Gastrointestinal Secretions and Vomiting

Adrian Thomas

The two main gastrointestinal secretions are mucus and digestive enzymes. There are numerous pits or crypts throughout the gastrointestinal tract containing specialized secretory cells (e.g. crypts of Lieberkuhn in the small intestine). Tubular glands are present in the stomach (e.g. oxyntic glands) and proximal duodenum. Specialized glands include the salivary glands, pancreas and liver.

The presence of food in the gastrointestinal tract causes direct stimulation of mucous (goblet) cells and nearby glands, which release digestive enzymes. The mucus protects the epithelium and acts as a lubricant. Mucous cells and glands are also stimulated by local enteric reflexes in response to distension or irritation. Parasympathetic stimulation increases secretion from salivary, oesophageal, gastric, pancreatic, duodenal Brunner's and distal large intestinal glands. Secretion from the rest of the small intestine and proximal large intestine is controlled predominantly by local neural and hormonal stimuli. Sympathetic stimulation alone slightly increases gastrointestinal secretion, but in the presence of parasympathetic or hormonal stimulation can reduce secretion because it induces constriction of splanchnic blood vessels.

Basic mechanism of glandular secretions

Organic substances: synthesis of enzymes and other organic substances takes place in the endoplasmic reticulum of glandular cells. These are modified in the Golgi apparatus and stored in secretory vesicles until neural or hormonal signals induce their release by exocytosis.

Water and electrolytes: hormonal or neural stimulation is thought to initiate active transport of chloride across the basal membrane, positive ions then follow the electrical gradient, the increased intracellular osmolality draws in water, resulting in increased intracellular pressure and cell swelling. This disrupts the secretory border allowing leakage of water and electrolytes.

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Saliva

Saliva helps to maintain oral hygiene because it:

- washes away bacteria and food
- contains bactericidal agents (e.g. thiocyanate)
- contains proteolytic enzymes (e.g. lysozyme)
- contains antibodies.

Saliva comprises a serous secretion containing ptyalin and a mucous secretion. The parotid gland secretes only serous fluid, the submandibular and sublingual glands secrete both and the numerous buccal glands secrete only mucus. Together they secrete 800–1500 ml/day of saliva. Ptyalin and/or mucin are secreted in the acini (Figure 1); as the fluid passes through the ducts, sodium is actively reabsorbed in exchange for potassium, bicarbonate is secreted and chloride is reabsorbed. Therefore, saliva contains high concentrations of potassium and bicarbonate and low concentrations of sodium and chloride. When the rate of salivation is increased, the rate of flow through the ducts also increases, reducing reabsorption and secretion.

Regulation of secretion: the salivary glands are controlled mainly via the parasympathetic nervous system from the superior and inferior salivary nuclei in the brainstem. They are influenced by the adjacent medulla and pons, which are stimulated by taste and touch sensors in the mouth, tongue and pharynx. They are also influenced by the appetite area in the amygdala, prefrontal cortex and adjacent hypothalamus. Reflex salivation also occurs in response to gastrointestinal irritation.

Gastric secretion

Mucous cells line the gastric mucosa. Oxyntic (gastric) glands occur in the fundus and body of the stomach. The pyloric glands are confined to the antrum.

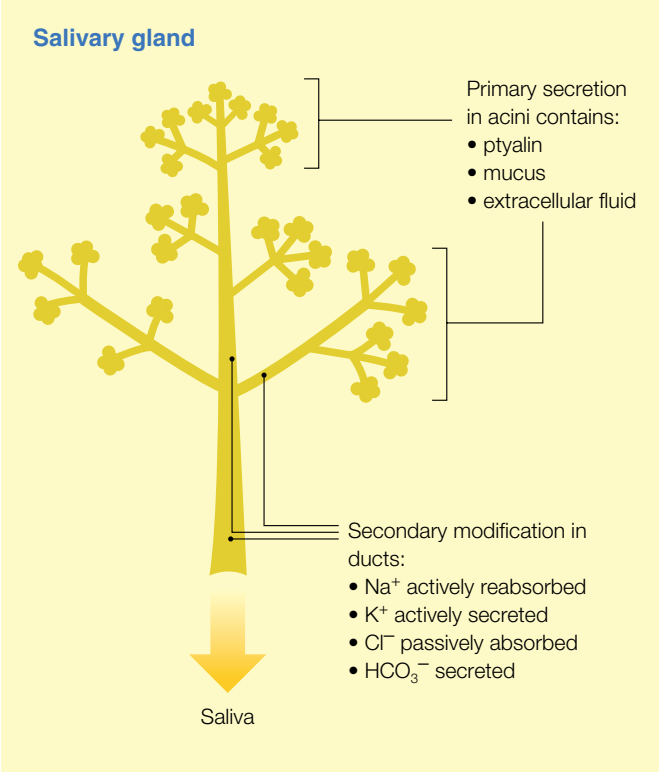
Mucous cells secrete large amounts of viscid alkaline mucus to protect the gastric mucosa from acid.

