Normal Stomach

The stomach develops from the distal part of the foregut. It is a saccular organ with a volume of 1200 to 1500 mL, but a capacity of over 3000 mL. It extends from just left of the midline where it is joined to the esophagus, to just right of the midline where it connects to the duodenum. The concavity of the right, inner curve is called the lesser curvature, and the convexity of the left, outer curve is the greater curvature. An angle along the lesser curve, the incisura angularis, marks the approximate point at which the stomach narrows prior to its junction with the duodenum. The entire stomach is covered by peritoneum; an exaggerated peritoneal fold, the greater omentum, extends beyond the greater curvature to the transverse colon.

The stomach is divided into five anatomic regions (Fig. 17-12A). The cardia is the narrow conical portion of the stomach immediately distal to the gastroesophageal junction. The fundus is the dome-shaped portion of the proximal stomach that extends superolateral to the gastroesophageal junction. The body, or corpus, comprises the remainder of the stomach proximal to the incisura angularis. The stomach distal to this angle is the antrum, demarcated from the duodenum by the muscular pyloric sphincter.
Figure 17-12  Anatomy and histology of the stomach.  


The gastric wall, like the rest of the gastrointestinal tract, consists of mucosa, submucosa, muscularis propria, and serosa. The interior surface of the stomach exhibits coarse rugae (meaning “folds”). These infoldings of mucosa and submucosa extend longitudinally and are most prominent in the proximal stomach, flattening out when the stomach is distended. A finer mosaic-like pattern is delineated by small furrows in the mucosa. The delicate texture of the mucosa is punctuated by millions of gastric foveolae, or pits, leading to the mucosal glands.
The normal gastric mucosa has two compartments: the superficial foveolar (meaning leaflike) compartment and the deeper glandular compartment. The foveolar compartment is relatively uniform throughout the stomach. In contrast, the glandular compartment exhibits major differences in thickness and in glandular composition in different regions of the stomach (Fig. 17-12B, C). The foveolar compartment consists of surface epithelial cells (the foveolar cells) lining the entire mucosal surface as well as the gastric pits. The lush undulation of the mucosal surface and pits imparts the leaflike texture to the gastric mucosa. The tall, columnar mucin-secreting foveolar cells have basal nuclei and crowded, small, relatively clear mucin-containing granules in the supranuclear region. Deeper in the gastric pits are so-called mucous neck cells, which have a lower content of mucin granules and are thought to be the progenitors of both the surface epithelium and the cells of the gastric glands. Mitoses are extremely common in this region, as the entire gastric mucosal surface is totally replaced every 2 to 6 days. The glandular compartment consists of gastric glands, which vary between anatomic regions:

- **Cardia glands** contain mucus-secreting cells only.
- **Oxyntic (also called gastric or fundic) glands** are found in the fundus and body and contain parietal cells, chief cells, and scattered endocrine cells. The term *oxyntic* means acid-forming (derived from Greek, *oxynein*).
- **Antral or pyloric glands** contain mucus-secreting cells and endocrine cells.

The main cell types in these glands are the following:

- **Mucous cells** populate the glands of the cardia and antral regions and secrete mucus and pepsinogen II. The mucous neck cells in the glands of the body and fundus secrete mucus as well as group I and II pepsinogens.

- **Parietal cells** line predominantly the upper half of the oxyntic glands in the fundus and body. They are recognizable by their bright eosinophilia on H & E stained preparations, which are attributable to their abundant mitochondria. The apical membrane of the parietal cell is invaginated, forming an extensive intracellular canalicular system complete with microvilli. In the resting state, vesicles lie in close approximation to the canalicular system. These vesicles contain the proton pump, a unique hydrogen-potassium-ATPase (H⁺,K⁺-ATPase) that pumps hydrogen across membranes in exchange for potassium ions. Within minutes of parietal cell stimulation, the vesicles fuse with the canalicular system, thereby creating an apically directed acid-secreting membrane of enormous surface area. Parietal cells also secrete *intrinsic factor*, which binds luminal *vitamin B₁₂* in the duodenum and permits its absorption in the ileum.

