INE | INSTITUTE OF NUTRITIONAL ENDOCRINOLOGY

Digestion:
Hormones of the GI Tract

Dr. Ritamarie Loscalzo

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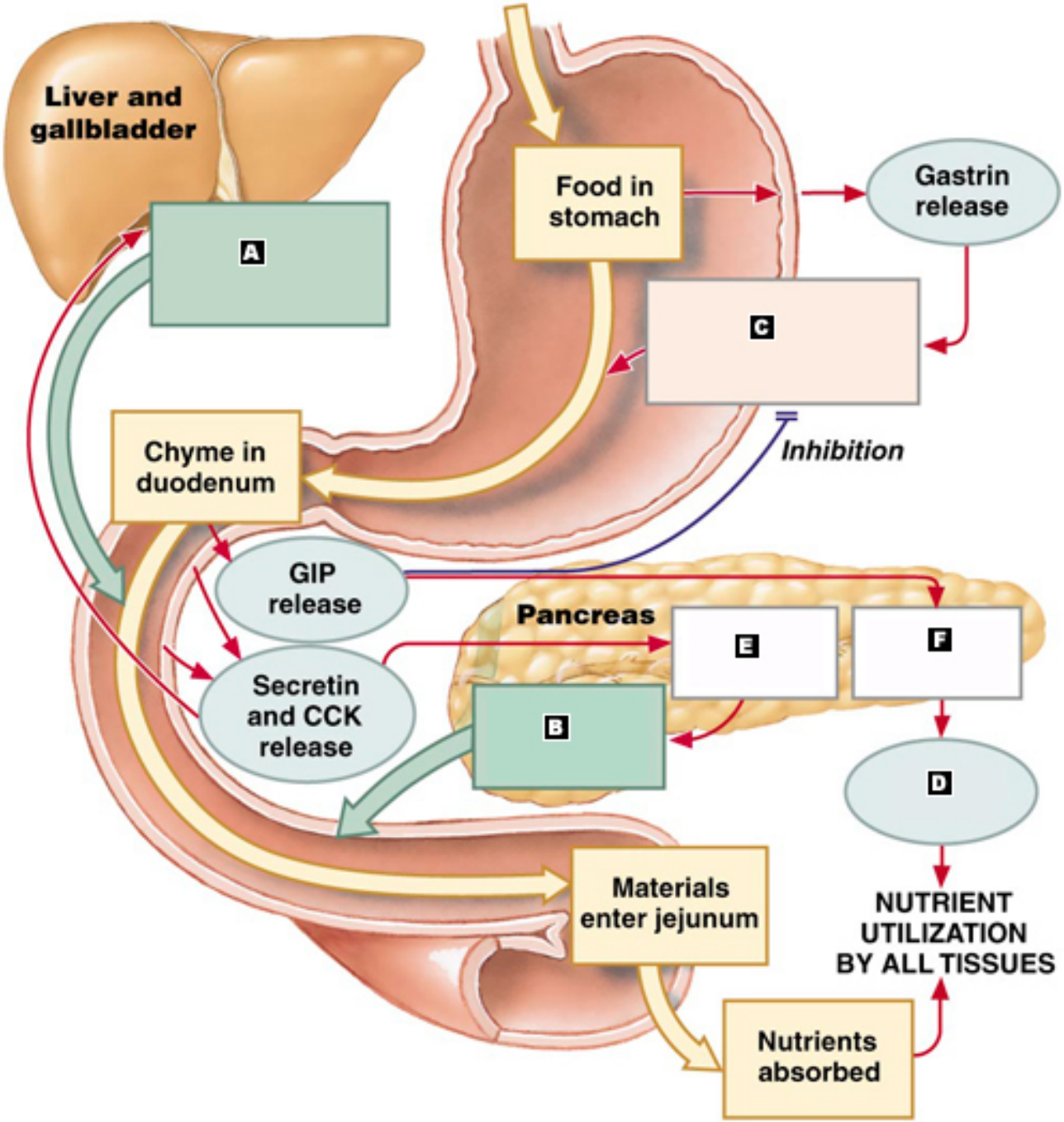


Major Gut Hormones

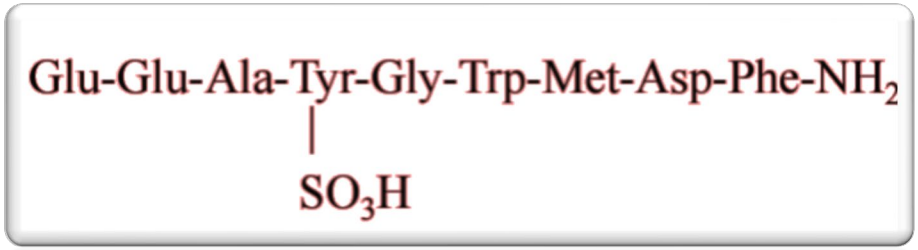
- ✓ **Gastrin:** stomach
- ✓ **Secretin:** duodenum
- ✓ **Cholecystokinin (CCK):** duodenum
- ✓ **Gastric inhibitory peptide (GIP):** duodenum
- ✓ **Glucagon-Like Peptide (GLP):** small intestine
- ✓ **Somatostatin:** stomach, duodenum, and pancreas
- ✓ **Motilin:** duodenum
- ✓ **Vasoactive Intestinal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