Oxyntic glands contain three types of cells: mucous neck cells (secreting mainly mucus but also some pepsinogen), peptic (chief) cells (secreting pepsinogen) and parietal (oxyntic) cells (secreting hydrochloric acid and intrinsic factor). The basic mechanism of pepsinogen and mucus secretion is described above. Pepsinogen is activated to pepsin in the presence of hydrochloric acid and pepsin. In an acid environment, pepsin is a powerful proteolytic enzyme. Intrinsic factor is necessary for absorption of vitamin B_{12} in the terminal ileum. During the secretion of hydrochloric acid (Figure 2) hydrogen ions from water in the parietal cell are actively secreted into the gastric lumen in exchange for potassium ions. The remaining hydroxyl ions are neutralized by hydrogen ions from carbonic acid. Bicarbonate ions diffuse from the cell to the extracellular fluid in exchange for chloride ions. Chloride ions are also transported into the lumen. Water passes into the lumen by osmosis.

Pyloric glands contain mainly mucous cells, but also secrete gastrin and small amounts of pepsinogen.

Regulation of gastric secretion: acetylcholine, gastrin and histamine bind to specific receptors on the secretory cells. Acetylcholine stimulates secretion of pepsinogen by the peptic cells, hydrochloric acid by the parietal cells and mucus by the mucous cells. Gastrin and histamine stimulate secretion of hydrochloric acid by the parietal cells but have little effect on the other cells. Amino acids, caffeine and alcohol also have weak stimulatory effects on gastric secretion.

Acid secretion – neural stimulation of acid secretion is initiated by higher CNS centres via the vagus nerve or by local reflexes. Local reflexes are triggered by gastric distension, acid



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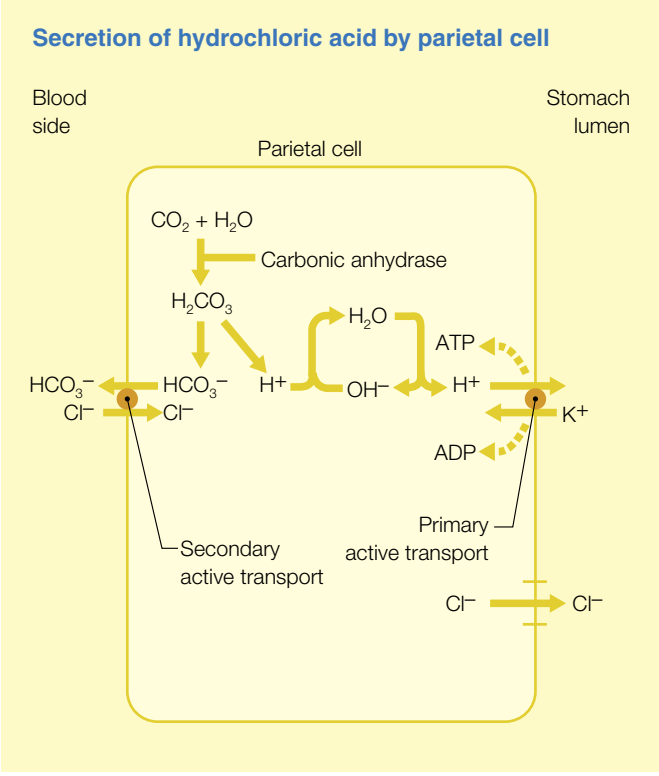

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pH and products of protein digestion. The nerves release acetylcholine, except for those supplying the gastrin-secreting cells (G cells) in the pyloric glands where an intermediate neuron secretes gastrin-releasing peptide. Gastrin enters the bloodstream and travels to the oxyntic glands in the body of the stomach where it stimulates the parietal cells to release hydrochloric acid and to a lesser extent the peptic cells to release pepsinogen. Acetylcholine, gastrin and histamine alone have little effect on gastric secretion. Histamine is continually present in small amounts and exerts its effect via the H_2-receptors on the parietal cells. This, together with vagal stimulation (either from higher CNS centres or local reflexes when food enters the stomach), releases gastrin and acetylcholine thus promoting large quantities of gastric acid to be released. Excess acidity produces neural inhibition of gastric secretion and blocks the secretion of gastrin from the G cells.

Pepsinogen secretion – pepsinogen is released from the peptic cells in response to neural stimulation (releasing acetylcholine) and the presence of gastric acid.