- **Chief cells**, concentrated more at the base of gastric glands, are responsible for the secretion of the proteolytic proenzymes *pepsinogen I* and *II*. Chief cells are notable for their basophilic cytoplasm, and ultrastructurally are classic protein-synthesizing cells, having an extensive rough endoplasmic reticulum, a prominent supranuclear Golgi apparatus, and numerous apical secretory granules. Upon stimulation of chief cells, the pepsinogens contained in the granules are released by exocytosis. The pepsinogens are activated to *pepsin* by the low luminal pH and inactivated above pH 6.0 upon entry into the duodenum.
Endocrine or enteroendocrine cells are scattered among the epithelial cells of gastric and antral glands. The cytoplasm of these triangular cells contains small brightly eosinophilic granules, which are concentrated on the basal aspect of the cell. These cells can act in an endocrine mode, releasing their products into the circulation, or a paracrine mode, via secretion into the local tissue. In the antral mucosa, most of the endocrine cells are the gastrin-producing cells, or G cells. In the body (gastric) mucosa, the endocrine cells produce histamine, which binds the histamine-2 (H2) receptor on the parietal cells to increase acid production. These cells are also referred as enterochromaffin-like (ECL) cells. Other ECL cells in the gastric mucosa include D cells (producing somatostatin) and X cells (producing endothelin). These cells play an important role in modulating acid production.

Gastric Mucosal Physiology

ACID SECRETION

The hallmark of gastric physiology is secretion of hydrochloric acid, divided into three phases.

- The cephalic phase, initiated by the sight, taste, smell, chewing, and swallowing of palatable food, is mediated by vagal activity.

- The gastric phase involves stimulation of stretch receptors by gastric distention and is mediated by vagal impulses; it also involves gastrin release from endocrine cells, the G cells, in the antral glands. Gastrin release is promoted by luminal amino acids and peptides and possibly by vagal stimulation.

- The intestinal phase, initiated when food containing digested protein enters the proximal small intestine, involves a number of polypeptides besides gastrin.

All signals converge on the gastric parietal cell to activate the proton pump:

- Acetylcholine released from cephalic-vagal or gastric-vagal afferents stimulates the parietal cell via the muscarine-3 cholinergic receptor, resulting in an increase in cytosolic Ca²⁺ and subsequent activation of the proton pump.

- Gastrin activates a gastrin receptor, resulting in an increase of cytosolic Ca²⁺ within the parietal cells.

- An oxyntic gland ECL cell plays a central role: gastrin and vagal afferents induce the release of histamine from the ECL cell, thereby stimulating the H₂ receptor on parietal cells. This pathway is considered to be the most important for activation of the proton pump.

Activation of some receptors on the parietal cell surface inhibit acid production. They include receptors for somatostatin, prostaglandins of the E series, and epidermal growth factor.

MUCOSAL PROTECTION

At maximal secretory rates the intraluminal concentration of hydrogen ion is 3 million times greater than that of the blood and tissues. The "mucosal barrier" protects the gastric mucosa from autodigestion and consists of:
Mucus secretion: The thin layer of surface mucus in the stomach and duodenum exhibits a diffusion coefficient for H+ that is one quarter that of water. Acid- and pepsin-containing fluid exits the gastric glands as "jets" passing through the surface mucus layer, entering the lumen directly without contacting surface epithelial cells.

Bicarbonate secretion: Surface epithelial cells in both the stomach and duodenum secrete bicarbonate into the boundary zone of adherent mucus, creating an essentially pH-neutral microenvironment immediately adjacent to the cell surface.

The epithelial barrier: Intercellular tight junctions provide a barrier to the back-diffusion of hydrogen ions. Epithelial disruption is followed rapidly by restitution, in which existing cells migrate along the exposed basement membrane to fill in the defects and restore epithelial barrier integrity.

Mucosal blood flow: The rich mucosal blood supply provides oxygen, bicarbonate, and nutrients to epithelial cells and removes back-diffused acid.

Prostaglandin synthesis: Production of prostglandins by the mucosal cells impacts on many other components of mucosal defense. For example, prostglandins favor production of mucus and bicarbonates, and they inhibit acid secretion by parietal cells. In addition, by their vasodilatory action, prostglandins E and I improve mucosal blood flow. Drugs that block prostglandin synthesis reduce this cytoprotection and thus promote gastric mucosal injury and ulceration.

When the mucosal barrier is breached, the muscularis mucosa limits injury. Superficial damage limited to the mucosa can heal within hours to days. When damage extends into the submucosa, weeks are required for complete healing. Imperfect as our understanding of these defensive mechanisms may be, they are clearly a physiologic marvel, or our gastric walls would suffer the same fate as a piece of swallowed meat.

In addition to the well-characterized barrier function and digestive function of the gastric mucosa, mucosal endocrine cells also produce hormones that are involved in growth regulation. Ghrelin is a recently identified growth hormone that regulates body growth and appetite via a possible effect on the gastrointestinal-hypothalamic-pituitary axis. [12]