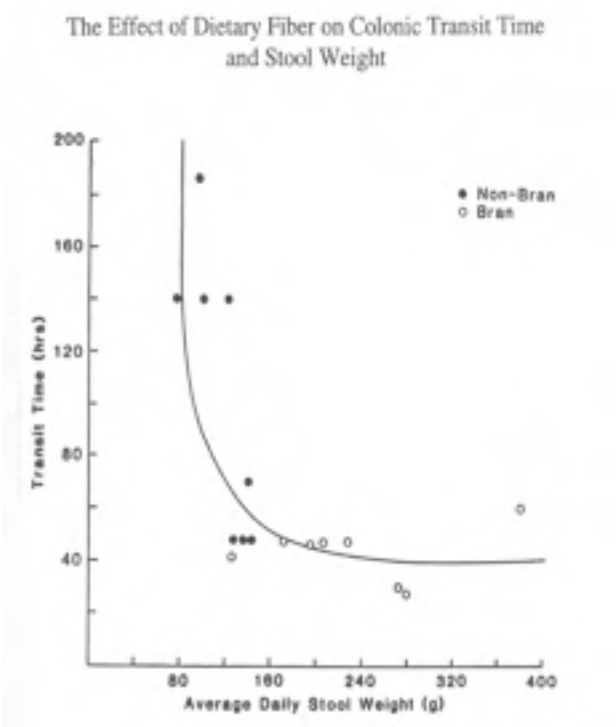
The rectum is both a storage organ and provides motile force for defecation. Distension initiates rectal contraction by local reflexes in the enteric nervous system. The increased pressure triggers the reflex relaxation of the internal anal sphincter which is made up of smooth muscle. At this point the external sphincter (skeletal muscle) contracts until voluntary relaxation. Rectal smooth muscle has a high frequency of slow waves so rectal contents propelled retrograde if defecation fails to occur. This aids in the absorption of rectal suppositories.

Hirschprungs Disease

1. Myenteric plexus in colon normally exerts a net inhibitory influence

2. When neurons are absent in rectum the aganglionic Segment is contracted resulting in a large distended Colon

3. Treatment is to surgically remove the segment



PD-INEL Fig. 8-8 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

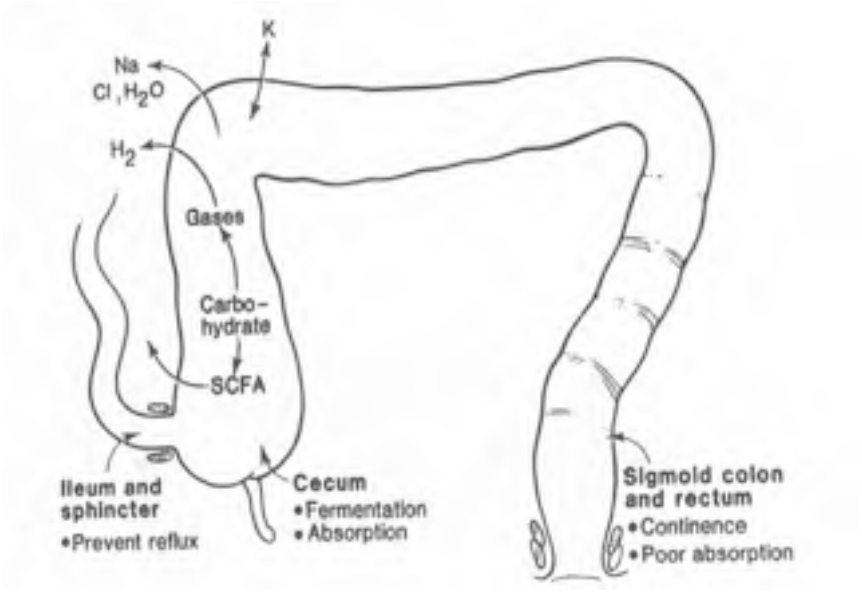
On typical Western diet as much as 3 days may be required for transit from the caeum to the rectum. Transit time is decreased to about 24-40 hours and stool weight increased when bran or fiber is added to the diet.