Phases of gastric secretion

Cephalic phase – this results from the thought, sight, smell or taste of food. Neural stimuli arise in the cerebral cortex, appetite centre or hypothalamus and are transmitted through the vagus.

Gastric phase – food entering the stomach elicits long vasovagal reflexes, local enteric reflexes and release of gastrin. This phase accounts for about 70% of total gastric secretion.

Intestinal phase – food mixed with gastric secretions (chyme) entering the proximal small intestine can stimulate modest gastric secretion. Mechanisms include duodenal gastrin release, absorbed amino acids, other hormones and reflexes.

Inhibition of gastric secretion: although chyme stimulates gastric secretion during the intestinal phase, it inhibits it during the gastric phase. This is initiated by the enterogastric reflex and gastrointestinal hormones, including secretin, in response to distension, hyper- or hypo-osmolar fluid, acid, protein breakdown products, fat or irritation in the duodenum.

Exocrine pancreatic secretion

The exocrine pancreas is structurally similar to the salivary glands. Digestive enzymes are secreted by the pancreatic acini and sodium bicarbonate is secreted by the ductules and ducts leading from the acini. Secretion is stimulated primarily by chyme in the duodenum.

Pancreatic enzymes: the pancreas secretes enzymes for:

- protein digestion (trypsin, chymotrypsin, carboxypeptidase)
- carbohydrate digestion (pancreatic amylase)
- fat digestion (pancreatic lipase, cholesterol esterase, phospholipase).

The proteolytic enzymes are produced in inactive forms (trypsinogen, chymotrypsinogen, procarboxypeptidase) which become active only in the gastrointestinal tract. Trypsinogen is converted to trypsin by enterokinase. Trypsin converts chymotrypsinogen to chymotrypsin, other proenzymes into active forms and can also activate trypsinogen (autocatalysis). The pancreatic enzymes are prevented from activation before reaching the gastrointestinal tract (which would cause destruction of the pancreas) by trypsin inhibitor.

Bicarbonate ions produced from carbon dioxide and water by carbonic anhydrase, are actively secreted (in exchange for chloride ions) by the ductular epithelial cells. The remaining hydrogen ions are exchanged for sodium ions in the bloodstream, the sodium ions continue into the duct to maintain electrical neutrality. Water follows by osmosis.

Regulation of secretion: pancreatic secretion is stimulated by acetylcholine (from parasympathetic nerves), cholecystokinin (from proximal small intestine when food enters) and secretin (from proximal small intestine when acid enters). Acetylcholine and cholecystokinin primarily stimulate the production of pancreatic enzymes from the acinar cells whereas secretin primarily stimulates the production of large quantities of sodium bicarbonate solution by the ductal cells, which is largely responsible for neutralizing the gastric acid. Pancreatic secretion occurs in three phases: cephalic, gastric and intestinal in the same way as gastric secretion.

Intestinal secretions

Mucus is secreted by Brunner's glands in the proximal small intestine. Throughout the intestine are numerous crypts of Lieberkuhn containing goblet cells (which produce mucus) and, in the small intestine, enterocytes (which produce large quantities of water). Enterocytes in the small intestinal villi also produce peptidases, disaccharidases and lipase.

Nausea and vomiting

Nausea is a conscious awareness of arousal of the vomiting centre or related areas of the brain. It often precedes vomiting and may be initiated by higher CNS centres or local irritation in the gastrointestinal tract.

Vomiting can be initiated by overdistension or irritation of the upper gastrointestinal tract, resulting in afferent impulses transmitted via the parasympathetic (vagus) and sympathetic nervous systems to the vomiting centre in the medulla. It can also be initiated by stimulation of other areas of the brain, especially the chemoreceptor trigger zone.

Certain drugs (including morphine) induce vomiting by direct stimulation of this area. In motion sickness, impulses arise from receptors in the labyrinth and are transmitted to the vestibular nuclei, then the cerebellum, before reaching the chemoreceptor trigger zone and eventually the vomiting centre. Higher CNS centres can also stimulate the vomiting centre (e.g. in states of psychological distress).

The vomiting centre initiates vomiting by transmitting impulses via cranial nerves V, VII, IX and X to the upper gastrointestinal tract and through the spinal nerves to the diaphragm and abdominal muscles. Antiperistalsis begins as far distally as the terminal ileum and rapidly propels the contents of the small intestine back to the stomach and duodenum, which contract vigorously. The vomiting centre then initiates a deep inhalation, opening of the upper oesophageal sphincter, closure of the glottis and lifting of the soft palate to prevent nasal reflux. The diaphragm and abdominal muscles contract and the lower oesophageal sphincter relaxes allowing vomiting to occur. ◆