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

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M1 - GI Sequence

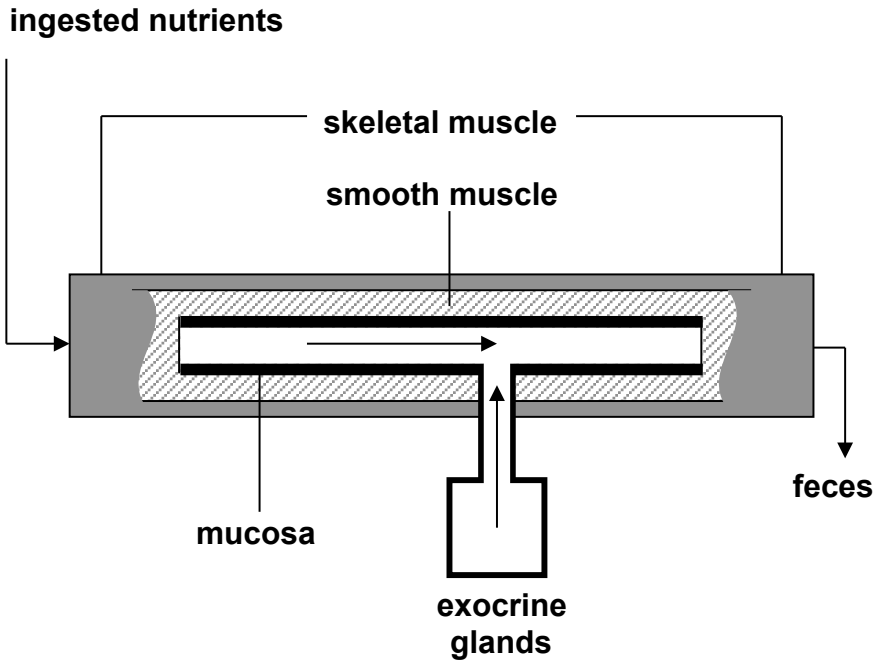
Nerves and Hormones

John Williams, M.D., Ph.D.