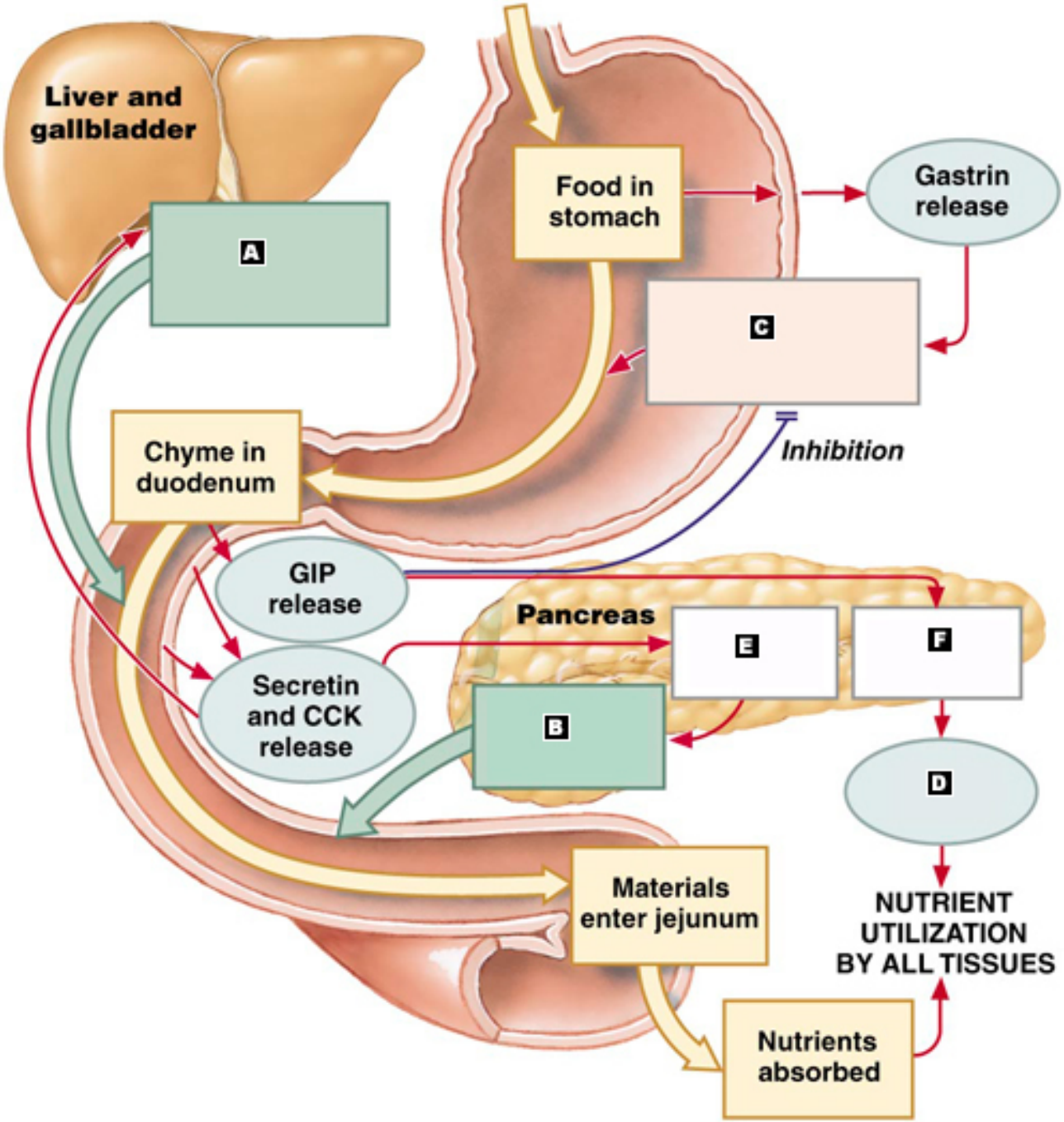
Major Digestive Hormones

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

Gastrin

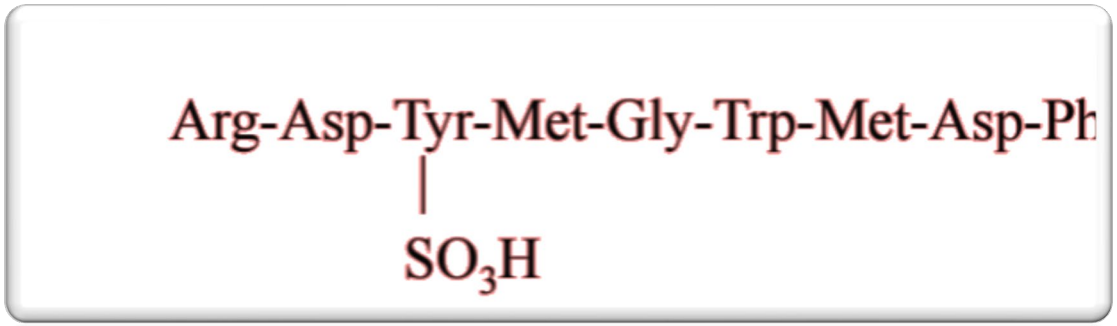
- ✓ Secreted by the stomach G cells in antrum
- ✓ Stimulated by arrival of food in stomach, particularly proteins, gastric distension, and vagus nerve
- ✓ Stimulates parietal cells to secrete hydrochloric acid (the only hormone to do this)
- ✓ Increases histamine release
- ✓ Increases gastric motility
- ✓ 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

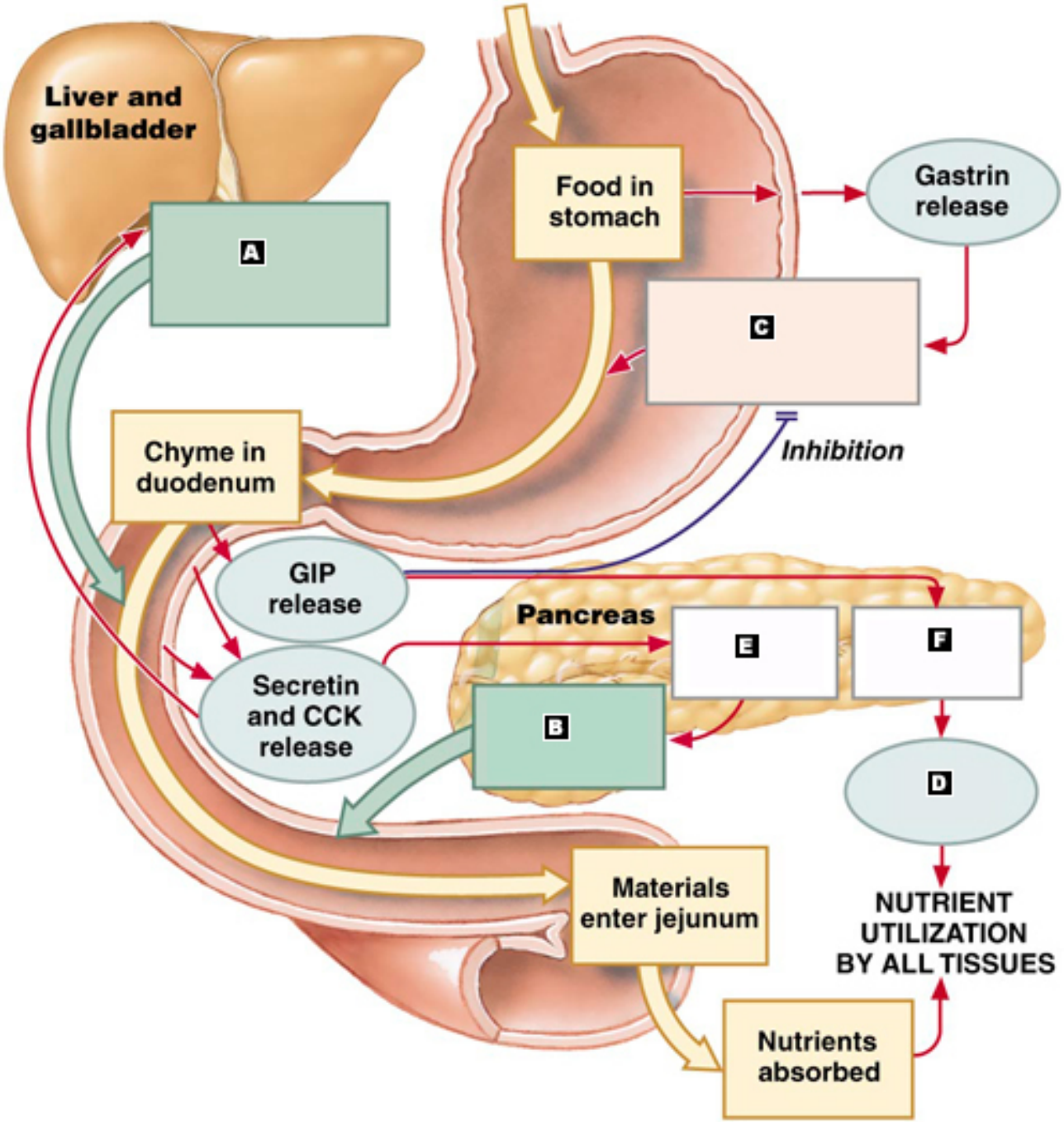




Cholecystokinin (CCK)

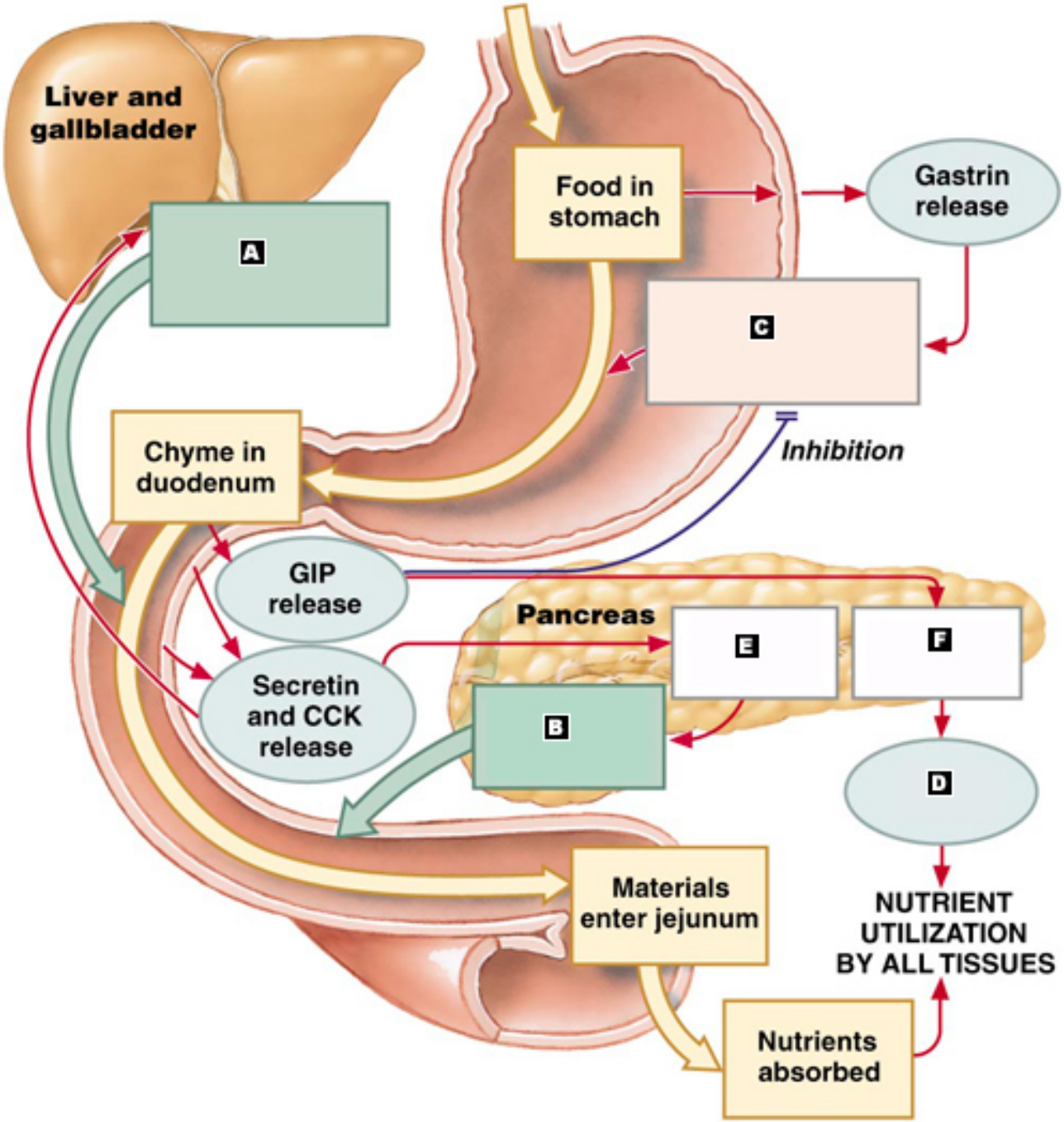
- ✓ Secreted by the duodenum
- ✓ Mainly stimulated by the presence of fat
- ✓ Slight stimulation by amino acids
- ✓ Stimulates the release of digestive enzymes by the pancreas
- ✓ Stimulates gall bladder contraction and relaxation of sphincter (the only hormone to do this)
- ✓ Decreases gastric emptying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





