

## Gastrointestinal secretory mechanisms

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CO COSTANZO, Linda S, *Physiology*, 2nd ed. Baltimore: Williams & Wilkins, 1998.

Secretion	Source	Target	Effect	Factors which stimulate secretion	Factors which inhibit secretion
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### HORMONES (released from endocrine cells in GI tract into portal circulation and eventually reach target cells; CO 208)

<b>Gastrin</b>	G cells in the mucosa of the gastric antrum and the duodenum (BL 384).	Reaches parietal cells via the bloodstream (BL 384).	<ul style="list-style-type: none"> <li>• ↑ gastric H<sup>+</sup> secretion</li> <li>• Stimulates growth of gastric mucosa</li> <li>• Stimulates gastric contractility (BL 364)</li> <li>• ↑ pancreatic juice (BL 390)</li> </ul>	<ul style="list-style-type: none"> <li>• Amino acids and small peptides (BL 387)</li> <li>• Distension of stomach</li> <li>• Vagus (via GRP)</li> </ul>	<ul style="list-style-type: none"> <li>• H<sup>+</sup> in stomach</li> <li>• Secretin (BL 387)</li> </ul>
<b>CCK</b> (cholecystokinin)	I cells of duodenum and jejunum		<ul style="list-style-type: none"> <li>• Stimulates contraction of gallbladder and relaxation of sphincter of Oddi (CO 227).</li> <li>• ↑ pancreatic enzyme.</li> <li>• ↑ HCO<sub>3</sub><sup>-</sup> secretion.</li> <li>• ↑ growth of exocrine pancreas and gallbladder.</li> <li>• ↓ gastric emptying (CO 231).</li> <li>• ↓ acid secretion by parietal cells (BL 387).</li> </ul>	<ul style="list-style-type: none"> <li>• Amino acids and small peptides (CO 225).</li> <li>• Fatty acids (CO 225).</li> </ul>	
<b>Secretin</b>	S cells of duodenum		<ul style="list-style-type: none"> <li>• ↑ pancreatic HCO<sub>3</sub><sup>-</sup> secretion</li> <li>• ↑ biliary HCO<sub>3</sub><sup>-</sup> secretion</li> <li>• ↓ gastric H<sup>+</sup> secretion</li> </ul>	<ul style="list-style-type: none"> <li>• H<sup>+</sup> in duodenum (CO 225).</li> <li>• Fatty acids in duodenum</li> </ul>	

<b>GIP</b> (gastric inhibitory peptide)	Duodenum and jejunum		<ul style="list-style-type: none"> <li>• ↑ insulin secretion</li> <li>• ↓ gastrin release (BL 387)</li> <li>• ↓ gastric H<sup>+</sup> secretion</li> </ul>	<ul style="list-style-type: none"> <li>• Fatty acids</li> <li>• Amino acids</li> <li>• Oral glucose</li> </ul>	
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**PARACRINES (released from endocrine cells in GI mucosa and diffuse over short distances to target cells; CO 210)**

<b>SST</b> (somatostatin)	Cells throughout the GI tract		<ul style="list-style-type: none"> <li>• Inhibits release of all GI hormones</li> <li>• ↓ gastric H<sup>+</sup> secretion</li> </ul>	H <sup>+</sup> in GI lumen	Vagal stimulation
<b>Histamine</b>	Mast cells of gastric mucosa	Diffuses to parietal cells, and there binds to H <sub>2</sub> receptors, activating adenylate cyclase (BL 384).	↑ gastric H <sup>+</sup> secretion directly and by potentiating (CO 223) the effects of gastrin and vagal stimulation (CO 210)		

**NEUROCRINES (released from neurons of GI tract and diffuse across synaptic cleft to target cell; CO 210)**

<b>VIP</b> (vasoactive intestinal peptide)	Neurons in the mucosa and smooth muscle of GI tract		<ul style="list-style-type: none"> <li>• Relaxation of GI smooth muscle and lower esophageal sphincter (CO 213)</li> <li>• ↑ pancreatic HCO<sub>3</sub><sup>-</sup> secretion</li> <li>• ↓ gastric H<sup>+</sup> secretion</li> </ul>	Vagal stimulation (CO 213)	
<b>GRP</b> (gastrin-releasing peptide, bombesin)	Vagus nerves that innervate G cells		• ↑ gastrin release from G cells		
<b>Enkephalins</b> (met-enkephalin and leu-enkephalin)	Nerves in mucosa and smooth muscle of GI tract		<ul style="list-style-type: none"> <li>• ↑ contraction of GI smooth muscle</li> <li>• ↓ intestinal secretion of fluid and electrolytes</li> </ul>		