Winter, 2009

University of Michigan
Medical School

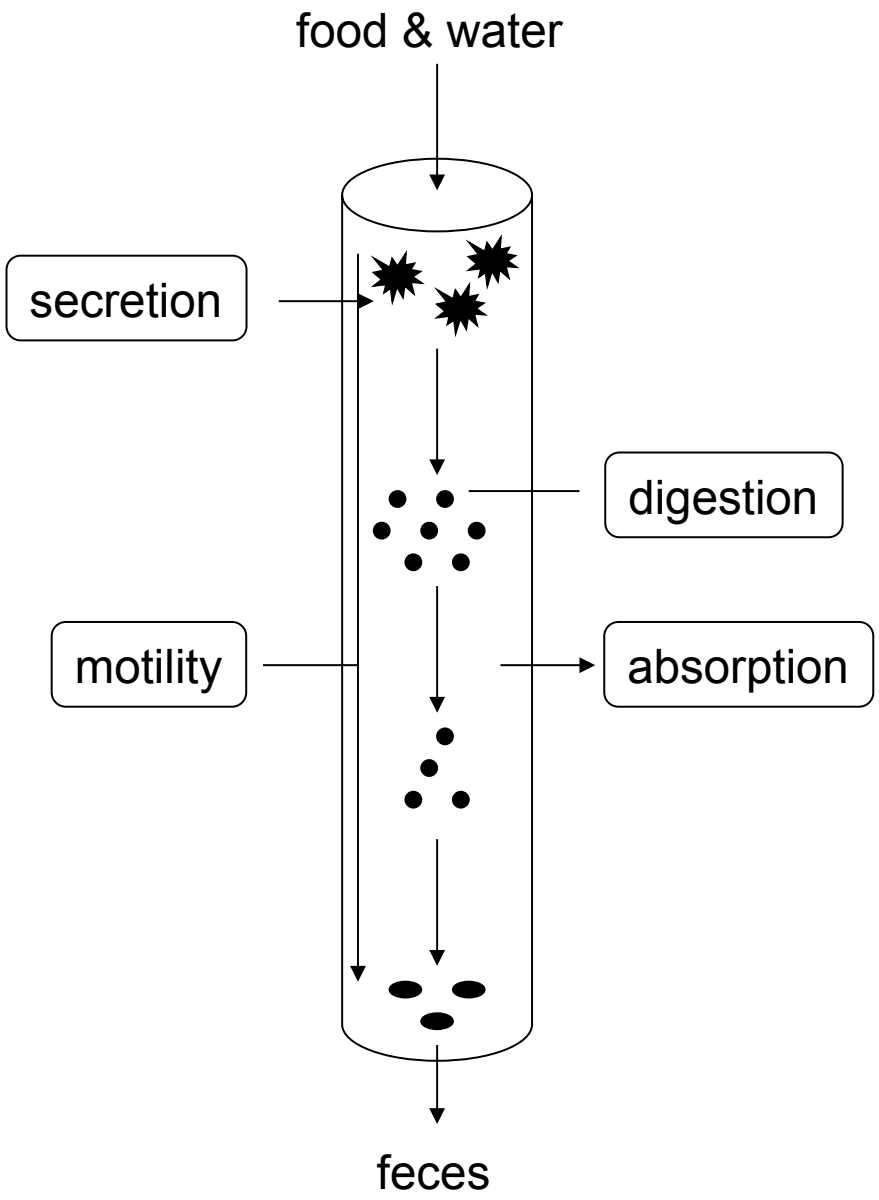
OVERVIEW OF GASTROINTESTINAL TRACT



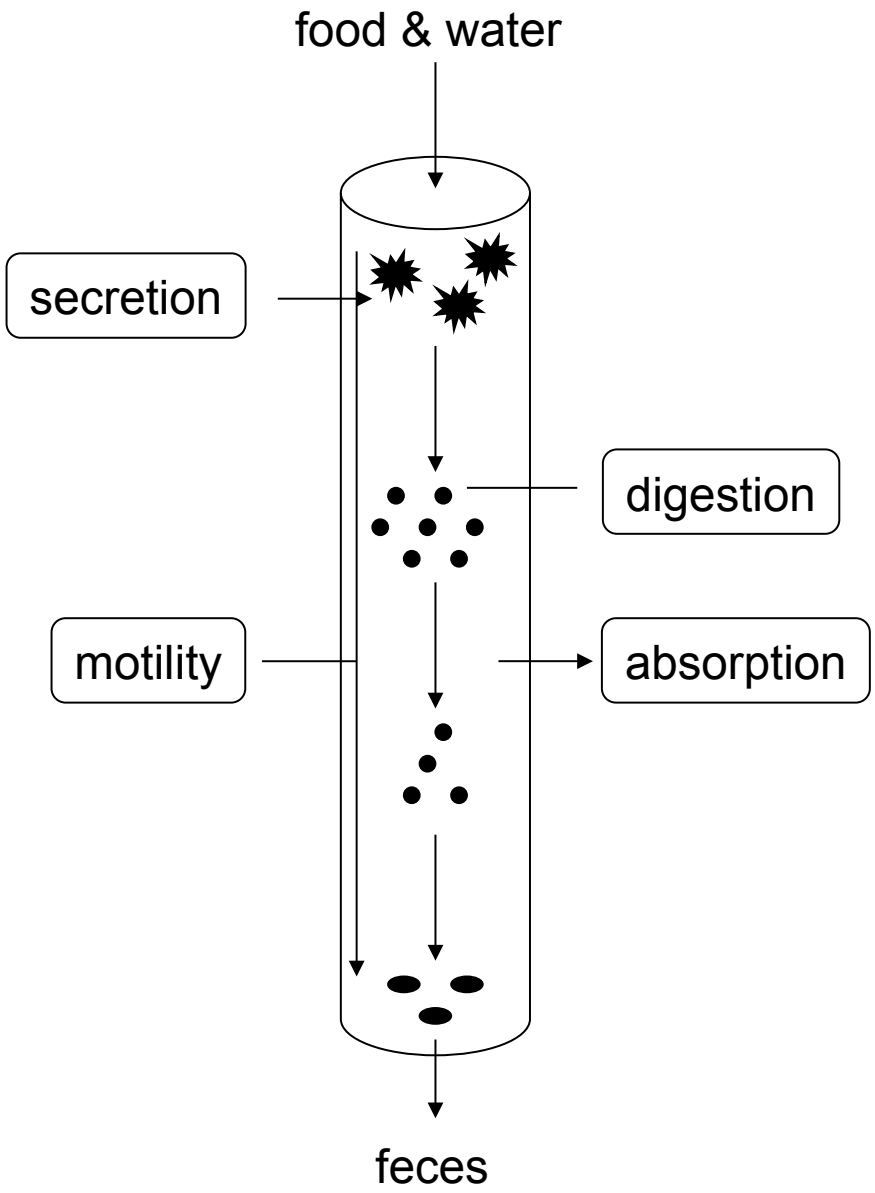
Gastrointestinal System

1. Salivary glands
2. Esophagus
3. Stomach
4. Small Intestine
5. Colon
6. Rectum
7. Pancreas
8. Liver
9. Gallbladder

BASIC PROCESSES OF THE GI TRACT



BASIC PROCESSES OF THE GI TRACT



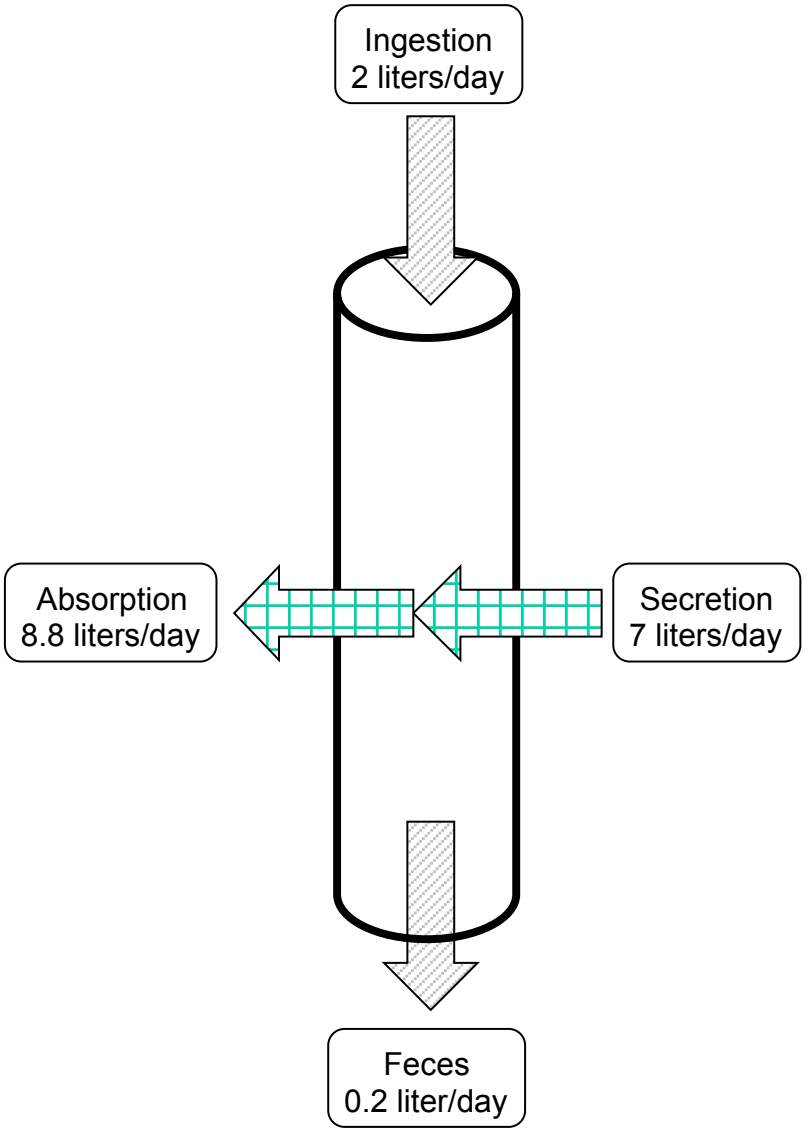
Motility

1. **Segmental Contractions**
2. **Propulsive Movements**
3. **Reservoir Function**

Digestion

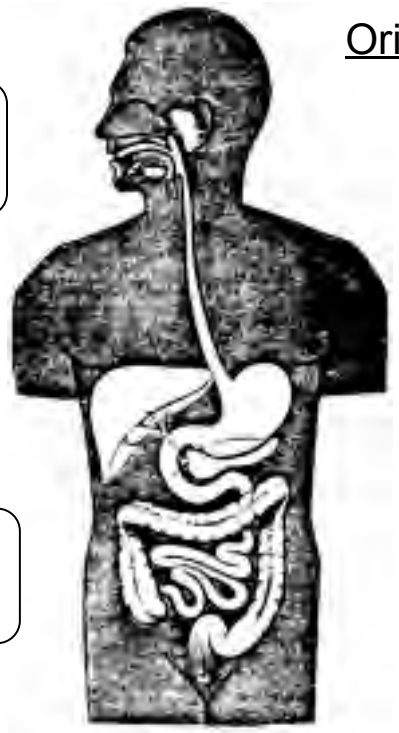
The chemical breakdown of food into molecules able to be absorbed

Overall Fluid Balance of the GI Tract



Saliva
Gastric Juice
Bile
Pancreatic Juice
Intestinal

Phases of GI Regulation



cephalic phase

gastric phase

intestinal phase

Origin of Stimuli

HEAD

STOMACH

INTESTINE

Cephalic Stimuli

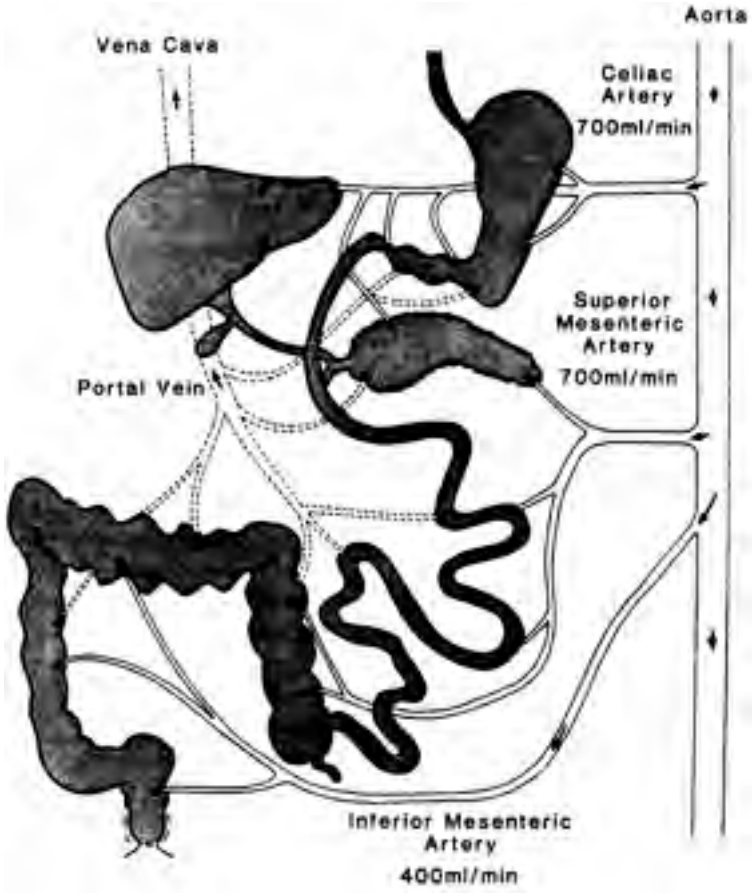
taste, smell, sight, emotions

Gastric and Intestinal Luminal Stimuli

mechanoreceptors - volume, pressure
chemoreceptors - amino acids, fatty acids, pH
osmoreceptors - osmolarity