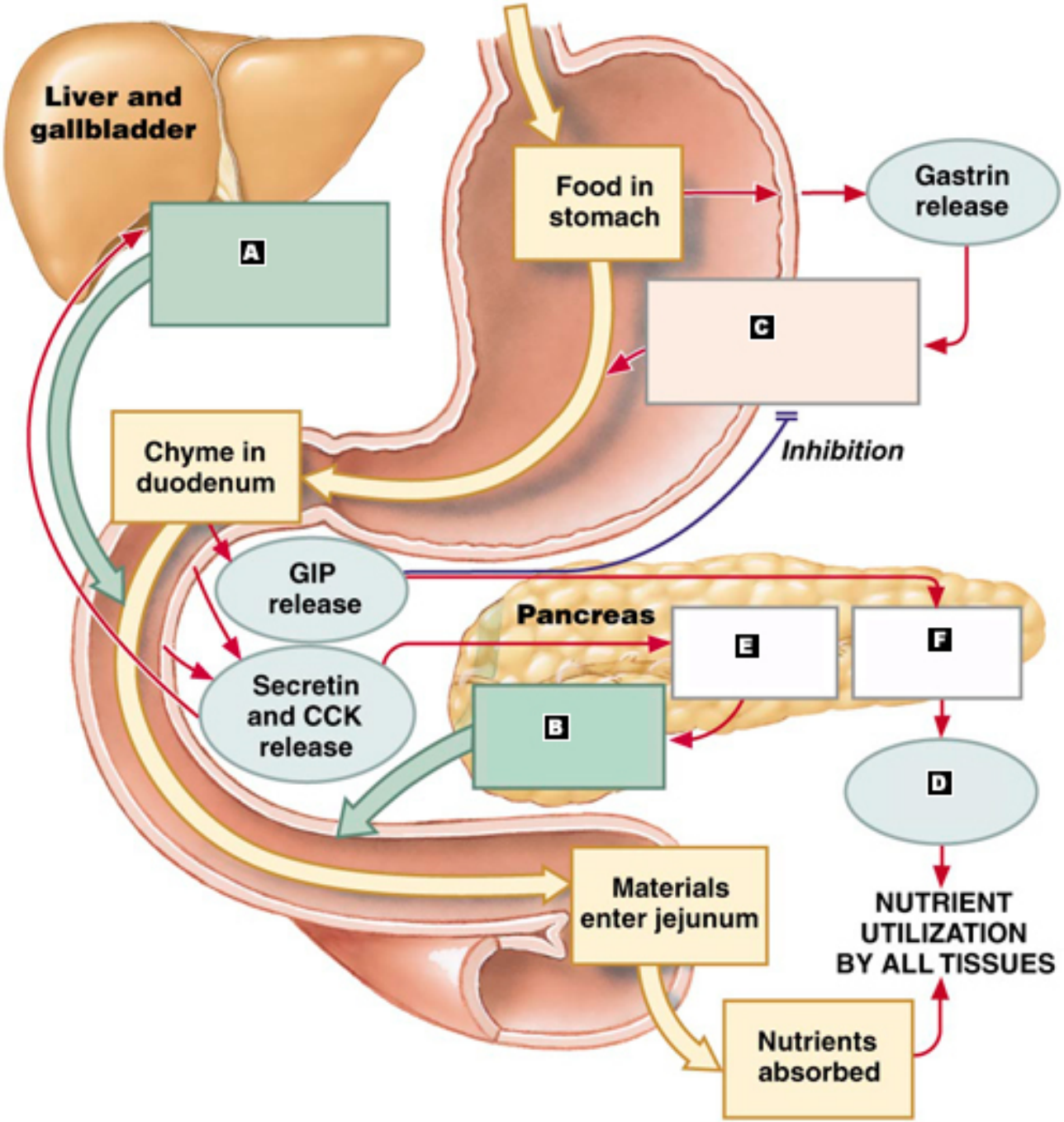
Secretin

- ✓ 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

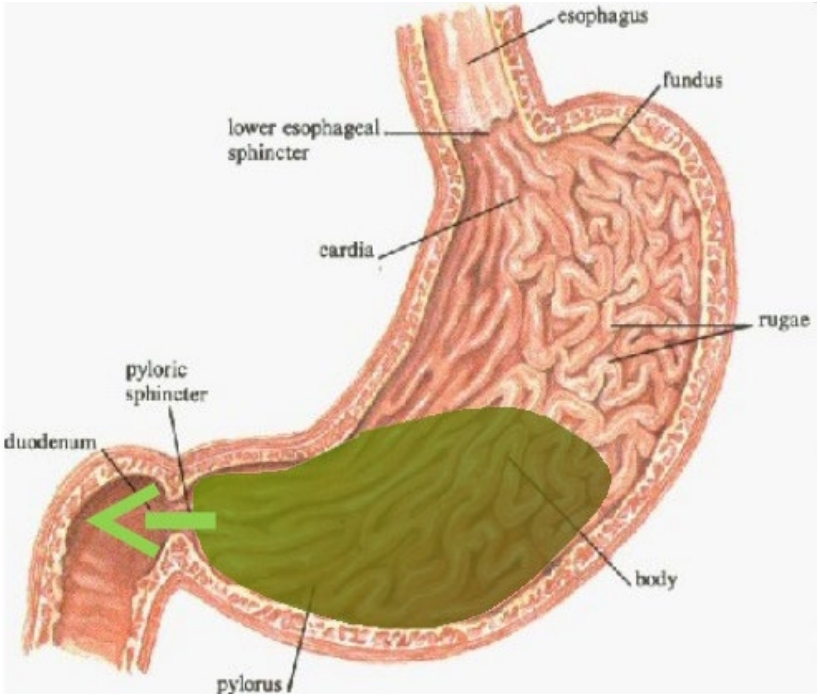
- ✓ AKA Growth Hormone Inhibitory Hormone (GHIH): 2 different forms: 14 in hypothalamus, 28 in stomach
- ✓ Stimulated by stomach acid and sympathetic nervous system
- ✓ Inhibited by parasympathetic nervous system
- ✓ Secreted by stomach, duodenum, and islet cells in pancreas - into stomach as well as 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