Composition of Gastrointestinal Gas			
	Stomach (%)	Intestine (%)	Flatus (%)
Nitrogen	79	64	61.2
Carbon dioxide	4	14	8.1
Hydrogen	0	19	19.8
Methane	0	9.8	7.3
Oxygen	17	0.7	3.6
	Swallowed air	*Bacterially Produced*	

PD-INEL Source Undetermined

Normally about 1 to 1½ liters per day of flatus

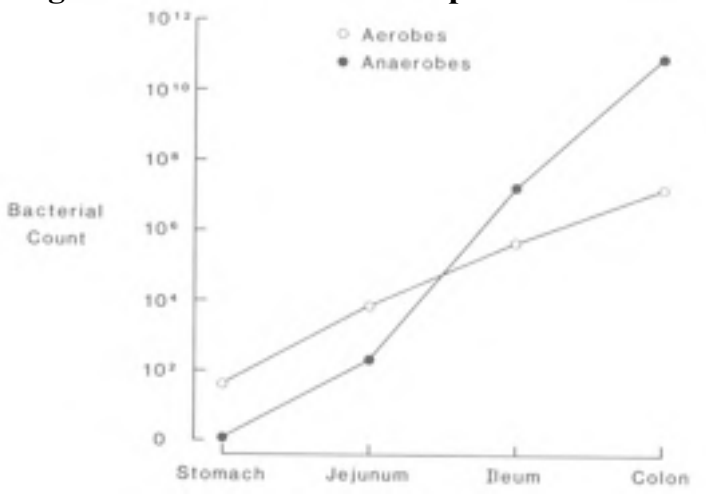
Role of the Cecum in Fermentation and Absorption



PD-INEL Levitt, MD, Bond, JH, Levitt, DG. "Gastrointestinal gas". *In* Johnson, L. *Physiology of the Gastrointestinal Tract*, Vol. 2. Raven Press, New York, NY; 1981.

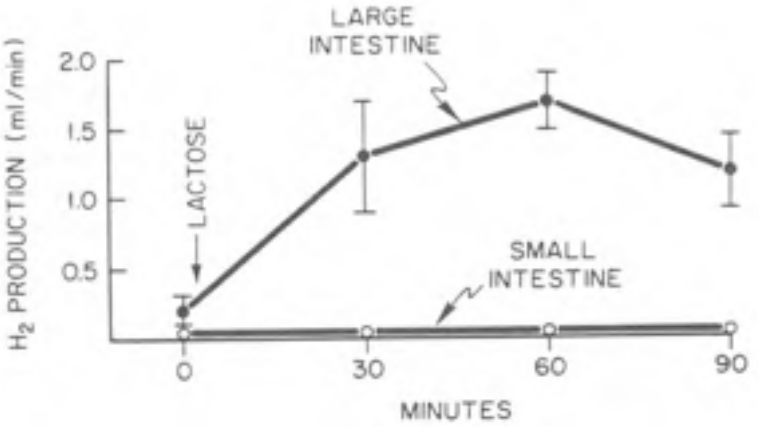
In addition to fermenting carbohydrate, intestinal bacteria metabolize bile acids and synthesize Vitamin K which can be absorbed.

