Digestion:
Hormones of the GI Tract

Dr. Ritamarie Loscalzo
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Major Gut Hormones

- **Gastrin**: stomach
- **Secretin**: duodenum
- **Cholecystokinin (CCK)**: duodenum
- **Gastric inhibitory peptide (GIP)**: duodenum
- **Glucagon-Like Peptide (GLP)**: small intestine
- **Somatostatin**: stomach, duodenum, and pancreas
- **Motilin**: duodenum
- **Vasoactive Intestinal Peptide (VIP)**: neurons in intestine, CNS, and urogenital tract
# Major Digestive Hormones

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Produced by</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrin</td>
<td>Stomach</td>
<td>Production of stomach acid and stomach motility</td>
</tr>
<tr>
<td>Cholecystokinin (CCK): trigger by fat</td>
<td>Small intestine</td>
<td>Production of pancreatic juices and emptying of gall bladder</td>
</tr>
<tr>
<td>Secretin</td>
<td>Duodenum</td>
<td>Stimulates bicarbonate production by pancreas, bile production by liver, and pepsin by stomach</td>
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<tr>
<td>Incretins: GIP: Gastric Inhibitory Peptide and GLP: Glucagon Like Peptide</td>
<td>Small intestine – affect insulin response</td>
<td>Increases insulin, inhibits glucagon release, slows rate of absorption of nutrients by reducing gastric emptying</td>
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<tr>
<td>Somatostatin</td>
<td>Stomach, intestine, pancreas</td>
<td>Inhibits gastrin, CCK, secretin, GIP, and also growth hormone, TSH, glucagon, and insulin</td>
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<tr>
<td>Dopamine</td>
<td>Brain and GI mucosa</td>
<td>Reduces motility and protects mucosa</td>
</tr>
<tr>
<td>Serotonin</td>
<td>Brain and GI mucosa</td>
<td>Inhibits gastric acid and stimulates mucus</td>
</tr>
<tr>
<td>Peptide YY (PYY)</td>
<td>Mainly ileum and colon, but a little in other parts of GI tract</td>
<td>Inhibits gastric motility, increases water and electrolyte absorption in colon, may suppress pancreatic secretion, increases efficiency of digestion</td>
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</tbody>
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Gastrin

- Secreted by the stomach G cells in antrum
- Stimulated by arrival of food in stomach, particularly proteins, gastric distension, and vagus nerve
- Stimulates parietal cells to secrete hydrochloric acid (the only hormone to do this)
- Increases histamine release
- Increases gastric motility
- Opens pyloric sphincter
- Relaxes ileocecal valve
- Stimulates growth of gastric mucosa
- Stimulates pepsinogen (inactive form of pepsin)
- Inhibited by low pH (<3)
- Inhibited by somatostatin, GIP, VIP, glucagon, and calcitonin
Cholecystokinin (CCK)

✓ Secreted by the duodenum
✓ Mainly stimulated by the presence of fat
✓ Slight stimulation by amino acids
✓ Stimulates the release of digestive enzymes by the pancreas
✓ Stimulates gall bladder contraction and relaxation of sphincter (the only hormone to do this)
✓ Decreases gastric emptying
✓ Induces satiety through hypothalamus
Secretin

- Secreted by the duodenum
- Stimulated by bile aid, fatty food, and acid in duodenum
- Most potent stimulator of the secretion of sodium bicarbonate by the pancreas
- Stimulates bile secretion and increases CCK
- Contracts pyloric sphincter
- Promotes growth and maintenance of pancreas
- Decreases gastric acid secretion and motility
- Inhibited by somatostatin
- Secretin family also includes GIP (Glucose-dependent Insulinotropic Peptide) and VIP (Vasoactive Intestinal Peptide)
Gastric Inhibitory Peptide (GIP)

- Member of secretin family
- Synthesized by neuroendocrine cells in mucosa of duodenum and jejunum
- Stimulated by glucose and fat in duodenum, acid in stomach
- Stimulates insulin release and glucose use by muscles (aka Glucose-dependent Insulinotropic Peptide)
- Stimulates lipogenesis by adipose tissue
- Inhibits gastric acid secretion and gastrin release
- Decreases stomach churning and slows the emptying in the stomach
- Receptors for it on beta cells of pancreas
- One of the family called incretins
- Hypersecretion leads to insulin resistance and obesity
Somatostatin

✓ AKA Growth Hormone Inhibitory Hormone (GHIH):
  2 different forms: 14 in hypothalamus, 28 in stomach
✓ Stimulated by stomach acid and sympathetic nervous system
✓ Inhibited by parasympathetic nervous system
✓ Secreted by stomach, duodenum, and islet cells in pancreas - into stomach as well as blood
✓ Inhibits all secretions: gastrin, VIP, GIP, secretin, motilin, GH, insulin and glucagon, pancreatic enzymes, and bile flow
✓ Increases fluid absorption and decreases intestinal secretions
✓ Decreases gastric secretion and motility
✓ Decreases absorption of glucose, amino acids, and triglycerides
Motilin

✓ Secreted by the duodenum
✓ Promotes intestinal motility - increases the migrating motor complex activity
✓ Stimulates the production of pepsin
✓ Rises after a meal or drinking water
✓ Accelerates gastric emptying and colonic transit
✓ Erythromycin is a motilin receptor agonist, leading to diarrhea and abdominal cramps
Vasoactive Intestinal Peptide (VIP)

- Secreted by neuroendocrine cells in intestine (and also CNS and urogenital tract)
- Stimulated by chyme entering duodenum
- Increases intestinal motility and secretions
- Relaxes smooth muscle
- Inhibits gastric secretion
- Dilates intestinal capillaries
- Receptors in small intestine and large intestine
- Also receptors in lung, heart, brain, kidney, and spleen
Other GI Neuroendocrine Peptides