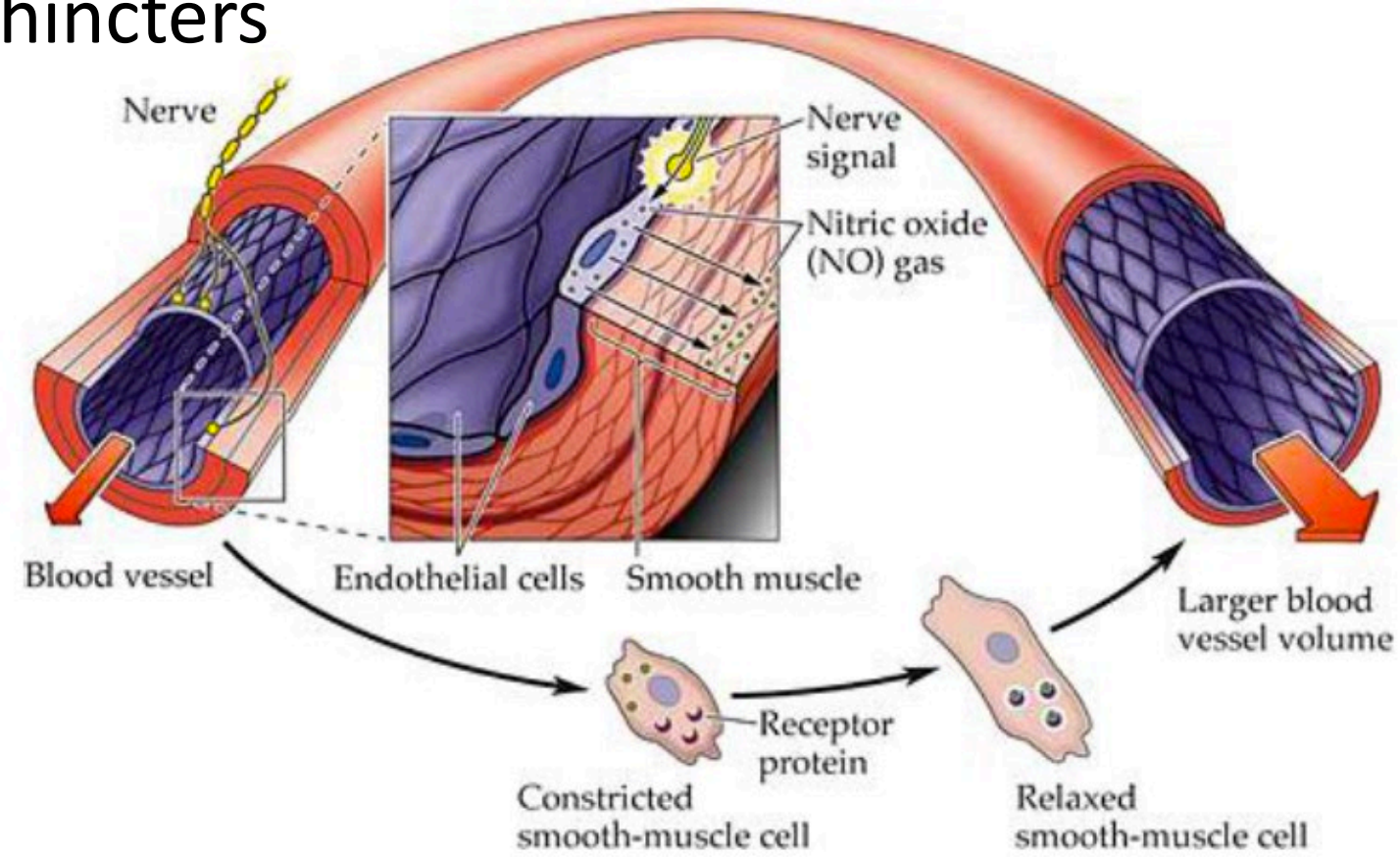


Other GI Neuroendocrine Peptides

- ✓ **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

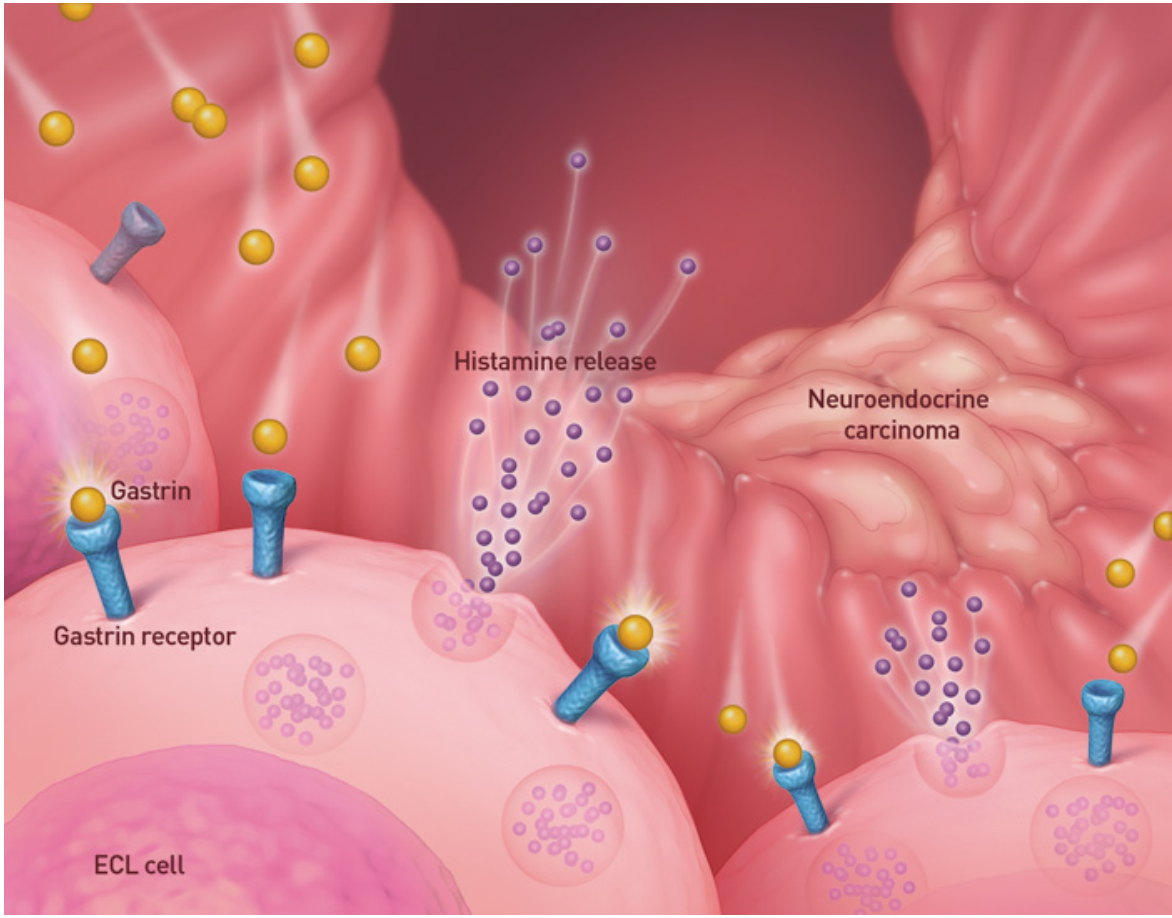
Nitric Oxide

- ✓ 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

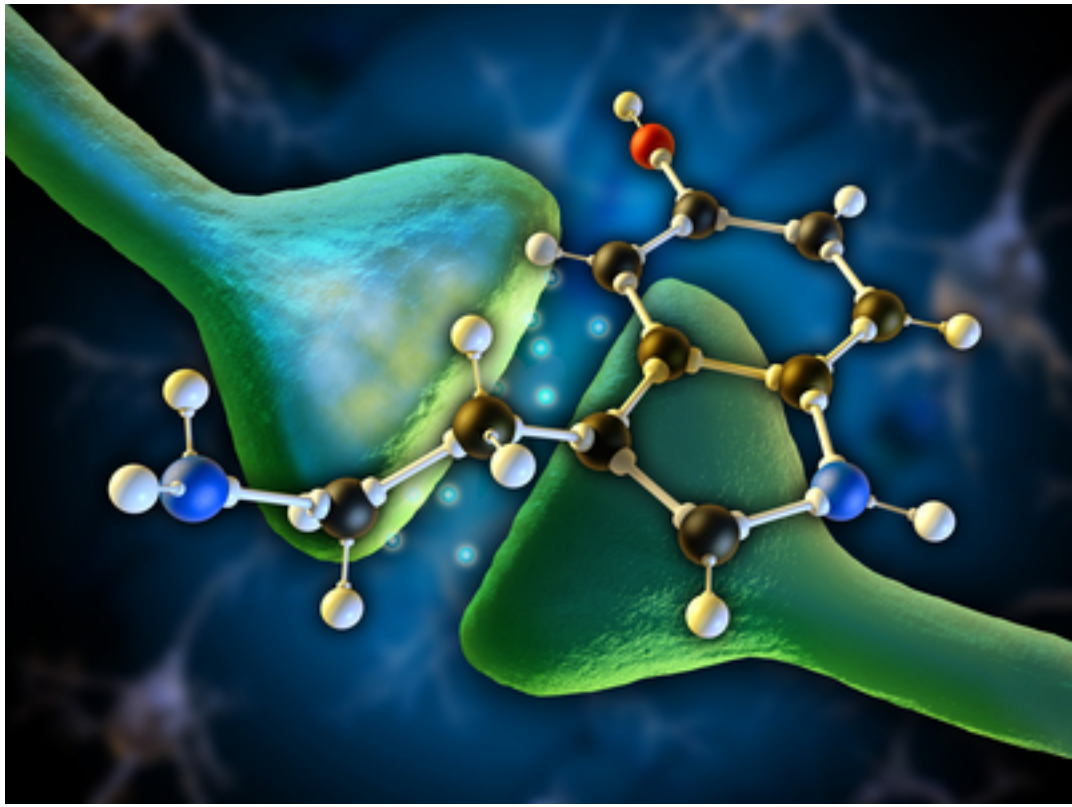


Peptide YY

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

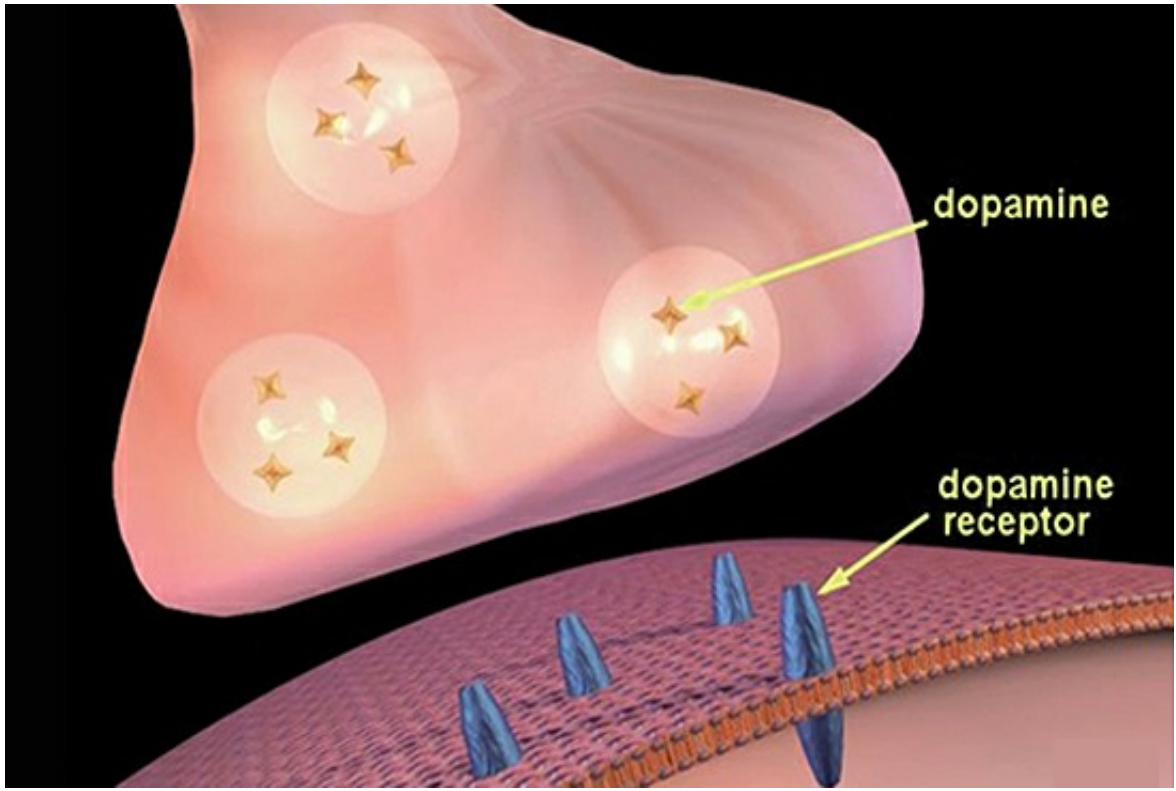