Magnitude of the Bacterial Population in the Gut



PD-INEL Fig. 8-4 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

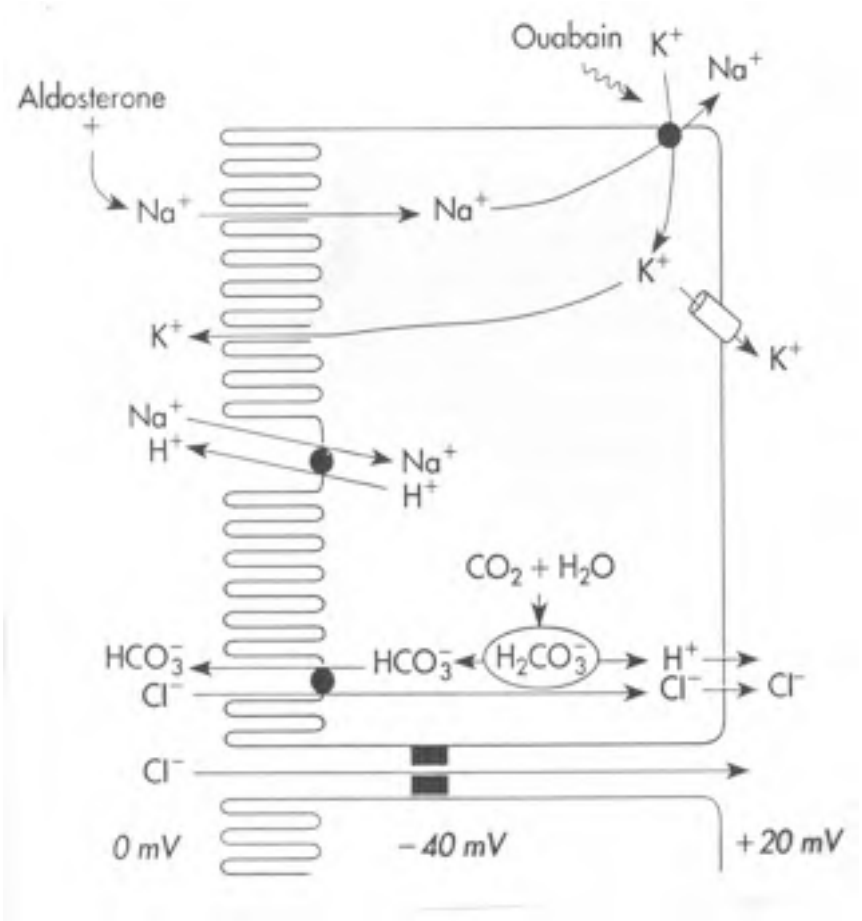
Hydrogen Gas Production in the Small Intestine and Colon in Response to Lactose



PD-INEL Levitt, MD, Bond, JH, Levitt, DG. "Gastrointestinal gas". *In* Johnson, L. *Physiology of the Gastrointestinal Tract*, Vol. 2. Raven Press, New York, NY; 1981.

Ingestion of certain foods such as beans rich in indigestible carbohydrates leads to increase in hydrogen content and increased flatus.

