**Review**

**Helicobacter pylori and gut hormones**

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*Helicobacter pylori* infection has been found to decrease the expression of antral somatostatin and to increase the release of the acid-stimulating hormone gastrin. The reversal of these changes in gut hormones by the eradication of *H. pylori*, and in-vivo and in-vitro studies in animals either infected with *H. pylori* or exposed to *H. pylori*-related materials may support the somatostatin-gastrin link theory in the pathophysiology of *H. pylori* infection. The following mechanisms have been proposed to explain the *H. pylori* infection-associated changes in gut hormones: (1) ammonia produced by *H. pylori* and monochloramine, (2) effect on somatostatin receptor subtype-2, (3) action of lipopolysaccharide from *H. pylori* on somatostatin receptor, (4) inflammatory cells and mediators, and (5) bacterial strain diversity. *H. pylori* infection can alter gastric acid secretion in both directions. The elevated acid secretion in patients with duodenal ulcer is decreased by *H. pylori* eradication, and is accompanied by the normalization of gut hormones in patients whose *H. pylori*-induced gastritis is limited to the antrum with hyperacidity. Corpus gastritis and the subsequent development of mucosal atrophy induced by *H. pylori* result in decreased acid secretion, although the mechanism underlying *H. pylori*-induced atrophy in some subjects remains unclear. Hypoacidity enhances corpus atrophy and increases gastrin secretion, mediated via a physiological suppression of somatostatin release, features that are also observed in *H. pylori* infection. Therefore, the capacity of acid secretion and distribution of gastritis or atrophy should be taken into consideration when we discuss the affect of *H. pylori* on gut hormones.

**Key words:** gastric acid, gastrin, gastritis, *Helicobacter pylori*, somatostatin

**Introduction**

*Helicobacter pylori* is now known to be the major etiologic agent of chronic active gastritis, and it also plays a crucial role in gastric and duodenal ulcer (DU) disease, as well as in gastric carcinoma.¹ ² *H. pylori* infection can alter acid secretion in both directions. Corpus gastritis and the subsequent development of mucosal atrophy induced by *H. pylori* infection result in a decrease of acid secretion. In contrast, DU patients have approximately twice the normal parietal mass, which increases their maximal acid secretory capacity. Several investigators have demonstrated that the elevated acid secretion in DU patients decreases after *H. pylori* eradication.³ The distribution of gastritis and gastric acid secretory capacity seem to be crucial in determining the clinical outcome of *H. pylori* infection. For instance, it has been proposed that high acid secretion leads to DUs, while low acid secretion is found in patients with gastric ulcers and gastric cancer.⁴

Gastric acid secretion is regulated by many factors involving the autonomic nervous system and gut hormones. Among several hormones affecting gastric acid secretion directly or indirectly, the most important regulatory peptides in the gastric mucosa include gastrin and somatostatin (SST). In order to understand the relationship between hormonal peptides and gastric acid secretion in *H. pylori* infection, it seems important to distinguish DU in which gastritis is limited to the antrum, with high acid secretion, from gastric ulcer and pangastritis, in which corpus gastritis and atrophy are present, accompanied by low acid output.

In this review, the SST and gastrin link in *H. pylori* infection is summarized, and discussed with specific at-
tention being paid to gastric acid secretion, as well as gastritis distribution. The mechanisms speculated to underlie *H. pylori*-induced gastric peptide regulation are also reviewed.

**Somatostatin (SST)**

SST is a tetradecapeptide, originally discovered in sheep hypothalamus, which showed an inhibitory effect on growth hormone release. In 1971, the presence of SST-containing D cells (see below for definition) in the canine antral mucosa was suggested by Fujita and Kobayashi, who demonstrated the degranulation of secretory vesicles from certain endocrine cells of the antral mucosa in response to luminal acidification.

Studies of SST have revealed the existence of a whole family of SST-related peptides, which includes the tetradecapeptide (SST-14), an amino-terminal-extended SST (SST-28), and larger preprohormone forms. SST-14 and SST-28 are the two biologically active forms of SST.

In mammals, the gastrointestinal tract and pancreas contain the largest amounts of SST. Chromatographic studies have shown the predominant form of SST in the human stomach to be the tetradecapeptide, whereas there is a relative increase in the proportion of SST-28 further down the gastrointestinal tract.

Most of the gastrointestinal SST immunoreactivity is confined to the mucosal layer, where it is localized in epithelial endocrine cells, called D cells. In the antrum, the D cells have apical membranes that are exposed to the lumen (“open cells”). In the corpus, the D cells are of the “closed” type; they are not exposed to the luminal surface of the mucosa.

By inhibiting gastrin release, SST plays an important role in the regulation of gastric acid secretion. In the antral mucosa, the open D cell releases SST in response to increased acidity in the gastric lumen. Because the apical surface of D cells opens onto the gastric lumen, changes in pH may be sensed directly through chemoreceptors on the apical membranes. Other studies suggest that gastric acid stimulates mucosal nerve endings, releasing calcitonin gene-related peptide (CGRP), which stimulates the release of SST. CGRP released from the primary afferent terminals of splanchnic nerves stimulates the release of SST from D cells. Vasoactive intestinal peptide released from the mucosal nerves stimulates SST release in the stomach. Adrenergic agonists stimulate SST secretion in the stomach, but cholinergic stimuli inhibit SST secretion (Fig. 1).

**Gastrin and *H. pylori* infection**

Gastrin peptides are released into the circulation from G cells in the gastric antrum and duodenum after stimulation by food intake, and strongly stimulate the parietal cells in the corpus to secrete acid (Fig. 1). The two main forms of gastrin in plasma are gastrin-17 and gastrin-34. These are equipotent on a molar basis, but gastrin-34 has a longer plasma half-life. About 95% of antral

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**Fig. 1.** Gastrin release is stimulated by extramural cholinergic and intramural cholinergic and non-cholinergic factors, and inhibited by somatostatin. Somatostatin release is stimulated by luminal (acid), paracrine, and hormonal factors (gastrin), and by intramural noncholinergic factors, and is inhibited by extramural cholinergic factors. CCK, Cholecystokinin; PYY, peptide YY; CGRP, calcitonin gene-related peptide; VIP, vasoactive intestinal peptide; GRP, gastrin-releasing peptide; Ach, acetylcholine. Adapted from reference 9, with permission.