Serotonin

- ✓ Produced by brain and GI mucosa
- ✓ Inhibits gastric acid
- ✓ Stimulates mucus
- ✓ Promotes the development and maintenance of neurons and interstitial cells
- ✓ Promotes motility



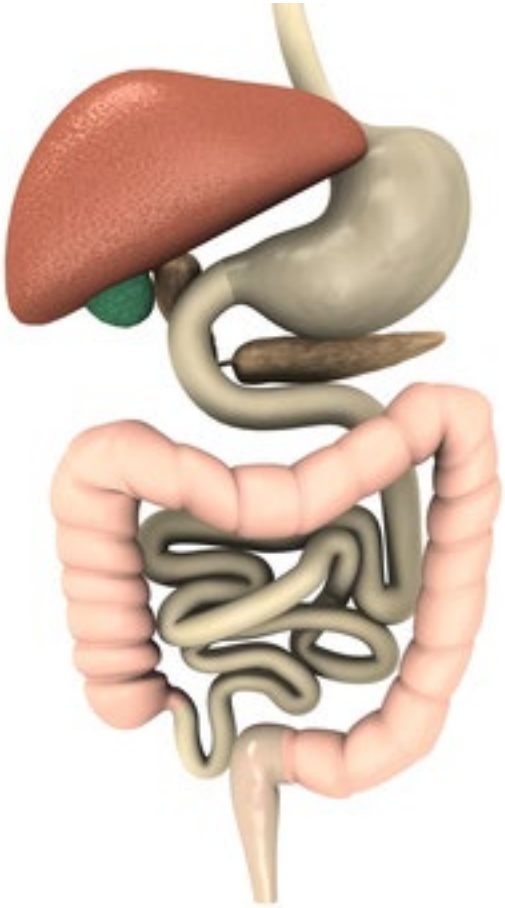
Dopamine

- ✓ Produced by brain and GI mucosa
- ✓ Reduces motility and protects mucosa
- ✓ Thought to control nausea and vomiting