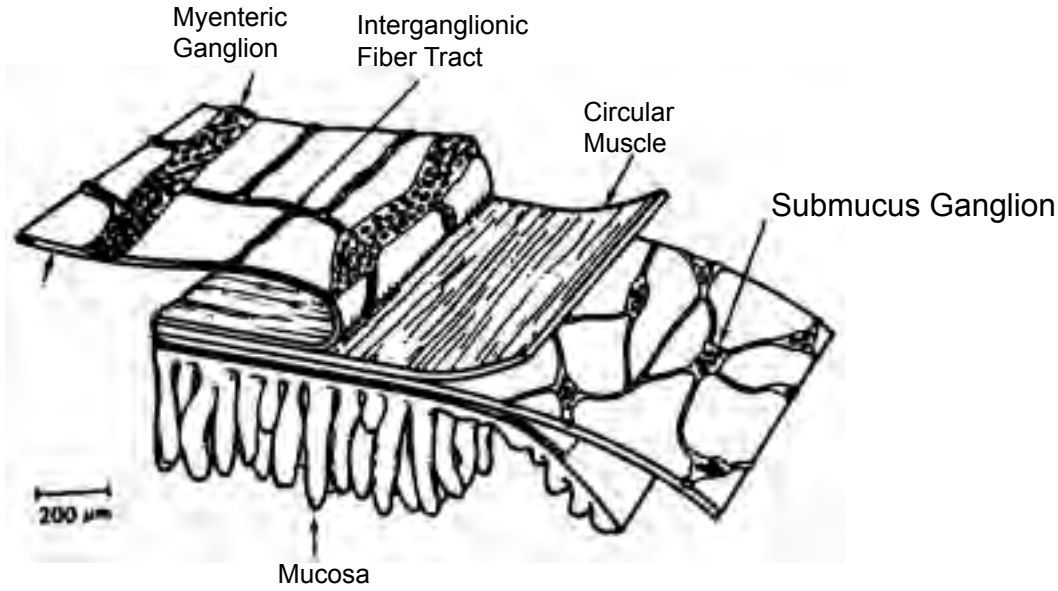
 John Williams modified from Guyton, AC. *Textbook of Medical Physiology,* 6th ed. W.B. Saunders Philadelphia, PA; 1981: 784.

SPLANCHNIC CIRCULATION



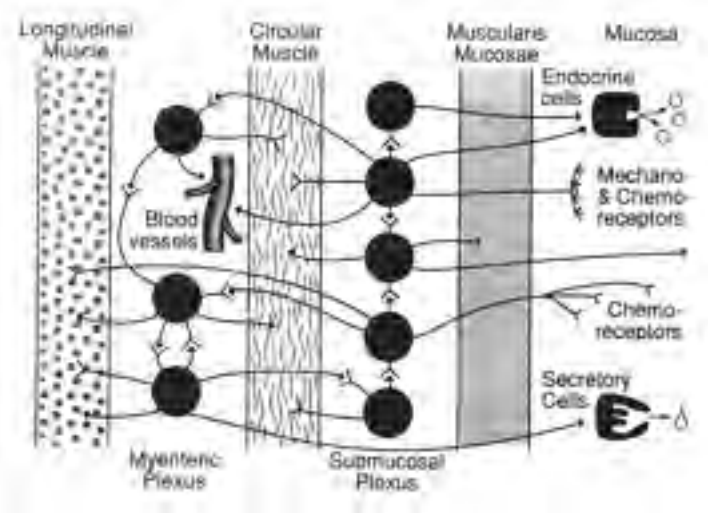
 Granger, D, *et al*. *Clinical Gastrointestinal Physiology.* W.B. Saunders, Philadelphia, PA; 1985: 28.

ENTERIC NERVOUS SYSTEM



Short Reflex Pathways

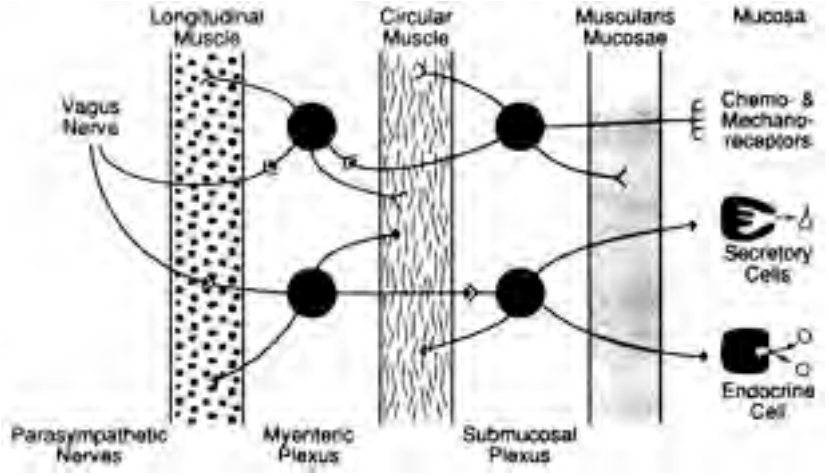
(within ENS)



Source: Undetermined

Long Reflex Pathways

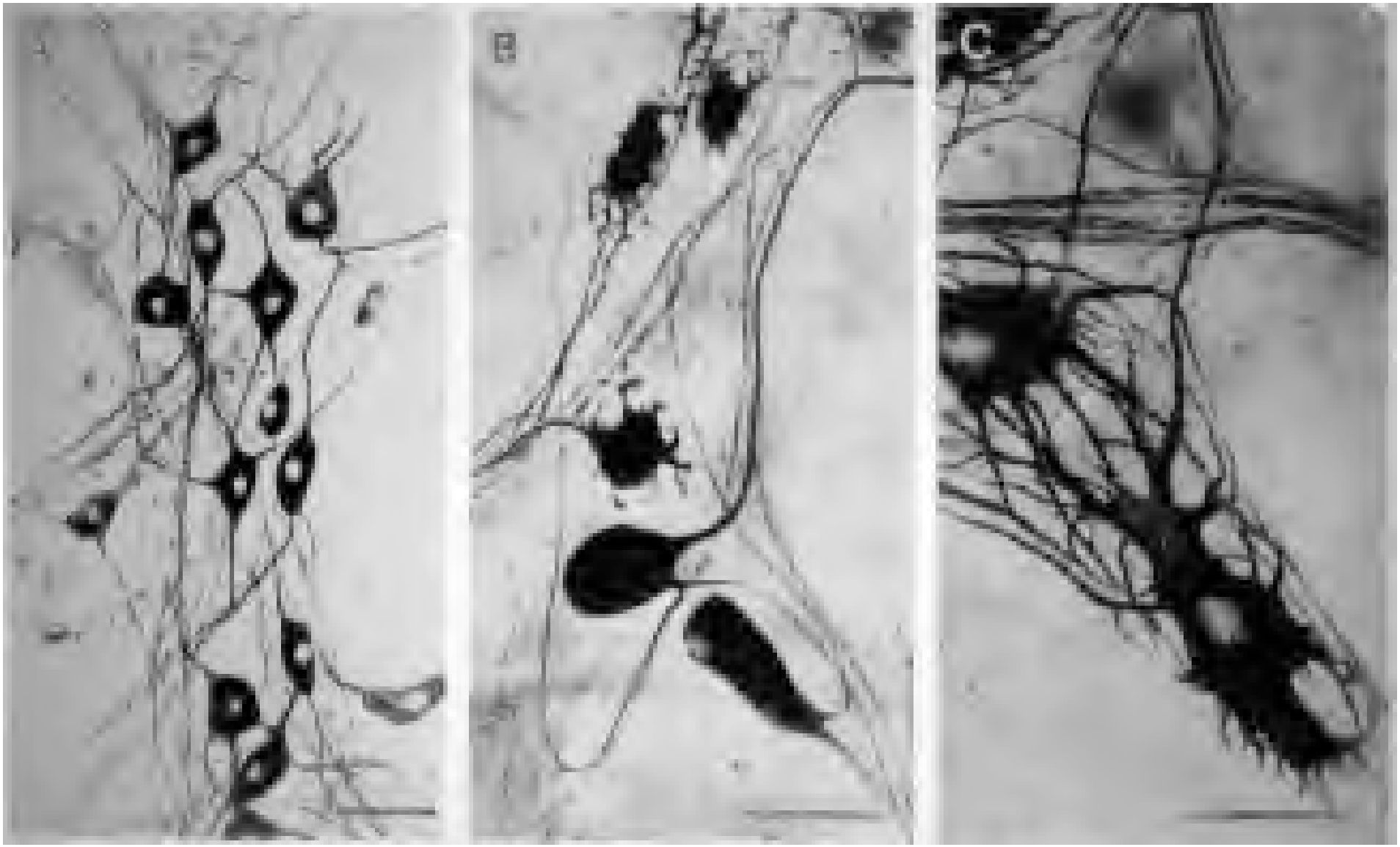
(involve CNS)



