Physiology of the Upper GIT: Oesophagus

• As substances enter into the esophagus, the lower esophageal sphincter (LES), an area of smooth muscle near the distal end of the esophagus, relaxes to allow their entry into the stomach.

• The LES usually remains contracted to prevent the reflux of gastric contents into the esophagus.

• However, peristaltic contractions of the esophageal muscles allows the LES to remain open until all food has entered the stomach.
  – Therefore LES is the primary barrier for the prevention against gastric reflux into the esophagus,
Gastric glands

(a) Three-dimensional view of layers of stomach
Role of histamine in gastric acid secretions

- Special endocrine cells of the stomach, known as enterochromaffin-like (ECL) cells have receptors for Ach and gastrin and are the source of histamine.

- Histamine binds to the H2 receptors on the parietal cells resulting in activation of adenylyl cyclase
  - This leads to an increase in intracellular second messenger cAMP.

- Activation of cAMP dependent protein kinases results in stimulation of H+-K+ pump.
Gastric and oesophageal defences against acidity

The high acid concentration in the gastric lumen requires defence mechanisms to protect the oesophagus and the stomach.

- The primary oesophageal defence is the lower oesophageal sphincter (LES) which prevents reflux of acidic gastric contents into the oesophagus.
<table>
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<th>Factor</th>
<th>Description</th>
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<tr>
<td>Proteins in food</td>
<td>Proteins in food provide <strong>buffering</strong> in the lumen; consequently, the gastric luminal pH is usually above 3 after a meal.</td>
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<td>Somatostatin</td>
<td>If the buffering capacity of protein is exceeded or if the stomach is empty, the pH of the gastric lumen will fall below 3. When this happens, the <strong>endocrine cells (D cells) in the antrum secrete somatostatin</strong>, which <strong>inhibits the release of gastrin and, thus, gastric acid secretion.</strong></td>
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<td>Acidification of the duodenal lumen.</td>
<td>Acidification stimulates the release of secretin, which inhibits the release of gastrin, and several peptides, collectively known as enterogastrones (e.g. cholecystokinin, gastrin releasing peptide) which are released by intestinal endocrine cells.</td>
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Pathophysiology of PUD
NSAIDs: Topical effects of NSAIDs on GI Mucosa

- Formulations such as enteric-coated aspirin, buffered aspirin, NSAID prodrugs, and parenteral or rectal preparations may spare topical effects on the gastric mucosa,

- However, they all have the potential to cause a gastric ulcer because of their systemic inhibition of endogenous prostaglandins.
Types of PUD

• PUD encompasses both gastric and duodenal ulcers.

• Ulcers are defined as breaks in the mucosal surface <5 mm in size, with depth to the submucosa.

• Duodenal ulcers (DUs) and gastric ulcers (GUs) share many common features in terms of pathogenesis, diagnosis, and treatment, but several factors distinguish them from one another.