of the stomach are lined with different types of specialized cells. The oxyntic or acid-producing region of the stomach is found in the fundus and body, where gastric glands contain characteristic parietal cells, which secrete both acid and intrinsic factor. These glands also contain zymogen-rich chief cells, which synthesize pepsinogen, and enterochromaffin-like endocrine cells, which secrete histamine. Antral glands have different endocrine cells, including gastrin-secreting G cells and somatostatin-secreting D cells.

The duodenum, the most proximal portion of the small intestine, forms a C-shaped loop around the head of the pancreas and is in continuity with the pylorus proximally and the jejunum distally (see Fig. 36-1 and Video 36-1). Angular changes in course divide the duodenum into four portions. The first part of the duodenum is the duodenal bulb or cap and is characterized by a smooth, featureless luminal surface. The remainder of the duodenum has characteristic circular folds known as the *plica circularis* or *valvulae conniventes*, which increase the surface area available for digestion. Similar to the stomach, the duodenal wall is formed by mucosa, submucosa, muscularis, and serosa layers. The duodenal mucosa is lined with columnar cells forming villi surrounded by crypts of Lieberkühn. The submucosa includes characteristic Brunner glands that produce bicarbonate-rich secretions involved in acid neutralization. The innervation of the duodenum is similar to the stomach.

GASTRODUODENAL MUCOSAL SECRETIONS AND PROTECTIVE FACTORS

Although hydrochloric acid (HCl) is the primary gastric secretion, the stomach also secretes water, electrolytes (hydrogen [H+], sodium [Na+], potassium [K+], chloride [Cl^-], and bicarbonate [HCO_3]), enzymes (pepsin and gastric lipase), and glycoproteins (intrinsic factors and mucin) to assist in a wide variety of physiologic functions. The digestion of proteins and triglycerides, as well as the complex process of vitamin B_{12} absorption, begins in the gastric lumen. Gastric acid also prevents the development of enteric microbial colonization and systemic infections. The normal human stomach contains about 1 billion parietal cells that are stimulated to secrete H+ ions by three different pathways: neurocrine, paracrine, and endocrine (Fig. 36-2). The neurocrine pathway involves the vagal release of acetylcholine, which stimulates H+ ion generation through a parietal cell muscarinic M_3 receptor. The paracrine pathway is mediated by release of histamine from mast cells and enterochromaffin-like (ECL) cells in the stomach. Histamine binds to histamine-2 receptors on parietal cells, activating adenylate cyclase, which, in turn, leads to an increase in adenosine 3′,5′-cyclic monophosphate (cAMP) levels and subsequent generation of H+ ions. The secretion of gastrin from antral G cells constitutes the endocrine pathway, which acts both directly on the parietal cell and indirectly by stimulating histamine secretion from ECL cells. The hydrogen-potassium adenosine triphosphatase (H+, K+-ATPase) enzyme, or proton pump, located at the apical surface of the parietal cell, is the final step of acid secretion. A negative feedback loop governs both gastrin release and acid secretion, preventing postprandial acid hypersecretion. Somatostatin, produced by D cells in the gastric corpus and fundus, inhibits release of gastrin from G cells and may also reduce acid secretion from parietal cells and histamine release from ECL cells. Acid is necessary to convert pepsinogen, secreted from gastric chief cells, into pepsin, a proteolytic enzyme that is inactive at a pH greater than 4. Parietal cells also secrete intrinsic factor, a glycoprotein that binds to ingested vitamin B_{12}, allowing its absorption in the terminal ileum.

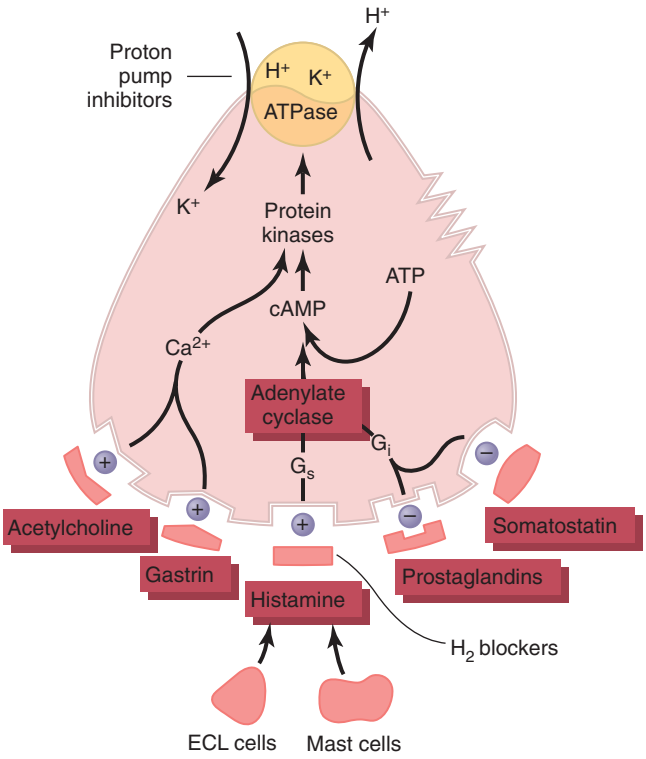

FIGURE 36-2 Schematic representation of acid secretion by the parietal cell. Each transmitter has a specific receptor located on the basolateral surface of the parietal cell. Stimulation of these receptors leads to activation of intracellular second messenger systems. Gastrin and acetylcholine promote the accumulation of intracellular calcium, whereas histamine causes a stimulatory G protein (G_s) to activate adenylate cyclase, which, in turn, generates cyclic adenosine monophosphate (cAMP). These intracellular messengers then activate protein kinases, which activate the proton pump (the H+, K+-ATPase enzyme), located at the apical surface of the parietal cell, to secrete H+ ion in exchange for K+ ions. Prostaglandins and somatostatin inhibit parietal cell function by binding to receptors that act through inhibitory G proteins (G_i) to inhibit adenylate cyclase. *Long arrows* indicate sites of action of various drugs that inhibit acid secretion. ECL, Enterochromaffin-like endocrine cells.

Several mechanisms are involved in maintaining the protective mucosal barrier. Mucus and HCO_3 constitute the first line of defense. Mucus forms a stable layer that prevents H+ ion backdiffusion and lubricates the mucosa, protecting against mechanical damage and maintaining a significant pH gradient between the gastric lumen and the epithelial cell surface. Endogenous epithelial defensive factors, such as cell migration and proliferation, permit a constant and rapid renewal of the mucosa and ensure the continuity of the epithelium and the integrity of the tight intercellular junctions. Subepithelial defensive factors such as an adequate mucosal blood flow constitute a second line of protection and play a crucial role in maintaining a normal pH environment and thereby the integrity of the gastroduodenal mucosa.