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

NEUROTRANSMITTERS INVOLVED IN GI REGULATION

NON-PEPTIDES	PEPTIDES
Acetylcholine	Substance P
Norepinephrine	CCK
Serotonin	Somatostatin
Nitric Oxide	VIP
Dopamine	Enkephalin
Purinergic (adenosine, ATP)	



PD-INEL Fig. 2 Johnson, L. *Physiology of the Gastrointestinal Tract*, Vol. 1, 2nd ed. Raven Press, New York, NY; 1987: 4.

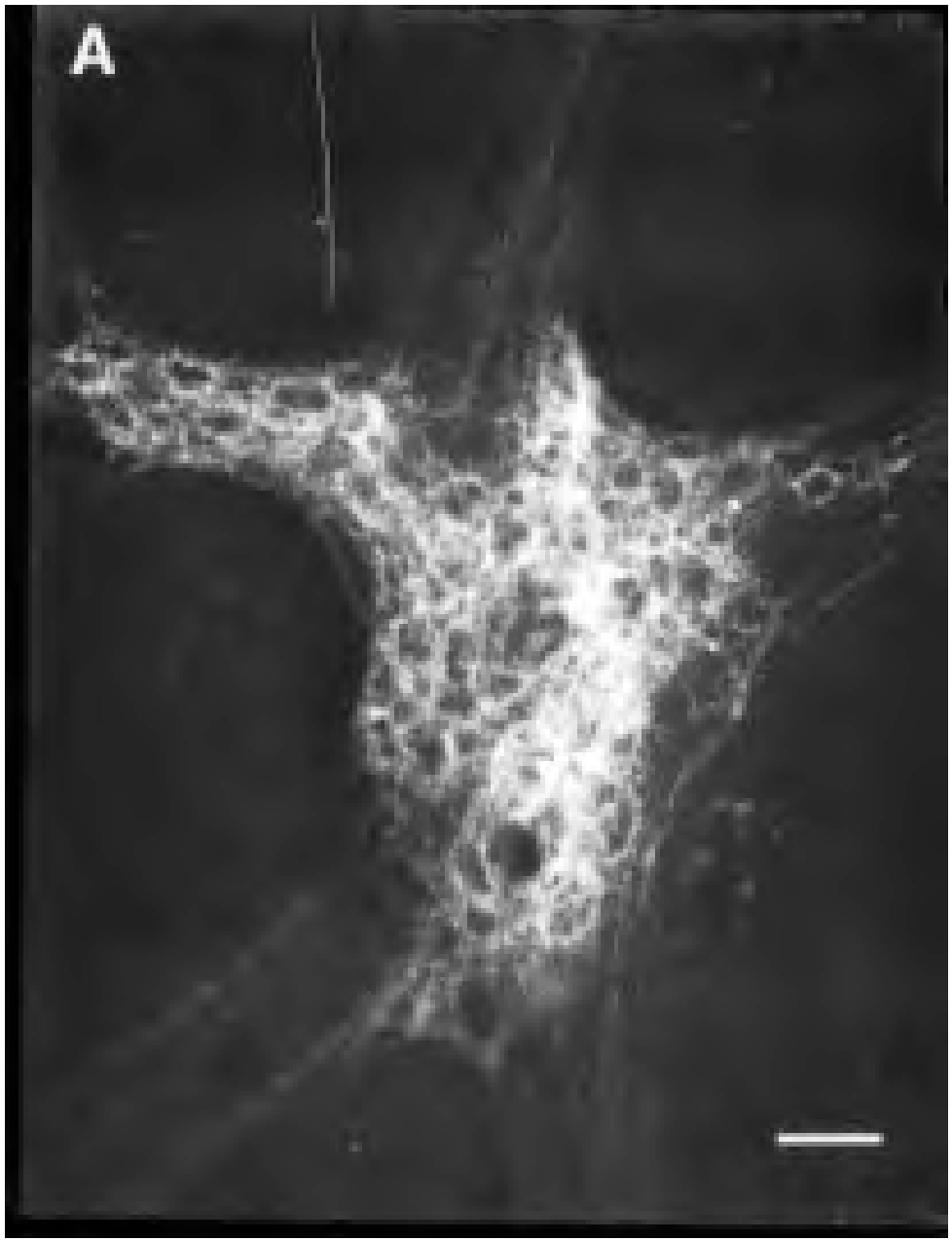
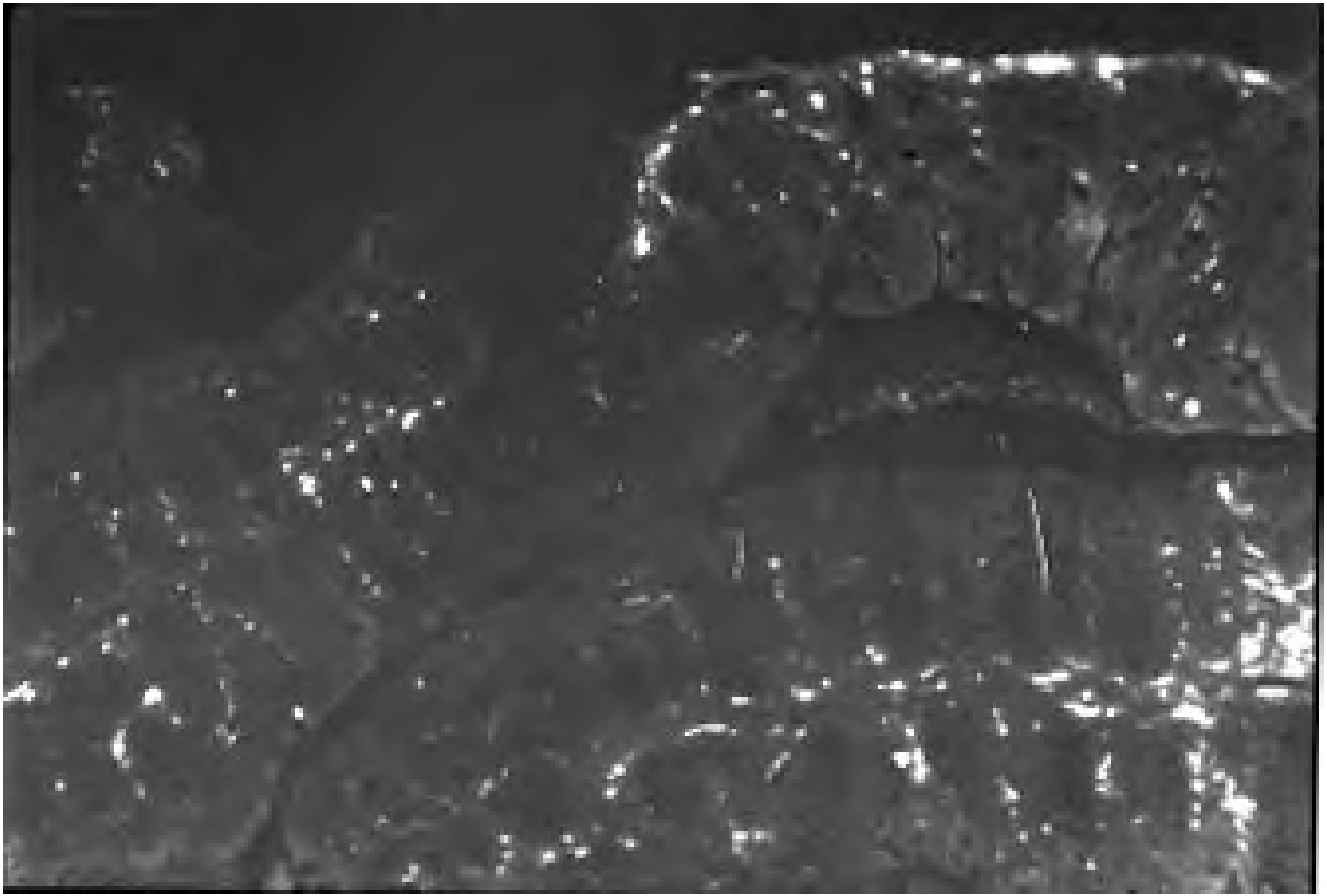