Ion Transport Pathways in the Human Colon

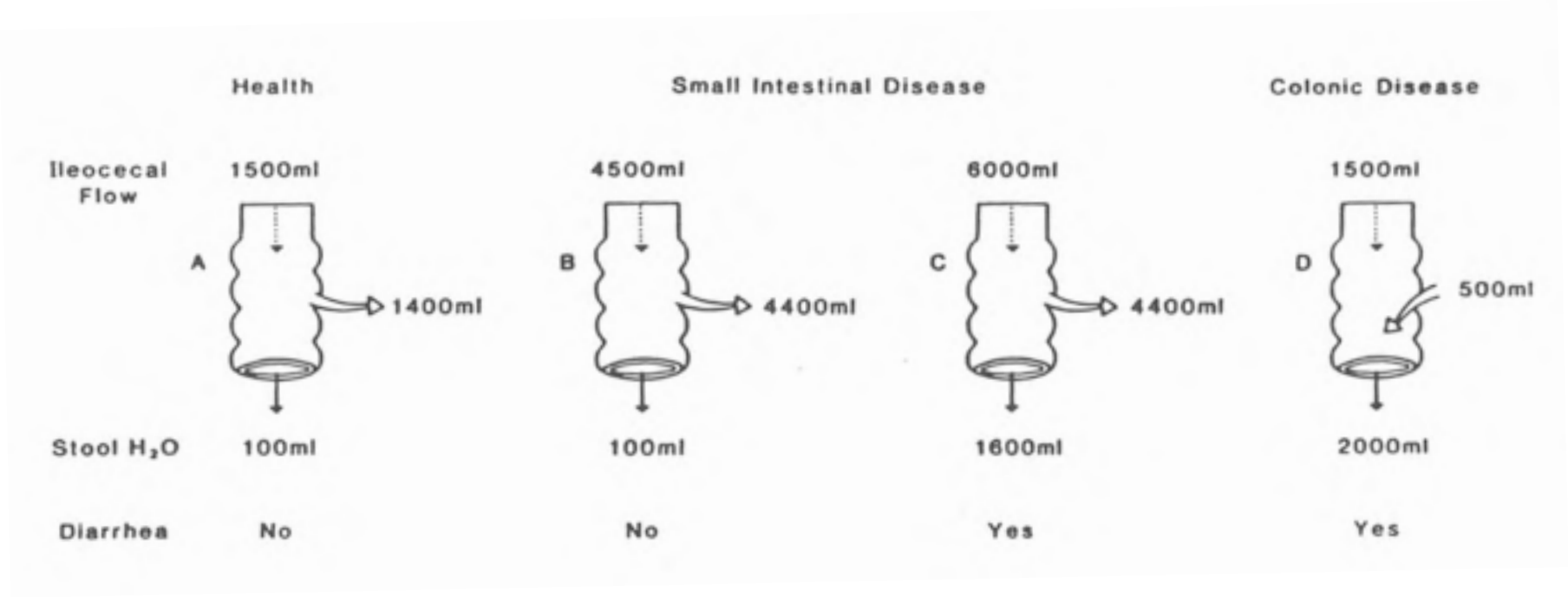


PD-INEL Fig. 12-3 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 130.

Colonic Salt and Water Absorption

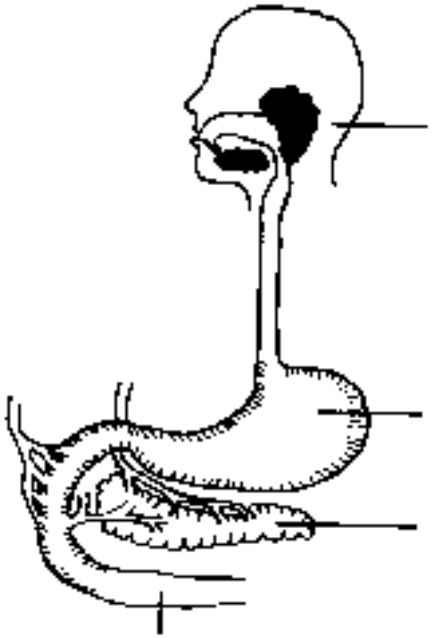
The human colon absorbs sodium and chloride and thereby also absorbs about 1.5 l/day of water. The colon does not possess the Na^+ linked organic solute transporters such as SGLT1 present in the small intestine. Na^+ is absorbed by two primary pathways. In the proximal colon, Na^+-H^+ exchange in the apical membrane is coupled to a $Cl^-HCO_3^-$ exchanger resulting in net absorption of NaCl. Absorption of short chain fatty acids is also facilitated by Na^+-H^+ exchange and results in Na butyrate absorption. In the more distal colon electrogenic Na^+ absorption predominates. Na^+ enters across the apical membrane down its electrochemical gradient through an amiloride sensitive sodium channel. The number of these channels is regulated by aldosterone and when the body is Na^+ depleted, Na^+ retention by the colon is very efficient. The Na^+ that enters the cell is then pumped out across the basolateral membrane by the Na^+-K^+ ATPase. NaCl can also be secreted by the crypts similar to the small intestine. K^+ can undergo net absorption or secretion by the colon. Recently a colonic H^+-K^+ ATPase distinct from the gastric enzyme has been identified in the distal colon. This enzyme secretes H^+ and absorbs K^+. The colon is a relatively tight epithelia which allows the lumen to become hypotonic. It is likely that water absorption is by transcellular rather than paracellular transport and involves aquaporins.

Relationship Between Ileocecal Flow, Colonic Water Absorption and Stool Water In Health and in Various Disease States



PD-INEL Fig. 8-2 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985. Modified (see additional source information).