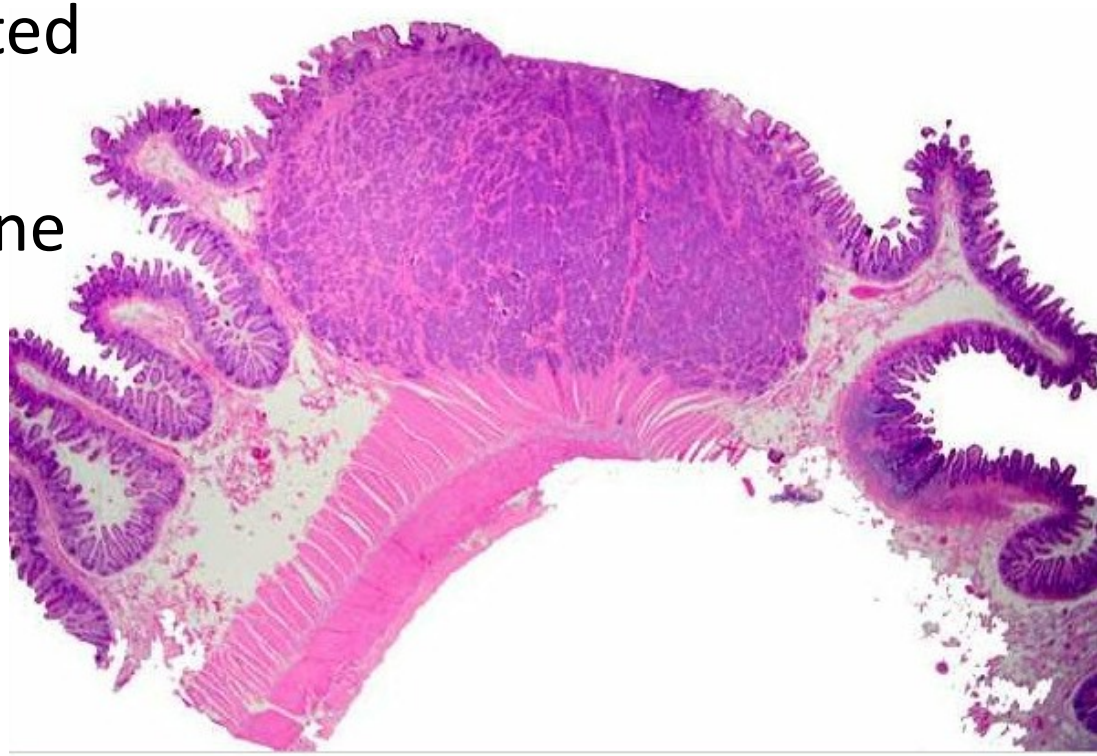
Bombesin

- ✓ 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

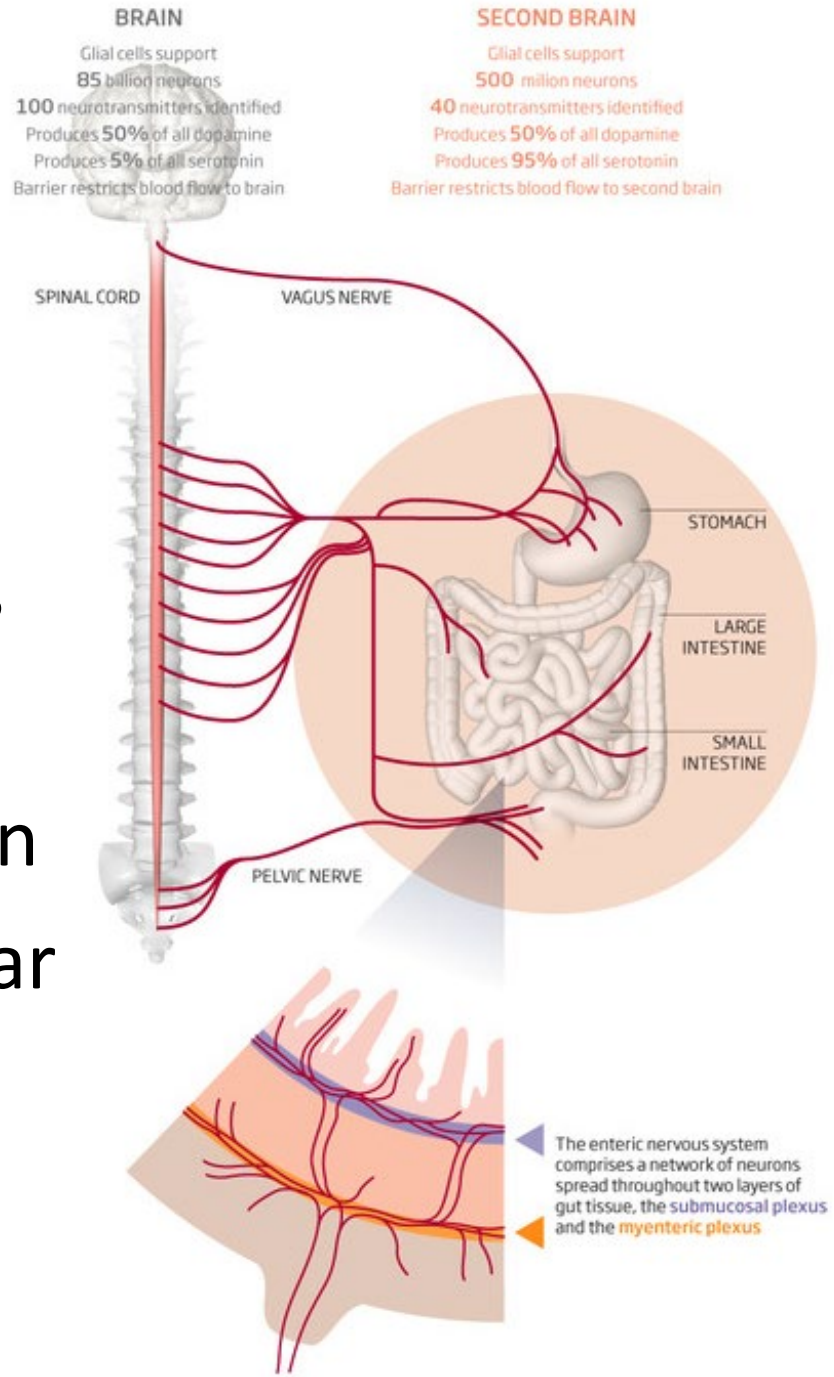
- ✓ Produced by neuroendocrine cells
- ✓ Potent inhibitor of insulin release
- ✓ Enhances meal-stimulated gastric acid secretion
- ✓ Can be used to determine the presence of a neuroendocrine tumor and as a means to monitor the efficacy of treatment



[NEUROENDOCRINE TUMOR, WELL DIFFERENTIATED (CARCINOID)]. Well-differentiated neuroendocrine tumor, also known as carcinoid tumor, most commonly occurs in ileum and accounts for about 25–30% of NET in this location. Small tumors may be limited to mucosa with or without extension into the submucosa. Larger tumors may invade into the muscularis propria and serosa. This tumor extends from mucosa through muscularis propria.

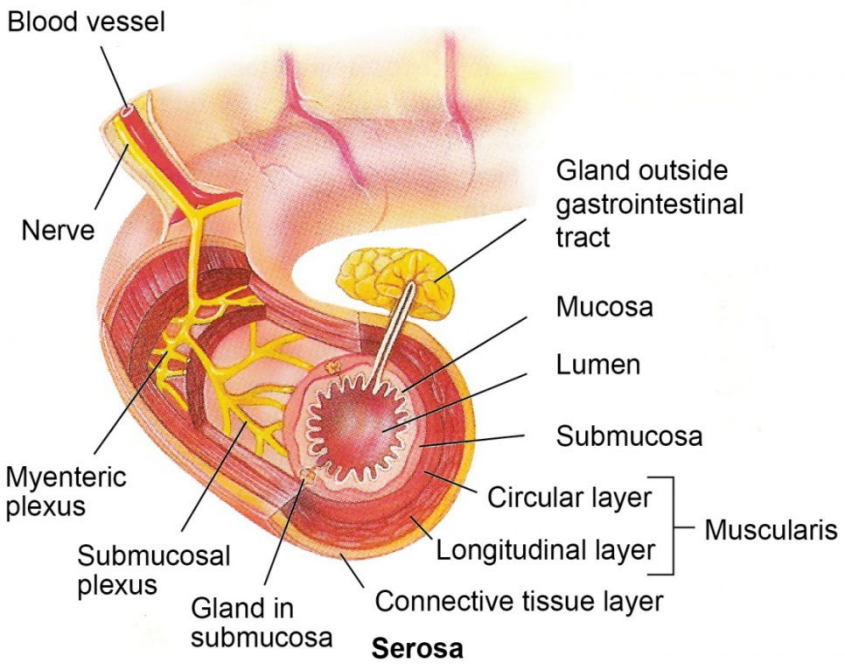
Calcitonin Gene-Related Peptide

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



Enteroglucagon

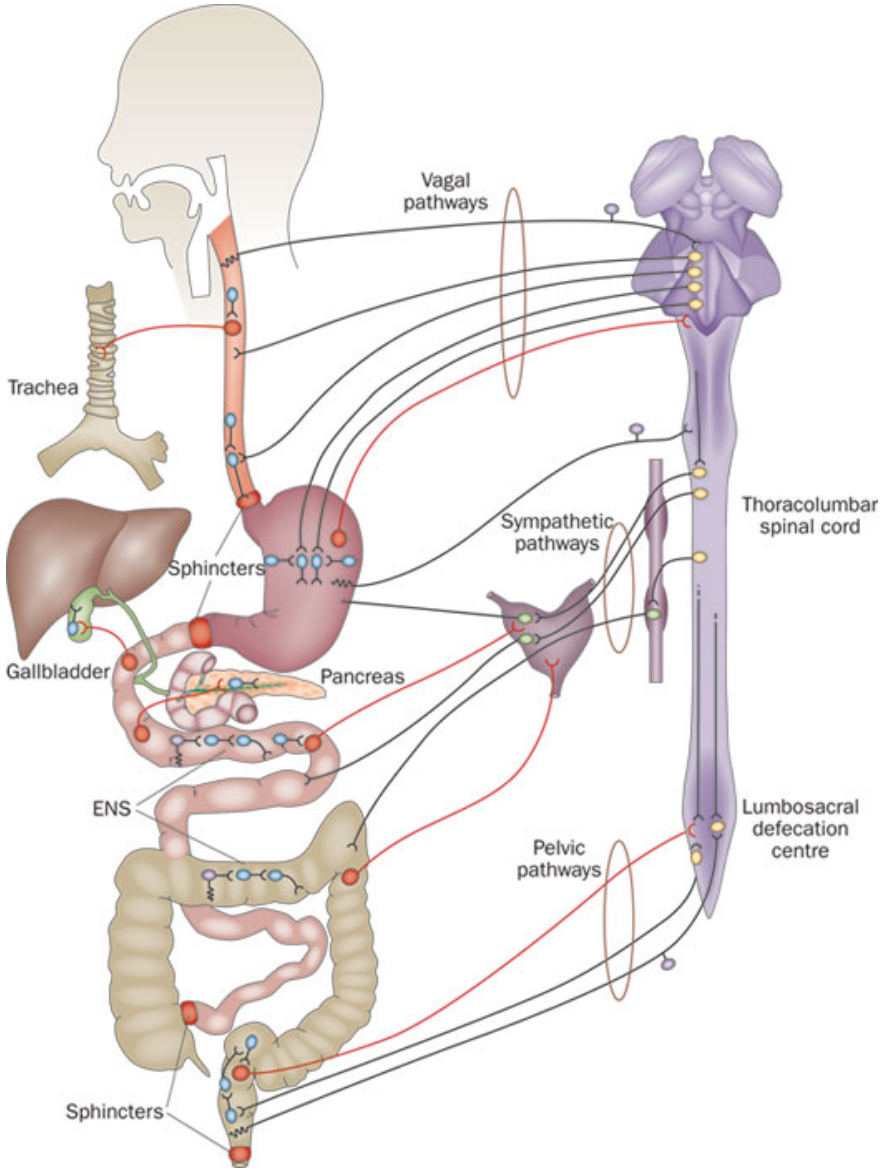
- ✓ Produced by small intestine and pancreas
- ✓ Found in high concentrations in the mucosa of the ileum, colon, and rectum
- ✓ Inhibits insulin secretion
- ✓ Trophic effect on the small intestinal mucosa
- ✓ Released after a mixed meal, particularly of carbohydrate and long-chain fatty acids