 Fig. 9 Johnson, L. *Physiology of the Gastrointestinal Tract*, Vol. 1, 2nd ed. Raven Press, New York, NY; 1987: 21.



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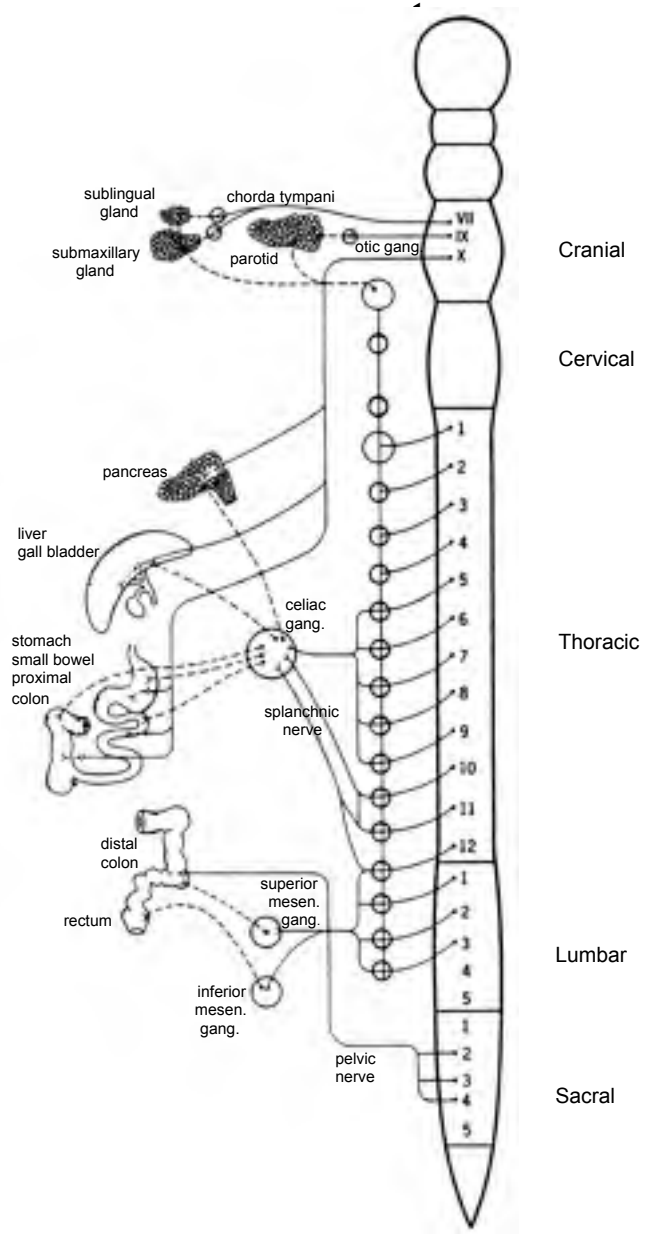
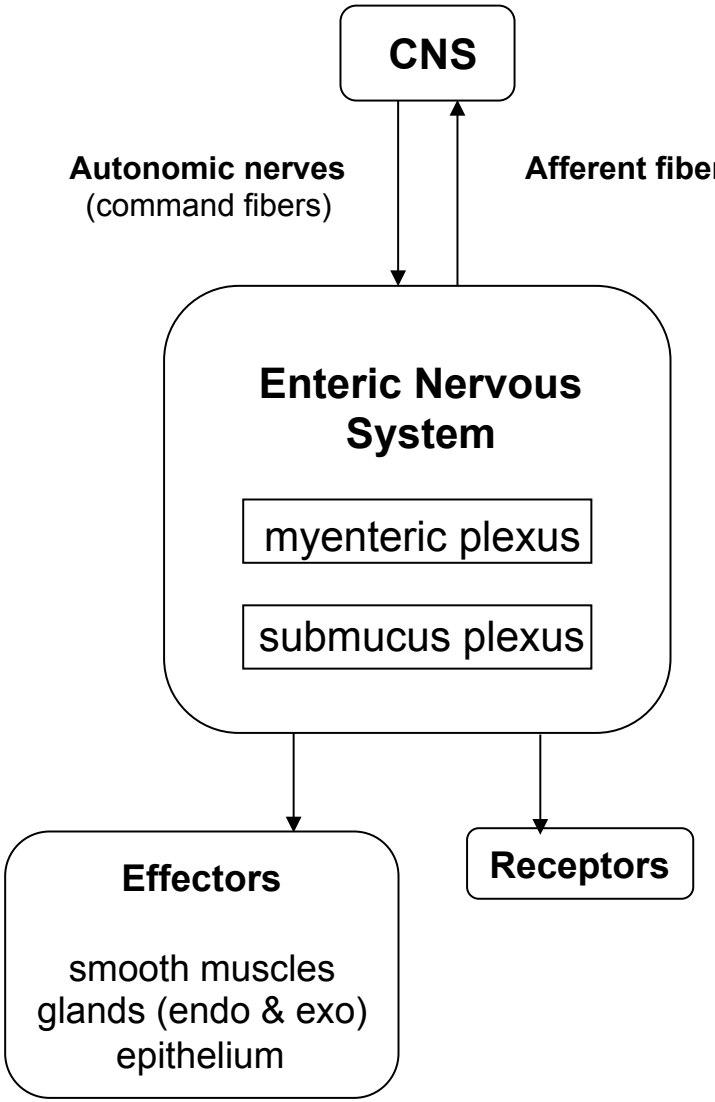
Extrinsic parasympathetic and sympathetic innervation of the digestive tract