REVIEW



Amylase

Pepsin
Lipase

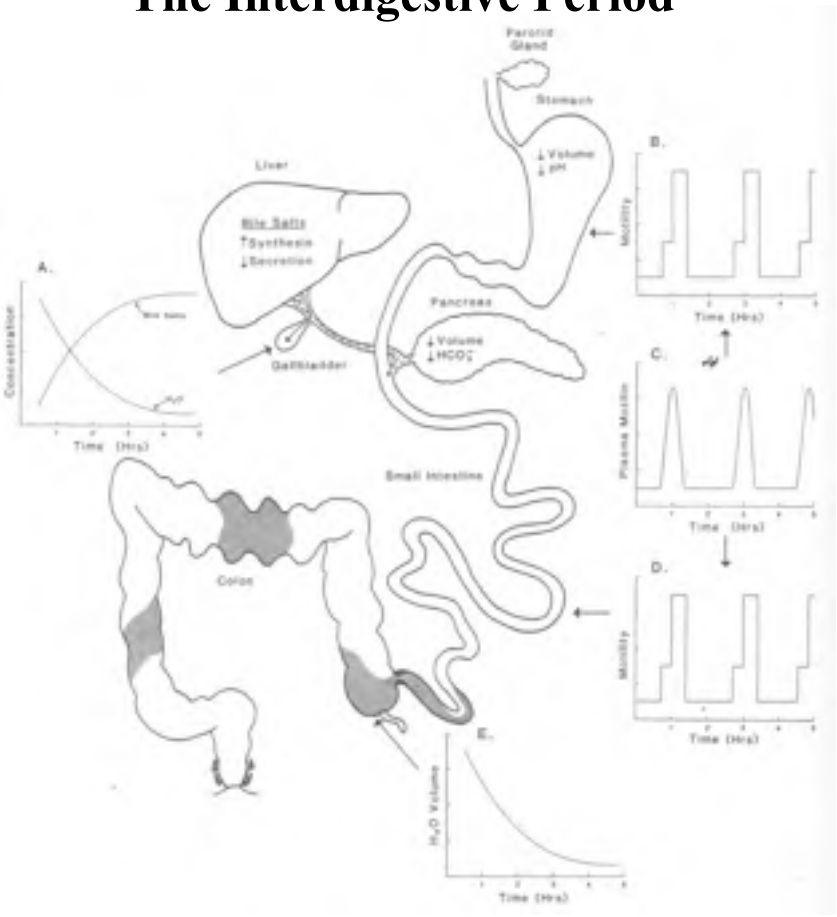
Amylase
Trypsin
Chymotrypsin
Carboxypeptidase
Elastase
Lipase - Colipase
Phospholipase A_2
Cholesterol esterase - nonspecific lipase