✓ Nitric Oxide: Intestine
✓ Histamine: Stomach
✓ Peptide YY: Ileum and colon
✓ Serotonin: Brain and gut mucosa
✓ Dopamine: Brain and gut mucosa
✓ Bombesin: Gut and pancreas
✓ Chromogranins: Neuroendocrine cells
✓ Calcitonin Gene-Related Peptide: Enteric nerves
✓ Enteroglucagon: Small intestine, pancreas
Nitric Oxide

✓ The ultimate smooth muscle relaxer
✓ Reduces motility
✓ Relaxes sphincters
Histamine

✓ Produced by enterochromaffin-like cells (ECL cells) of the stomach
✓ Stimulated by gastrin
✓ Increase HCl secretion from parietal cells
Peptide YY

- Produced by large intestine
- Inhibits food intake
- Acts on stomach and intestine to slow down the movement of food through the digestive tract
Serotonin

✓ Produced by brain and GI mucosa
✓ Inhibits gastric acid
✓ Stimulates mucus
✓ Promotes the development and maintenance of neurons and interstitial cells
✓ Promotes motility
Dopamine
✓ Produced by brain and GI mucosa
✓ Reduces motility and protects mucosa
✓ Thought to control nausea and vomiting
Bombesin

- Produced throughout the gut and in the pancreas
- Stimulates release of cholecystokinin (CCK) and gastrin
- Stimulates release of motilin
- Stimulates pancreatic enzyme secretion
- Trophic effects on the developing gut
- Potent chemoattractant of macrophages and lymphocytes and enhances the phagocytic process in macrophages
Chromogranins

✓ Produced by neuroendocrine cells
✓ Potent inhibitor of insulin release
✓ Enhances meal-stimulated gastric acid secretion
✓ Can be used to determine the presence of a neuroendocrine tumor and as a means to monitor the efficacy of treatment
Calcitonin Gene-Related Peptide

- Produced by enteric nerves
- Inhibits gastric acid
- Inhibits pancreatic secretion
- Causes relaxation of vascular smooth muscle
Enteroglucagon

✓ Produced by small intestine and pancreas
✓ Found in high concentrations in the mucosa of the ileum, colon, and rectum
✓ Inhibits insulin secretion
✓ Trophic effect on the small intestinal mucosa
✓ Released after a mixed meal, particularly of carbohydrate and long-chain fatty acids
✓ Amount secreted is proportional to the amount of unabsorbed food entering the colon
✓ High concentrations found in conditions associated with loss of the small-intestinal absorptive capacity
✓ Sometimes called glicentin
More GI Neuroendocrine Peptides

- **Galanin:** Enteric nerves
- **Neuropeptide Y:** Enteric nerves
- **Neurotensin:** Ileum
Galanin

✓ Produced by enteric nerves, especially in liver and pancreatic islets
✓ Inhibits intestinal smooth-muscle contraction
✓ Inhibits postprandial insulin release
Neuropeptide Y

✓ Produced by enteric nerves
✓ Regulates intestinal blood flow
✓ Often co-localized with noradrenaline
✓ Found in both extrinsic adrenergic nerves to the myenteric plexus and in intrinsic nerves in the myenteric and submucosal plexi
✓ Highest concentrations in upper intestine and distal colon
✓ Potent vasoconstrictor
✓ Inhibits intestinal secretion and depresses colonic motility
Neurotensin

✓ Produced in the ileum
✓ Affects gut motility
✓ Increases jejunal and ileal fluid secretion
✓ Inhibits gastric acid secretion and gastric emptying
✓ Stimulates pancreatic exocrine and intestinal secretion
✓ Plasma concentrations rise postprandially, particularly after fatty food
GI Neuroendocrine Peptides

- **Ghrelin**: Stomach stimulates appetite, increases gastric emptying
- **Glucagon-like peptide-2**: Ileum, colon
  - Stimulates motility and absorption and has trophic effects on the intestine
- **Pancreatic polypeptide**: Pancreas
  - Inhibits pancreatic and biliary secretion
- **Trefoil peptides**: Stomach, intestine
  - Mucosal protection and repair
- **Enkephalins**: Stomach, duodenum
  - Opiate-like
- **Substance P**: Enteric nerves, function unclear
- **Growth hormone-releasing factor**: Small intestine, function unclear
Integration of Neural and Endocrine Gut Functions

- Thoughts, taste, smell of food, and chewing activate parasympathetic nervous system via acetylcholine (ACh)
- ACh stimulates parietal cells to increase acid secretion
- ACh increases gastrin, inhibits somatostatin
- Sympathetic input (activity, stress): increases somatostatin release → inhibition of gastric secretion and motility
Local Reflex Integration of Neural and Endocrine Functions

- **Mechanoreceptors**: GI tract walls detect movement of food
  - Stomach distension causes activation of the parasympathetic system
  - This increases gastrin, leading to acid release, and decreases somatostatin

- **Chemoreceptors detect nutrients and pH**
  - Amino acids, alcohol, or caffeine in the stomach increases gastrin release
  - Fatty acids in the duodenum cause release of CCK
http://www.drritamarie.com/go/YTControlOfTheGITract
http://www.drritamarie.com/go/YTDigestiveHormones

*The Belly Fat Effect*, Mike Mutzel

http://www.drritamarie.com/go/EndoDigestionPPT

http://www.drritamarie.com/go/EndocrineDigestionPPT

http://www.drritamarie.com/go/GIHormones