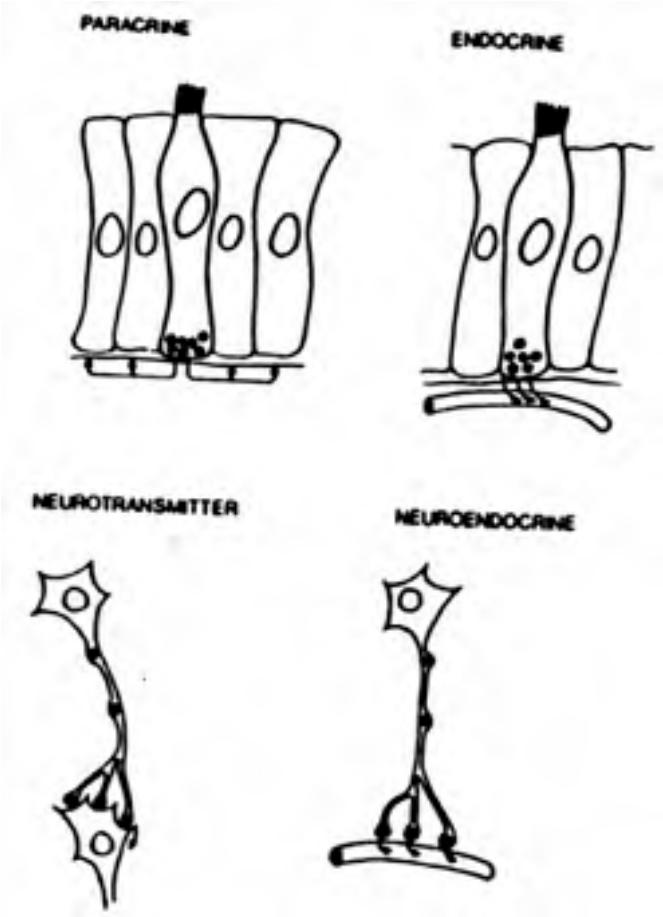


Solid lines represent preganglionic and broken lines represent postganglionic fibers.

PD-INEL Fig. 1-6 Granger, D, *et al*. *Clinical Gastrointestinal Physiology.* W.B. Saunders, Philadelphia, PA; 1985: 12.