<b>ACh</b> (Acetylcholine)	Released near parietal cells by cholinergic nerve terminals (BL 384)		<ul style="list-style-type: none"> <li>• ↑ gastric contractility (BL 364).</li> <li>• ↑ enzyme secretion by acinar cells (CO 226).</li> <li>• ↑ contraction of gallbladder (CO 227).</li> <li>• Potentiates effect of secretin on <math>\text{HCO}_3^-</math> secretion (CO 226).</li> </ul>	<ul style="list-style-type: none"> <li>• Amino acids, small peptides.</li> <li>• Fatty acids (CO 226).</li> </ul>	
<b>α-adrenergic agonists</b> (BL 384), including ACh			↓ $\text{HCO}_3^-$ secretion		
<b>NO</b> (nitric oxide)			• Relaxation of lower esophageal sphincter		
<b>Substance P</b> (a tachykinin)	Nerves and endocrine cells		<ul style="list-style-type: none"> <li>• ↑ smooth muscle contraction.</li> <li>• Inhibits acid secretion and intestinal absorption.</li> </ul>		

## IONS

<b>H<sup>+</sup></b> (in HCl)	Gastric parietal cells secrete HCl into the lumen of the stomach (via an $\text{H}^+/\text{K}^+$ -ATPase) and concurrently absorb $\text{HCO}_3^-$ into the bloodstream (CO 221).				Chyme in the duodenum inhibits $\text{H}^+$ secretion both directly and via hormonal mediators (viz. GIP and secretin) (CO 223).
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**OTHER**

<b>Intrinsic factor</b> (BL 383, 409), a glycoprotein	Parietal cells of stomach		<ul style="list-style-type: none"> <li>• Required for normal absorption of vitamin B<sub>12</sub>.</li> <li>• This is the most important secretion of the stomach; gastrin and pepsin are not essential (Dr. Rao).</li> </ul>		
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**ENZYMES**

<b>Pepsinogen</b> (→ pepsin)	Secreted primarily by the chief cells of the gastric glands (BL 382).		Get cleaved to pepsins (active forms) and act as proteases (BL 382).	Most agents that stimulate parietal cells to secrete acid also elicit release of pepsinogens (BL 388), such as ACh, gastrin, acid, secretin and CCK.	
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**PANCREATIC SECRETIONS**

<b>Pancreatic exocrine secretion</b>	Acinar cells (BL 389)		<ul style="list-style-type: none"> <li>• Includes enzymes important for the digestion of all the major classes of foodstuffs (BL 389): trypsin(ogen), chymotrypsin(ogen), (pro)carboxypeptidase.</li> <li>• Pancreatic secretion includes a high concentration of HCO<sub>3</sub><sup>-</sup> (to neutralize chyme) (CO 224).</li> </ul>	Various (BL 390; CO 216): <ul style="list-style-type: none"> <li>• Gastrin</li> <li>• Gastric distension</li> <li>• Amino acids and peptides in antrum</li> <li>• Secretin (which is released in response to acid in duodenum and upper jejunum)</li> <li>• CCK (potentiates secretin)</li> </ul>	Pancreatic polypeptide (secreted from enterochromaffin cells)
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### HEPATIC SECRETIONS (CO 226 ff.)

<b>Bile</b>	Synthesized in hepatocytes. Usually stored in the gallbladder (BL 396).		<ul style="list-style-type: none"> <li>• Bile contains bile acids, cholesterol, lecithin and bile pigments (BL 393).</li> <li>• Bile acids emulsify lipids (BL 393).</li> </ul>	<ul style="list-style-type: none"> <li>• CCK reaches the gallbladder via the bloodstream and stimulates emptying. Gastrin also stimulates emptying, but not as strongly (BL 396).</li> <li>• Parasympathetic nervous system causes contraction of gallbladder (CO 216)</li> </ul>	
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### SALIVARY SECRETIONS (CO 216 ff.)

<b>Saliva</b>	Parotid, submandibular and sublingual salivary glands		<ul style="list-style-type: none"> <li>• <math>\alpha</math>-amylase (initial degradation of carbohydrates; cleaves <math>\alpha 1 \rightarrow 4</math> bond)</li> <li>• Lingual lipase (initial degradation of fats) (CO 231).</li> </ul>	<ul style="list-style-type: none"> <li>• Mostly stimulated by parasympathetic innervation.</li> <li>• Somewhat stimulated by sympathetic innervation.</li> </ul>	
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### GENERAL EFFECTS OF AUTONOMIC INNERVATION

	<b>Parasympathetic stimulation</b> (mediated by acetylcholine)	<b>Sympathetic stimulation</b> (mediated by norepinephrine)
Sphincters (except upper esophageal and external anal, which are not under autonomic control)	↓ contraction	↑ contraction
Vascular smooth muscle	↑ contraction	↓ contraction
Muscularis mucosae	↑ contraction	↓ contraction
Secretion	↑ secretory activity	↓ secretory activity
Overall activity of GI tract	↑ activity	↓ activity

**Chiefly stimulatory neuromodulators:** ACh, CCK, GRP, Serotonin, Tachykinins (e.g. substance P), VIP (stimulates secretion).

**Chiefly inhibitory neuromodulators:** ATP, dynorphins, enkephalins, NO, somatostatin, VIP (inhibits muscular contraction).