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

License: Unless otherwise noted, this material is made available under the terms of the Creative Commons Attribution–Non-commercial–Share Alike 3.0 License: http://creativecommons.org/licenses/by-nc-sa/3.0/

We have reviewed this material in accordance with U.S. Copyright Law and have tried to maximize your ability to use, share, and adapt it. The citation key on the following slide provides information about how you may share and adapt this material.

Copyright holders of content included in this material should contact open.michigan@umich.edu with any questions, corrections, or clarification regarding the use of content.

For more information about how to cite these materials visit http://open.umich.edu/education/about/terms-of-use.

Any medical information in this material is intended to inform and educate and is not a tool for self-diagnosis or a replacement for medical evaluation, advice, diagnosis or treatment by a healthcare professional. Please speak to your physician if you have questions about your medical condition.

Viewer discretion is advised: Some medical content is graphic and may not be suitable for all viewers.
Use + Share + Adapt

{ Content the copyright holder, author, or law permits you to use, share and adapt. }

- **Public Domain – Government**: Works that are produced by the U.S. Government. (USC 17 § 105)
- **Public Domain – Expired**: Works that are no longer protected due to an expired copyright term.
- **Public Domain – Self Dedicated**: Works that a copyright holder has dedicated to the public domain.
- **Creative Commons – Zero Waiver**
- **Creative Commons – Attribution License**
- **Creative Commons – Attribution Share Alike License**
- **Creative Commons – Attribution Noncommercial License**
- **Creative Commons – Attribution Noncommercial Share Alike License**
- **GNU – Free Documentation License**

Make Your Own Assessment

{ Content Open.Michigan believes can be used, shared, and adapted because it is ineligible for copyright. }

- **Public Domain – Ineligible**: Works that are ineligible for copyright protection in the U.S. (USC 17 § 102(b)) laws in your jurisdiction may differ

{ Content Open.Michigan has used under a Fair Use determination. }

- **Fair Use**: Use of works that is determined to be Fair consistent with the U.S. Copyright Act. (USC 17 § 107) laws in your jurisdiction may differ

Our determination **DOES NOT** mean that all uses of this 3rd-party content are Fair Uses and we **DO NOT** guarantee that your use of the content is Fair.

To use this content you should **do your own independent analysis** to determine whether or not your use will be Fair.
M1 - GI Sequence

Nerves and Hormones

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

Winter, 2009
OVERVIEW OF GASTROINTESTINAL TRACT

- Ingested nutrients
- Skeletal muscle
- Smooth muscle
- Mucosa
- Exocrine glands
- Feces

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

food & water

secretion

digestion

motility

absorption

feces
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

Ingestion
2 liters/day

Secretion
7 liters/day

Absorption
8.8 liters/day

Feces
0.2 liter/day

Saliva
Gastric Juice
Bile
Pancreatic Juice
Intestinal
Phases of GI Regulation

Cephalic Stimuli
taste, smell, sight, emotions

Gastric and Intestinal Luminal Stimuli
mechanoreceptors - volume, pressure
chemoreceptors - amino acids, fatty acids, pH
osmoreceptors - osmolarity

Origin of Stimuli
HEAD
STOMACH
INTESTINE

SPLANCHNIC CIRCULATION

ENTERIC NERVOUS SYSTEM

- Myenteric Ganglion
- Interganglionic Fiber Tract
- Circular Muscle
- Submucus Ganglion
- Mucosa
Short Reflex Pathways
(within ENS)

Long Reflex Pathways
(involve CNS)

Source: Undetermined

## NEUROTRANSMITTERS INVOLVED IN GI REGULATION

<table>
<thead>
<tr>
<th><strong>NON-PEPTIDES</strong></th>
<th><strong>PEPTIDES</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholine</td>
<td>Substance P</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>CCK</td>
</tr>
<tr>
<td>Serotonin</td>
<td>Somatostatin</td>
</tr>
<tr>
<td>Nitric Oxide</td>
<td>VIP</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Enkephalin</td>
</tr>
<tr>
<td>Purinergic (adenosine,</td>
<td></td>
</tr>
<tr>
<td>ATP)</td>
<td></td>
</tr>
</tbody>
</table>
Fig. 2 Johnson, L. Physiology of the Gastrointestinal Tract, Vol. 1, 2nd ed. Raven Press, New York, NY; 1987: 4.
Extrinsic parasympathetic and sympathetic innervation of the digestive tract

Solid lines represent preganglionic and broken lines represent postganglionic fibers.

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

CNS

Autonomic nerves
(command fibers)

Enteric Nervous System

myenteric plexus
submucous plexus

Afferent fibers

Effectors

smooth muscles
glands (endo & exo)
epithelium

Receptors

John Williams
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

Lumen

endocrine cell

stimuli

Neural

circulating hormones

GI Hormones

capillary

paracrines
MORPHOLOGY AND SECRETION BY GI ENDOCRINE CELLS

Lumen

endocrine cell

stimuli

paracrines

circulating hormones

GI Hormones

capillary

H+
Amino acids
Fatty acids

Neural
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 Exist as both non-sulfated
G-34 “big” gastrin 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

Major Physiological Effects:

1. Stimulation of Bile and Pancreatic HCO₃ 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

**Ghrelin** – oriexigenic peptide present in the gastric mucosa
DISTRIBUTION OF GI REGULATORY MOLECULES
Slide 4 – John Williams
Slide 5 – John Williams
Slide 6 – John Williams
Slide 7 – John Williams
Slide 10 – Source Undetermined
Slide 15 – Source Undetermined
Slide 16 – Fig. 1-6 Granger, D, et al. *Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985: 12.
Slide 17 – John Williams
Slide 18 – Source Undetermined
Slide 20 – John Williams
Slide 21 – John Williams
Slide 22 – Source Undetermined
Slide 23 – Source Undetermined
Slide 32 – Fig. 1-2 Granger, D, et al. *Clinical Gastrointestinal Physiology*. W.B. Saunders, Philadelphia, PA; 1985: 7.