Disaccharides:
- Maltase
- Sucrase
- Lactase
- Isomaltase

Peptidases:
- Aminopeptidase
- Carboxypeptidase
- Dipeptidase
- Enterokinase

PD-INEL Fig. 9-1 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

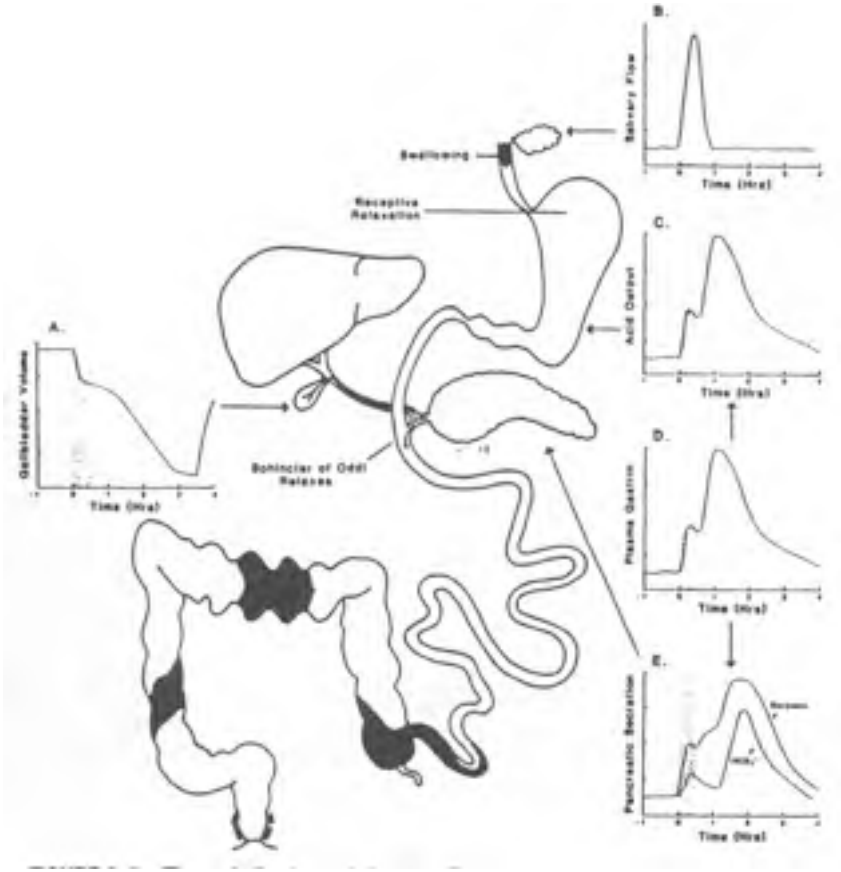
The Interdigestive Period



PD-INEL Fig. 9-2 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Figure 9-1. The interdigestive period. This period is characterized by low output of digestive secretions and the migrating motility complex (MMC). The contractile patterns in the stomach *(B)* and intestine *(D)* are correlated to the plasma concentration of motilin *(C)*. Water and electrolytes are being absorbed in the gallbladder *(A)* and cecum *(E)*.

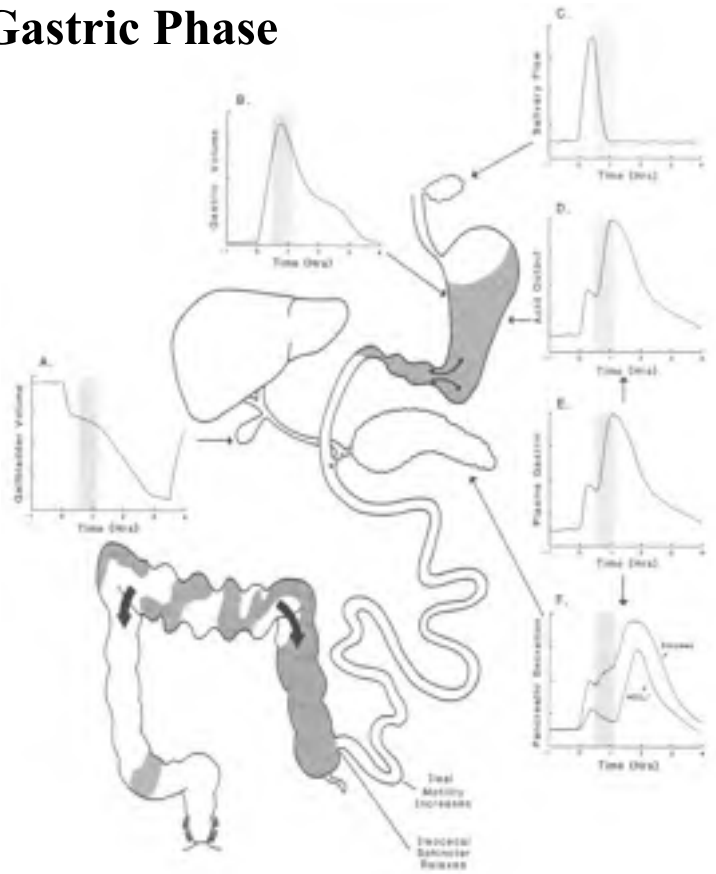
The Cephalic Phase



PD-INEL Fig 9-3 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

FIGURE 9-2. The cephalic phase of digestion. This period is characterized by an activated parasympathetic systems and a small rise in plasma gastrin (D). These neurohumoral factors increase salivary (B), gastric (C), and pancreatic (E) secretions. The gallbladder contracts and the sphincter of Oddi relaxes leading to a decrease in gallbladder volume (A).