BLOCK DIAGRAM FOR NEURAL CONTROL OF THE GI TRACT

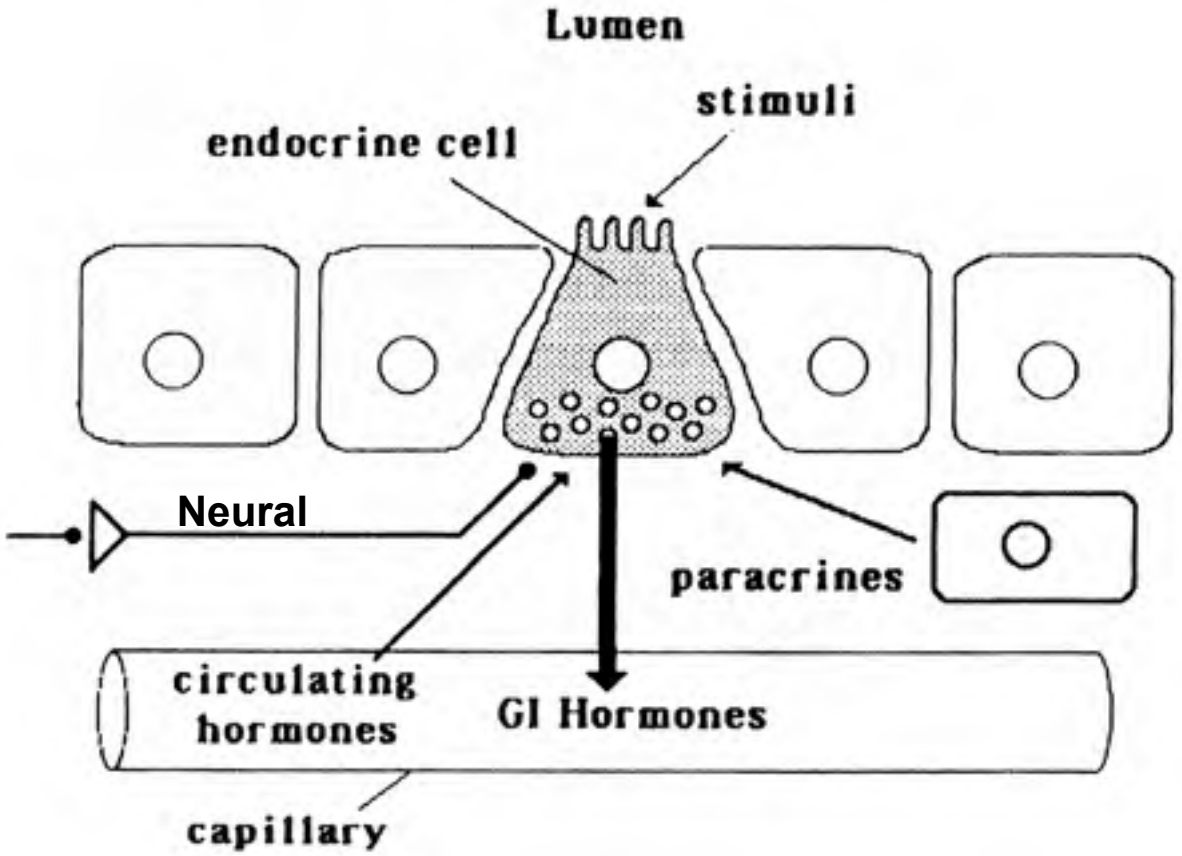




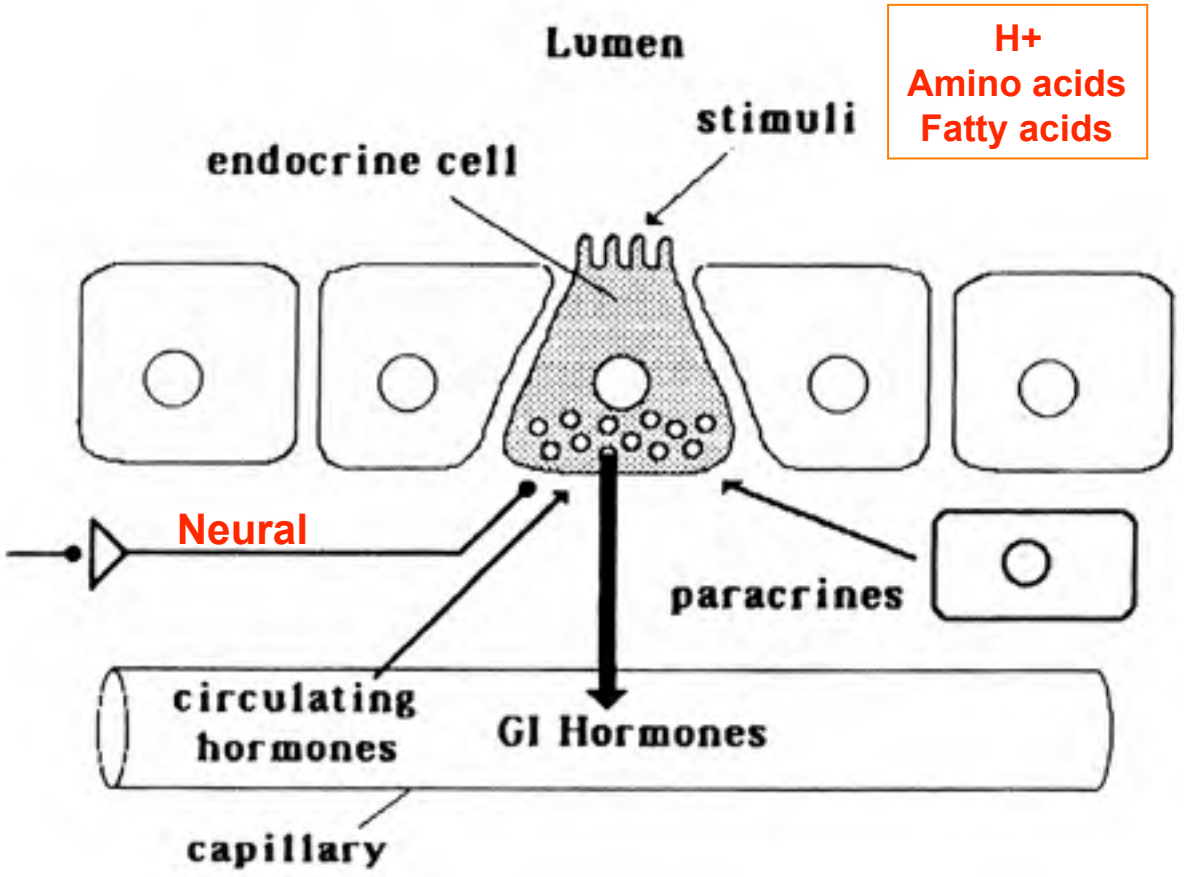
GENERAL PROCESSES AFFECTED BY GI REGULATORY MOLECULES

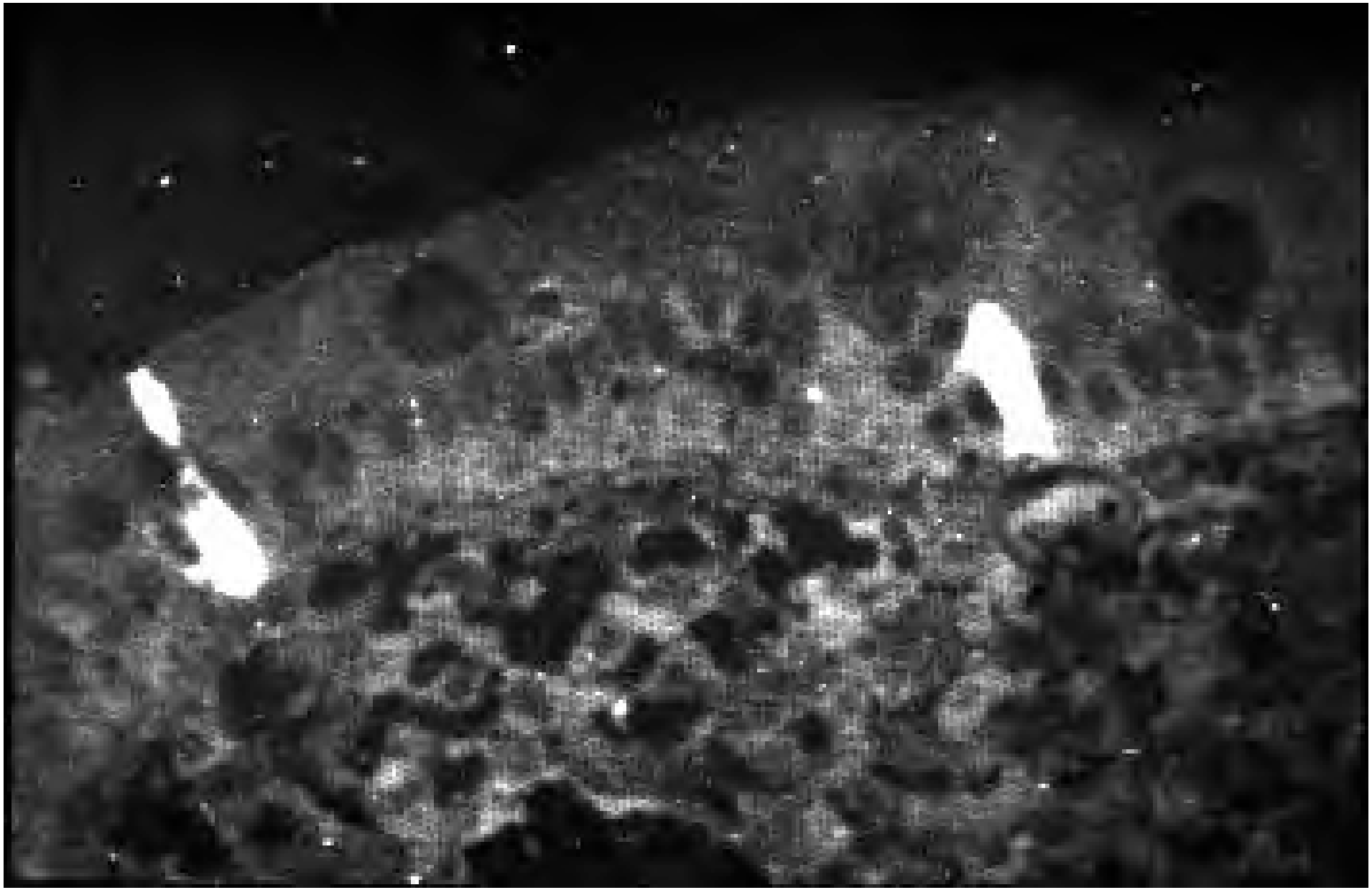
1. **GI Secretion (stomach, pancreas, intestine)**
2. **GI Motility (stomach, intestine, gallbladder)**
3. **Endocrine Secretion (pancreatic islets)**
   (Incretin)
4. **Growth of GI Organs**
5. **Food Intake**