- ✓ 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

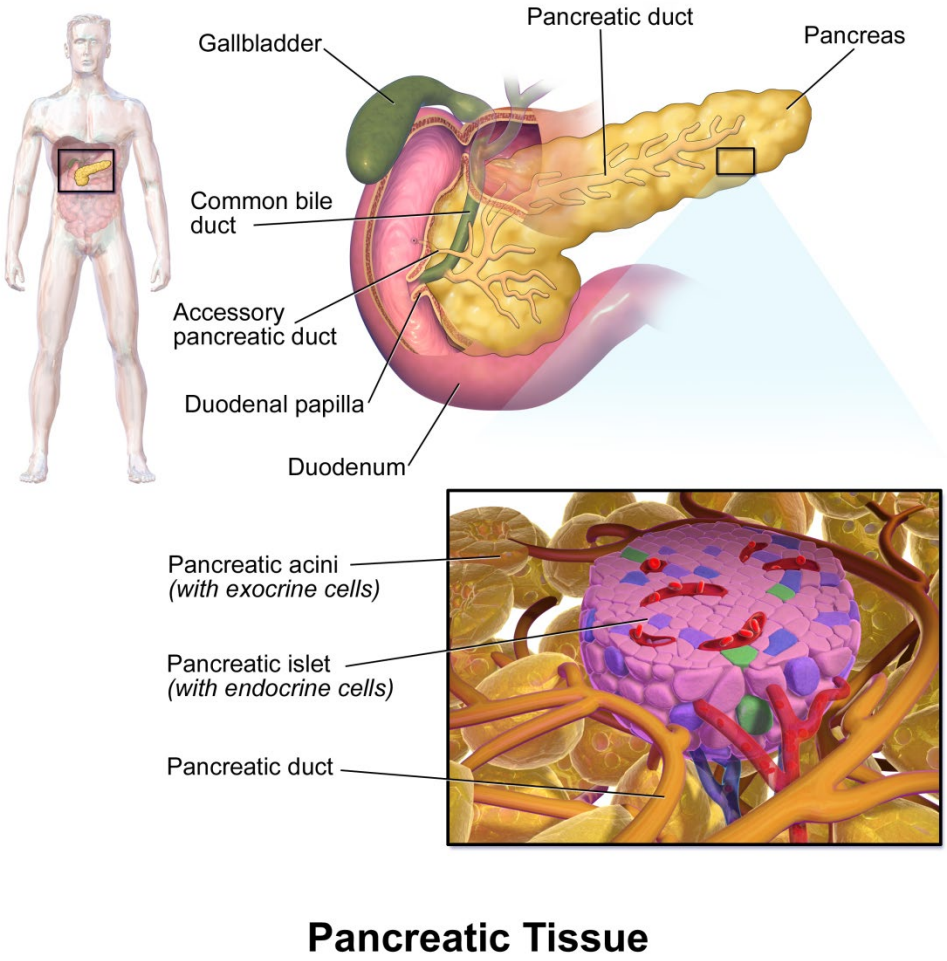
More GI Neuroendocrine Peptides

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



Galanin

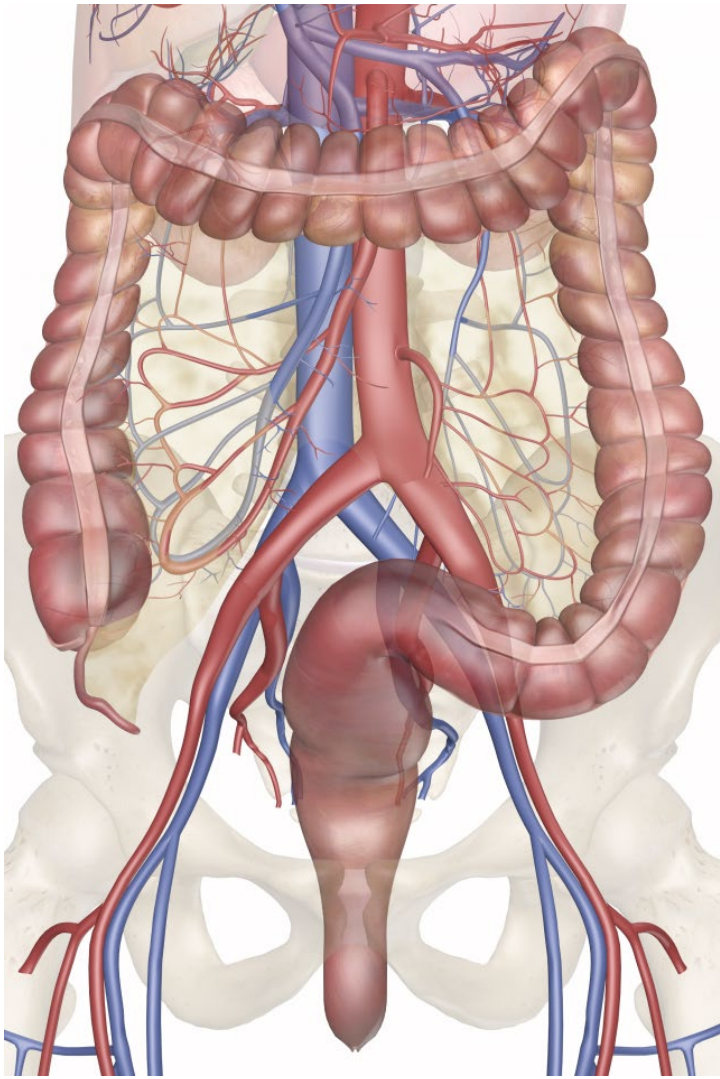
- ✓ Produced by enteric nerves, especially in liver and pancreatic islets
- ✓ Inhibits intestinal smooth-muscle contraction
- ✓ Inhibits postprandial insulin release