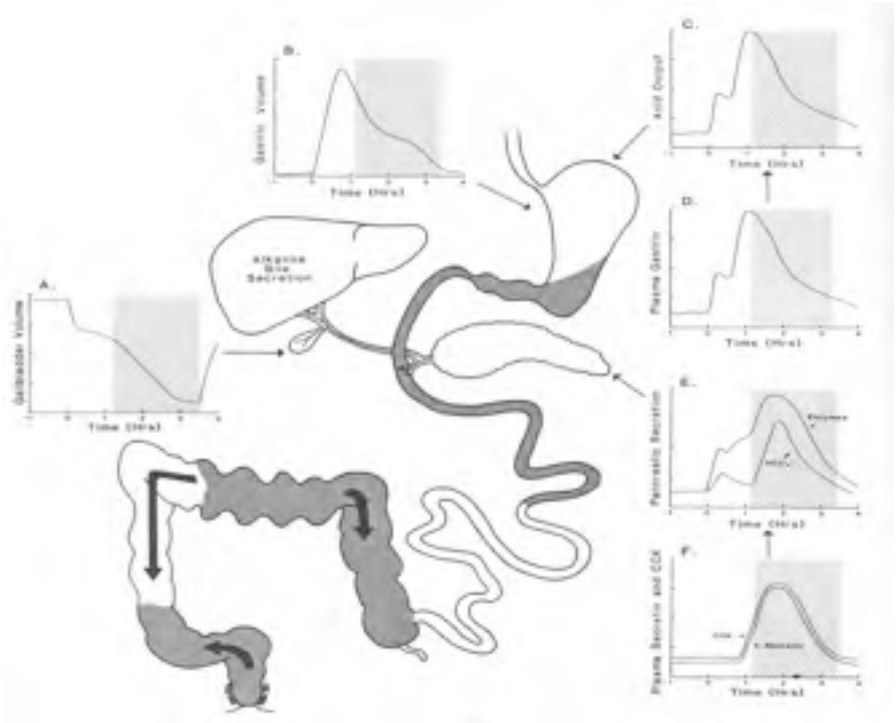
Gastric Phase



PD-INEL Fig. 9-4 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

FIGURE 9-3. The gastric phase of digestion. This period is characterized by a decreased parasympathetic drive and a further increase in plasma gastrin (E). Salivary secretion returns toward the basal level (C), whereas gastric (D) and pancreatic (F) secretions are further augmented. Gastric volume increases rapidly and subsequently declines as it empties (B). The gallbladder continues to empty (A). Motor reflexes from the stomach initiate ileal and colonic contractions; chyme moves into the cecum where it is mixed.

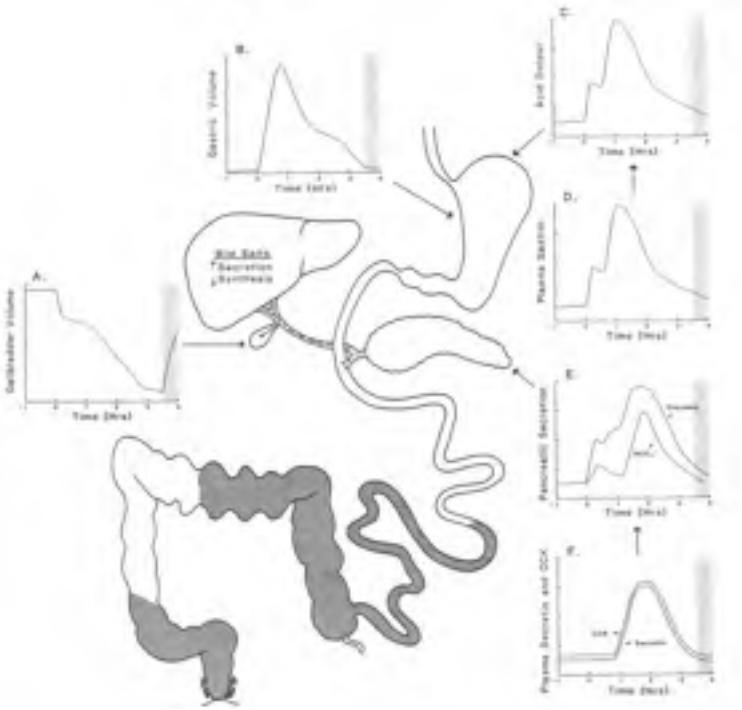
The Early Intestinal Phase



PD-INEL Fig. 9-6 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

FIGURE 9-4. The early intestinal phase of digestion. This period is characterized by a reduction in plasma gastrin levels (D) and a concomitant rise in plasma levels of secretin and CCK (F). The stomach continues to slowly empty its contents (B), while acid output falls dramatically (C). The pancreas elaborates an enzyme- and bicarbonate-rich secretion (E). There is intense contraction of the gallbladder (A). The motor pattern in the small bowel shifts from the MMC to irregular segmental and propulsive contractions, which mix the chyme with digestive secretions. Colonic motility includes patterns such as mass movements and retropulsion.