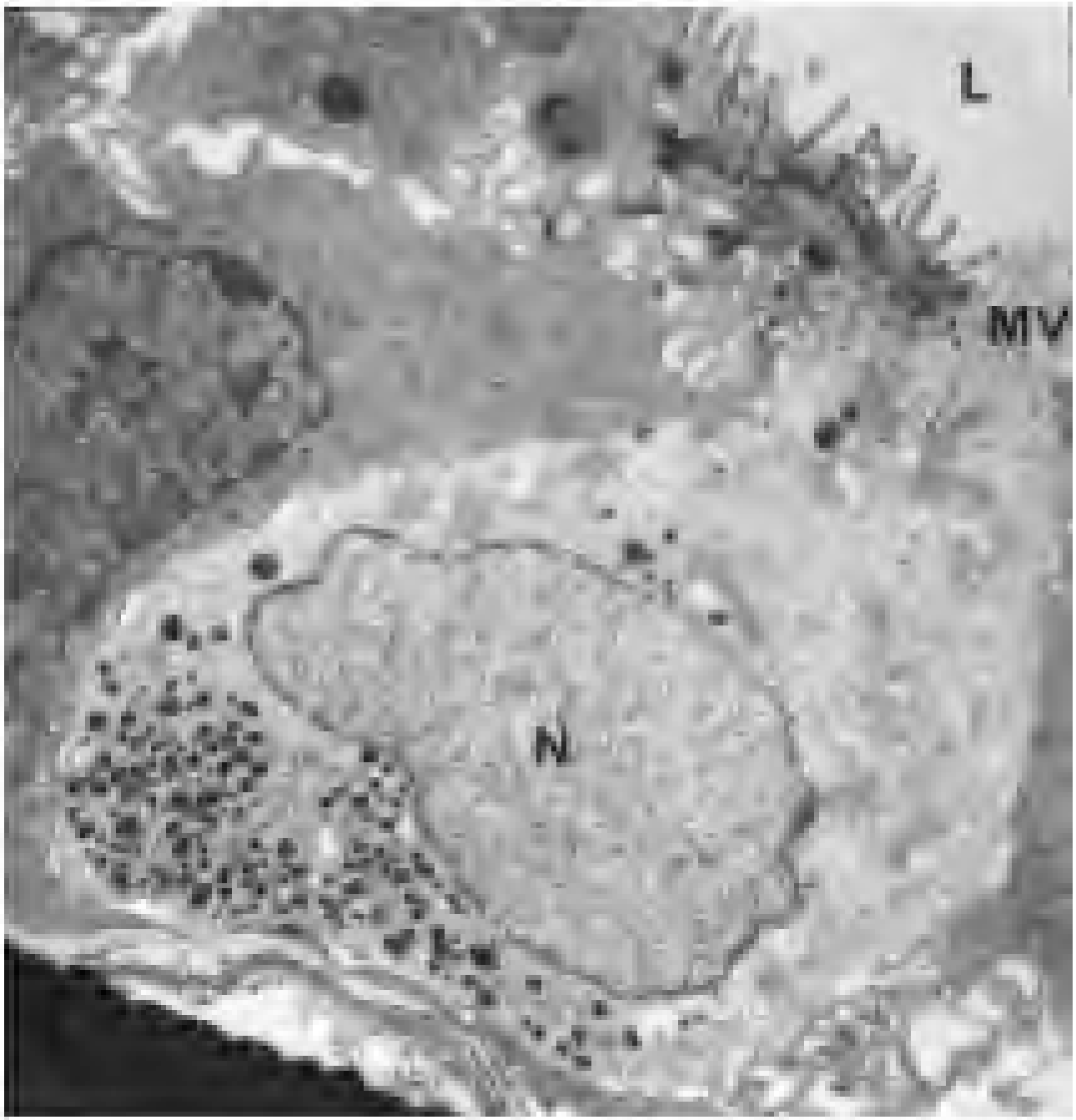
MORPHOLOGY AND SECRETION BY GI ENDOCRINE CELLS



MORPHOLOGY AND SECRETION BY GI ENDOCRINE CELLS







GASTRIN-CCK FAMILY

1. Gastrin

2. Cholecystokinin (CCK)

GASTRIN

Major Physiological Effects:

1. Gastric Acid Secretion
2. Gastric Mucosal Growth

Chemistry

G-4 minimal active fragment shared with CCK

G-5 Pentagastrin (synthetic)

G-17 "little" gastrin
G-34 "big" gastrin
> Exist as both non-sulfated and sulfated forms

Secretion

1. Synthesized by G cells in gastric antrum
2. Released in response to food in stomach

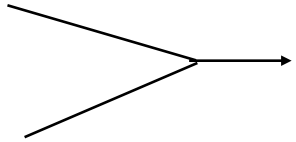
CHOLECYSTOKININ (CCK)

Major Physiological Effects:

1. Gallbladder Contraction
2. Pancreatic Enzyme Secretion
3. Inhibition of Gastric Emptying

Chemistry:

CCK-8
CCK-33
CCK-58



All contain sulfated tyrosine

Secretion:

1. Synthesized by I cells in duodenal and upper jejunal mucosa

2. Released in response to peptides and fatty acids in lumen of small intestine

Secretin-GIP-VIP-Glucagon Family

1. SECRETIN
2. GASTRIC INHIBITORY PEPTIDE (GIP)
3. GLUCAGON
4. VASOACTIVE INTESTINAL PEPTIDE (VIP)

Secretin-GIP-VIP-Glucagon Family

SECRETIN

Major Physiological Effects:

1. Stimulation of Bile and Pancreatic HCO_3 Secretion
2. Inhibition of Gastric Acid Secretion

Chemistry:

27 aa peptide

Secretion:

Secretin is synthesized by S cells in the duodenal mucosa and released in response to acid (pH <4.5) in the duodenal lumen

GASTRIC INHIBITORY PEPTIDE (GIP)

Major Physiological Effects:

1. **Stimulation of Insulin Secretion**
2. **Inhibition of Gastric Acid Secretion**

Secretion

Synthesized and released from a distinct type of duodenal endocrine cell in response to luminal nutrients

GLUCAGON

Found in both pancreas and gut but processed in islets to glucagon and in gut to GLP-1 and GLP-2

VASOACTIVE INTESTINAL PEPTIDE (VIP)

Widely distributed neuropeptide most often inhibitory to muscle but stimulates glandular secretion.
Tumors (VIPomas) result in secretory diarrhea

Other GI Regulatory Molecules

Histamine – paracrine regulator; major stimulant of gastric acid secretion

Bombesin or GRP (Gastrin Releasing Peptide) – neuropeptide; stimulates gastrin release

Motilin - intestinal GI hormone; regulates intestinal motility (MMC)

Enkephalins - neurocrine regulators of motility and secretion

Substance P – neuropeptide; usually excitatory

Somatostatin - universal inhibitory paracrine or endocrine regulatory peptide

GLP-1 (glucagon-like peptide 1) - formed by postranslational processing of proglucagon in intestine. An important regulator of insulin secretion and appetite

GLP-2 (glucagon-like peptide 2) - stimulates growth of intestinal mucosa

Inflammatory Mediators - Serotonin, cytokines, chemokines

Growth and Trophic Factors - Insulin, TGF α, IGF

Ghrelin – oriexigenic peptide present in the gastric mucosa

DISTRIBUTION OF GI REGULATORY MOLECULES

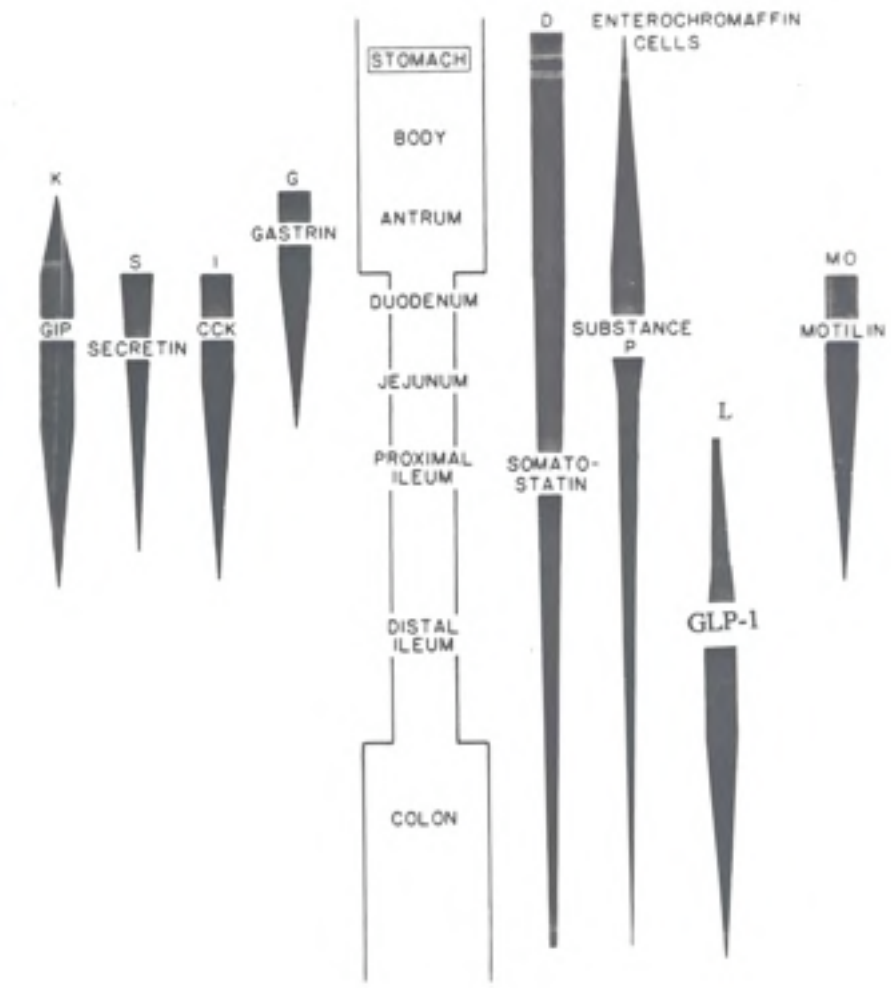


 Fig. 1-2 Granger, D, *et al*. *Clinical Gastrointestinal Physiology.* W.B. Saunders, Philadelphia, PA; 1985: 7.

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Slide 9 – Granger, D, *et al*. *Clinical Gastrointestinal Physiology.* W.B. Saunders, Philadelphia, PA; 1985: 28.

Slide 10 – Source Undetermined

Slide 11 – Granger, D, *et al*. *Clinical Gastrointestinal Physiology.* W.B. Saunders, Philadelphia, PA; 1985.

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