Pancreatic Tissue

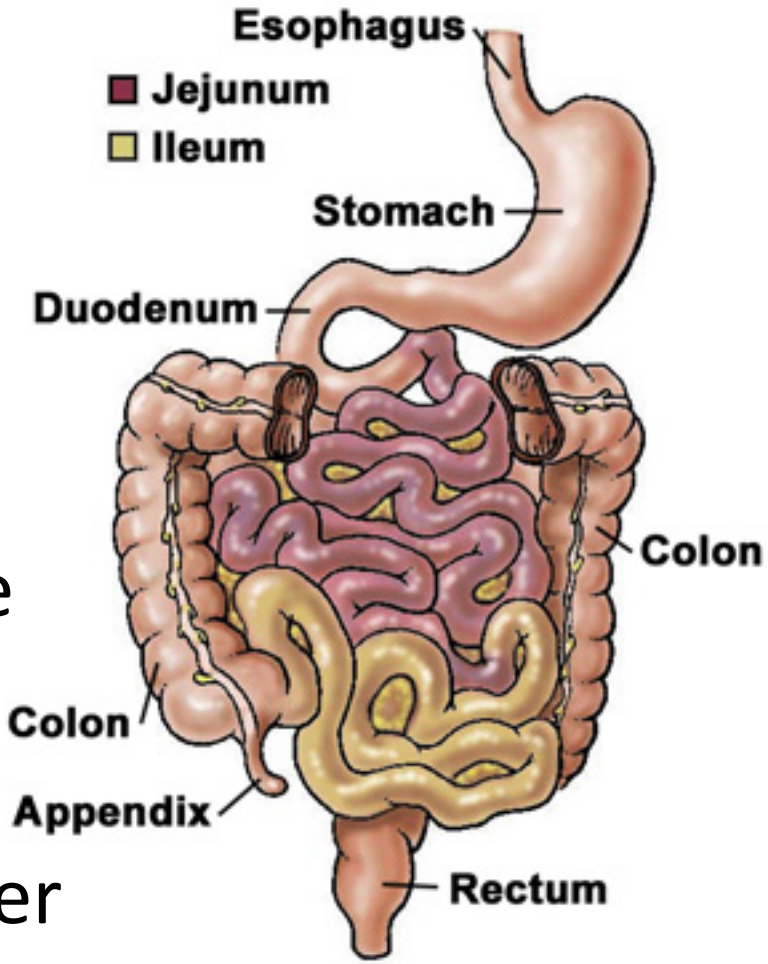
Neuropeptide Y

- ✓ 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



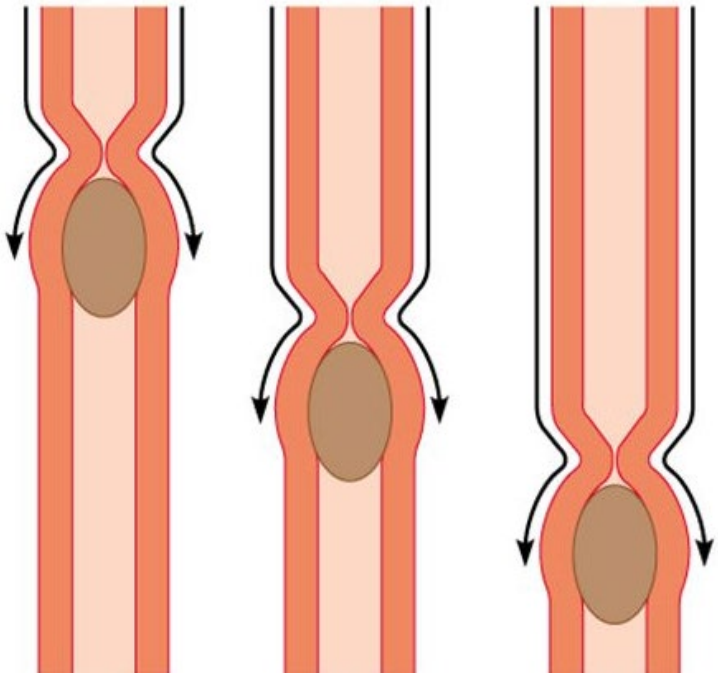
Neurotensin

- ✓ 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

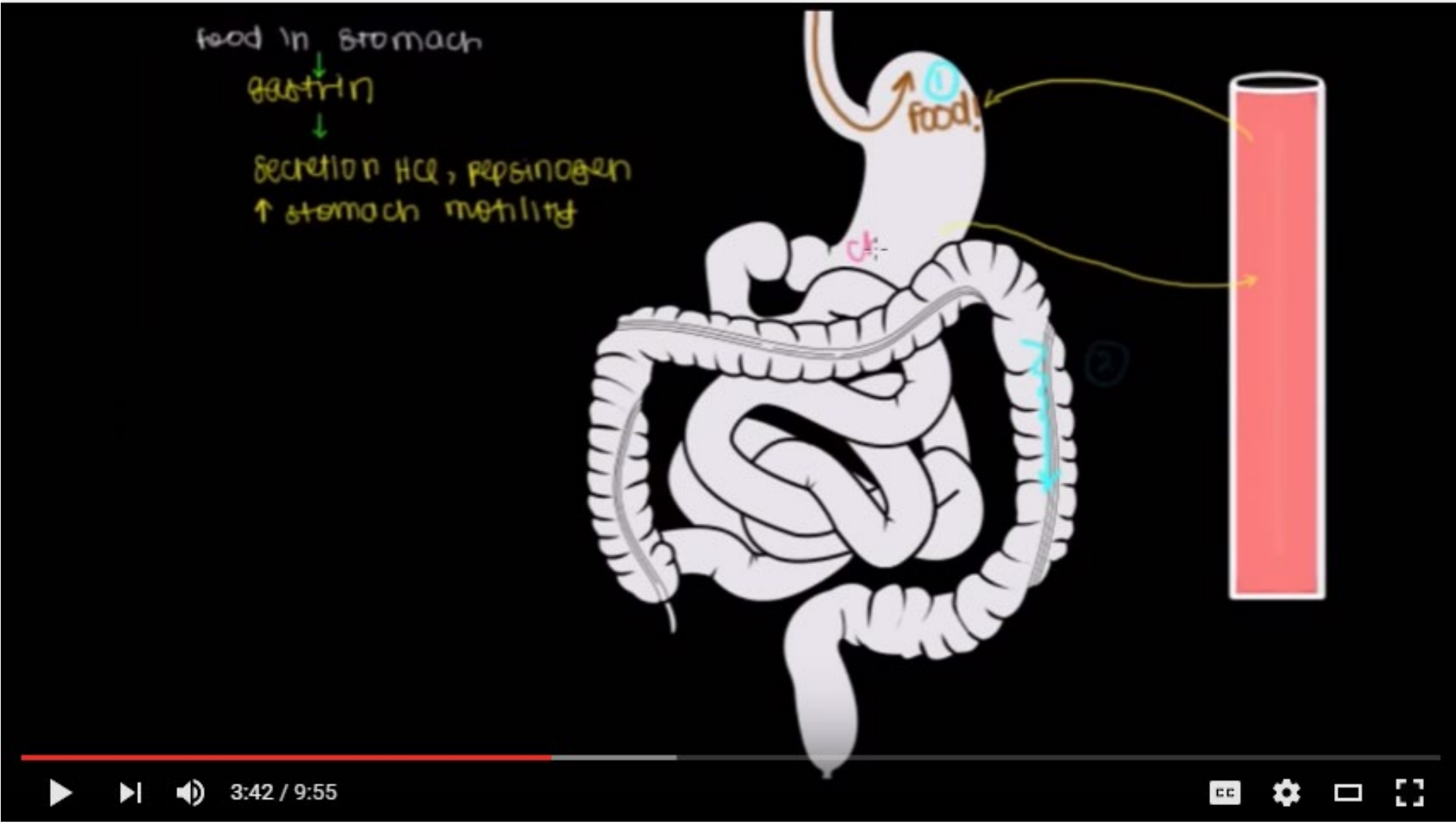


Integration of Neural and Endocrine Gut Functions

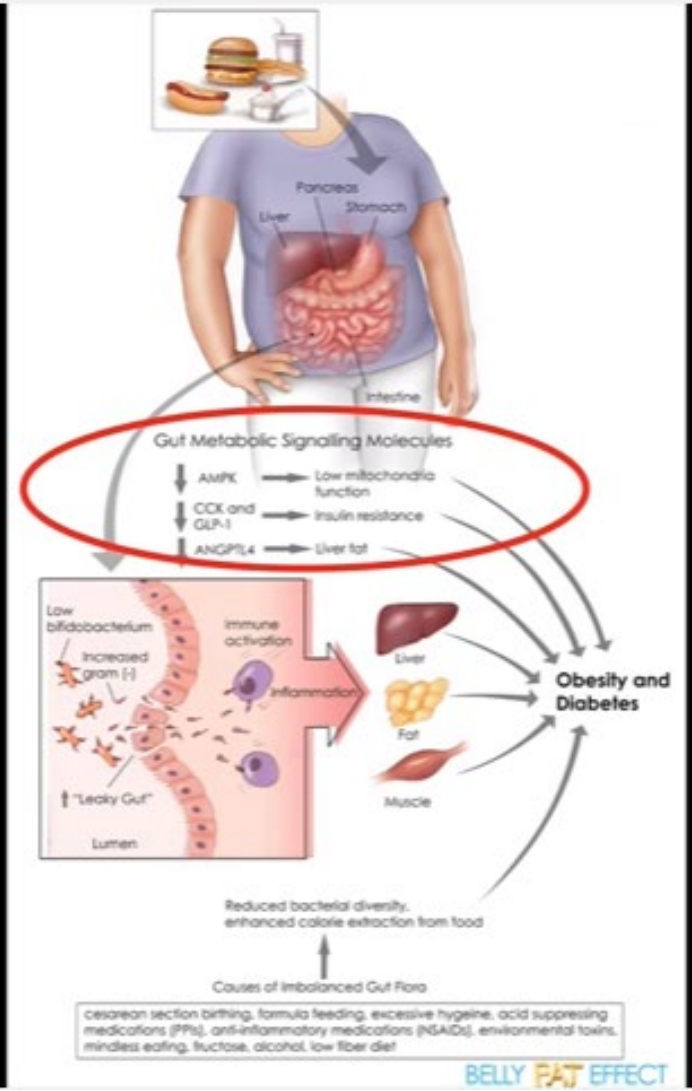
- ✓ Thoughts, taste, smell of food, and chewing activate parasympathetic nervous system via acetylcholine (ACh)
- ✓ ACh stimulates parietal cells to increase acid secretion
- ✓ ACh increases gastrin, inhibits somatostatin
- ✓ Sympathetic input (activity, stress): increases somatostatin release → inhibition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

References and Resources

- ✓ "Hormones of the Digestive System." *Boundless Anatomy and Physiology*. Boundless, 26 May. 2016.
- ✓ *The Belly Fat Effect*, Mike Mutzel
- ✓ http://www.drritamarie.com/go/EndoDigestionPPT
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- ✓ http://www.drritamarie.com/go/GIHormones