The Late Intestinal Phase



PD-INEL Fig. 9-1 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

FIGURE 9-6. The late intestinal phase. This period is characterized by a gradual return of the intestinal hormones (secretin and CCK) to their interdigestive plasma levels (D, F). Gastric (C) and (E) secretion rates and gastric volume (B) fall toward their basal levels. Bile salts, absorbed from the terminal ileum, stimulate hepatic bile salt secretion and inhibit bile salt synthesis. The gallbladder slowly fills with hepatic bile (A). When the rectum distends sufficiently, the urge to defecate is felt and the stool is passed.

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: 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 7: (All images) Source Undetermined

Slide 8: (Left) John Williams

Slide 8: (Right) Fig. 7-15 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985: 169.

Slide 9: (Left) Fig. 11-8 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 114.

Slide 9 (Right) Fig 7-18 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985: 174.

Slide 10: Source Undetermined

Slide 11: Source Undetermined

Slide 12: Fig. 8 Johnson, L. *Essential Medical Physiology* New York Raven Press 1992: 515.

Slide 13: (Both images) Source Undetermined

Slide 14: (Left) Fig. 11-14 Johnson, L. *Gastrointestinal Physiology*, 6th ed. Mosby Elsevier, St. Louis, MO; 2001: 136.

Slide 14: (Right) Source Undetermined

Slide 15: Fig. 9 Chang, E, Sitrin, M, Black, D. *Gastrointestinal, Hepatobiliary, and Nutritional Physiology.* Lippincott – Raven, Philadelphia, PA; 1996: 204.

Slide 16: Fig. 12-6 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 133.

Slide 17: (Left) John Williams

Slide 17: (Right) Source Undetermined

Slide 18: (Left) Figs. 7-7 and 7-8 from Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 18: (Right) Fig. 12-4 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007.

Slide 19: Source Undetermined

Slide 20: (Left) Fig. 5-1 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 42.

Slide 20: (Right) Source Undetermined

Additional Source Information

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

Slide 21: (Both images) Source Undetermined

Slide 22: (Left) Fig. 5-3 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 44.

Slide 22: (Right) Jim Sherman

Slide 23: (Left) Jim Sherman

Slide 23: (Right) Source Undetermined

Slide 24: (Top left) National Digestive Diseases Information Clearinghouse, http://digestive.niddk.nih.gov/ddiseases/pubs/barretts/

Slide 24: (Bottom left) Fig 7-30 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 24: (Bottom right) Fig. 8-6 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 25: Fig 7-30 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 26: Fig. 8-9 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 27: (Left) Fig. 8-8 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 27: (Right) Source Undetermined

Slide 28: (Left) Levitt, MD, Bond, JH, Levitt, DG. “Gastrointestinal gas”. *In* Johnson, L. *Physiology of the Gastrointestinal Tract*, Vol. 2. Raven Press, New York, NY; 1981.

Slide 28: (Top right) Fig. 8-4 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 28: (Bottom right) Levitt, MD, Bond, JH, Levitt, DG. “Gastrointestinal gas”. *In* Johnson, L. *Physiology of the Gastrointestinal Tract*, Vol. 2. Raven Press, New York, NY; 1981.

Slide 29: Fig. 12-3 Johnson, L. *Gastrointestinal Physiology*, 7th ed. Mosby Elsevier, Philadelphia, PA; 2007: 130.

Slide 30: Fig. 8-2 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985. Modified (see additional source information).

Slide 31: (Left) Fig. 9-1 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 31: (Right) Fig. 9-2 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Additional Source Information

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

Slide 32: (Left) Fig 9-3 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 32: (Right) Fig. 9-4 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 33: (Right) Fig. 9-6 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.

Slide 33: (Left) Fig. 9-1 Granger, D, *et al. Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985.