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M1 - GI Sequence

Stomach

John Williams, M.D., Ph.D.

Winter, 2009
FUNCTIONS OF STOMACH

1. Storage of ingested meal
2. Regulate rate of emptying into small intestine
3. Mix contents of stomach
4. Mechanical and Chemical Breakdown of food
5. Inhibit bacterial growth
6. Provide intrinsic factor for vitamin $B_{12}$ absorption
Regions of the Stomach

- Esophagus
- Cardia
- Lesser curvature
- Duodenum
- Pylorus
- Antrum (Gastrin)

- Fundus
- Greater curvature
- Body

(Parietal cells: HCl, Intrinsic factor, Chief cells: Pepsinogen)
Gastric Gland and Surface Pit from Body of the Stomach

Modified from Fig. 7 Johnson, L. Essential Medical Physiology. Raven Press, New York, NY; 1992: 482.
Location of Histamine in the Gastric Mucosa

Normal

Acid Inhibition

Sources Undetermined
## GASTRIC SECRETIONS

<table>
<thead>
<tr>
<th>Substance</th>
<th>Cell</th>
<th>Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCl</td>
<td>Parietal Cell</td>
<td>fundus-body</td>
</tr>
<tr>
<td></td>
<td>(Oxyntic cell)</td>
<td></td>
</tr>
<tr>
<td>Intrinsic Factor</td>
<td>Parietal Cell</td>
<td>fundus-body</td>
</tr>
<tr>
<td>Pepsinogen</td>
<td>Chief Cell</td>
<td>fundus-body-</td>
</tr>
<tr>
<td>antrum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucus</td>
<td>Mucus Cell</td>
<td>fundus-body-</td>
</tr>
<tr>
<td>antrum</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Volume:** 1.5-2.0 liters/day, isotonic

**basal rate:** 1.5 mmoles H⁺/hr

**max rate:** 6-40 mmoles H⁺/hr

**pH max:** 1.0
Ion Concentrations in Gastric Juice Relative to Secretory Rate

Fig. 9 Johnson, L. *Essential Medical Physiology*. Raven Press, New York, NY; 1992: 484.
Mechanism of HCL Secretion by Parietal Cells

- **H**<sup>+</sup>-**K**<sup>+</sup>-ATPase
- Carbonic anhydrase
- **CO**<sub>2</sub> → **CO**<sub>2</sub> + **H**₂**O**
- **HCO**<sub>3</sub><sup>-</sup> → **H**<sup>+</sup> + **HCO**<sub>3</sub><sup>-</sup>
- **Cl**<sup>-</sup> → **Cl**<sup>-</sup>
- **K**<sup>+</sup> → **K**<sup>+</sup>
- **Na**<sup>+</sup> → **Na**<sup>+</sup>
Schematic representation of the H+,K+ -ATPase heterodimer in the apical membrane of the parietal cell
Parietal Cell Vesicles Cycle between Resting and Secreting State
Secretory Transformation of Parietal Cells

canalculus

H.K, ATPase

tubulovesicles active pumps

Ca cAMP

ACh histamine
Receptors and Intracellular Messengers Regulating Parietal Cell H⁺ Secretion

Histamine

Gastrin

Vagal stimulation
Acetylcholine

Adenylate cyclase

ATP → cAMP → Ca²⁺ → Gastric hydrogen ion pump → K⁺ → \( H^+ \) → secretion

A B Sum A + B alone

potentiation
Role of the ECL Cell in Peripheral Regulation of Gastric Acid Secretion

Parietal Cell

Source Undetermined
INTEGRATED CONTROL OF GASTRIC ACID SECRETION
BY NEURAL AND HUMORAL PATHWAYS

1. Vagus acts directly on parietal cells and indirectly by effects on gastrin and histamine release.

2. Histamine released from enterochromaffin-like cells (ECL cells) reaches parietal cells by local diffusion.

3. Gastrin released from antral G cells reaches parietal cells by systemic circulation.

4. Inhibitory regulators include somatostatin released from D cells in antrum and body of stomach and intestinal hormones collectively termed “enterogastrone”, and prostaglandins from surface cells.
Gastrin release from G cells of the antrum is stimulated by luminal amino acids and digested proteins and is inhibited in a paracrine fashion by somatostatin in response to luminal acid. Somatostatin is released when pH is < 3.0.
METHODS FOR MEASURING ACID SECRETION

1. Gastric Aspiration
2. Intragastric Titration
3. Basal vs. Peak Acid Output
ACID SECRETION AND INTRAGASTRIC pH FOLLOWING A SIRLOIN STEAK MEAL

ACID SECRETION (mmol/hr)

TIME (min) AFTER MEAL

pH

TIME (min) AFTER MEAL
ACID SECRETION DURING SHAM FEEDING

ACID OUTPUT (mmol/hr)

TIME (minutes)

SHAM FEEDING

(n = 22)
ACID SECRETION IN RESPONSE TO INTRAGASTRIC SALINE (DISTENSION) AND FOOD

[Graph showing acid secretion over time in response to saline (distension) and food, with data points at 30, 60, 90, and 120 minutes, and a baseline (basal) level.]
Cephalic Phase of Gastric Secretion

sight, taste, smell, chewing, stress

Vagus Nerve

Enteric Nerve Plexus

G-Cell → ECL-Cell → Parietal Cell

GASTRIN

HCL
Gastric Phase Acid Secretion

long and short reflexes

G-Cell → ECL-Cell

G-Cell → Parietal cell

ECL-Cell → histamine

ACh → Parietal cell

Gastrin

somatostatin

D-Cell

peptides

amino acids

HCL → buffered by proteins in meal

distension

John Williams
Intestinal Phase Acid Secretion

- Nerves
- Hormones: enterogastrone, GIP, CCK, secretin
- luminal stimuli: fatty acids, acid, amino acids, hypertonic solutions, distension

inhibition of parietal cell and gastrin release
PEPSIN

1. Proteolytic enzyme secreted by chief cells as an inactive precursor, pepsinogen.

2. Release stimulated by vagal nerve and by presence of acid in stomach.

3. Activated by peptide cleavage at acid pH.

4. Initiates digestion of protein. It is an endopeptidase and active at acid pH.
THE MOLECULE OF INTRINSIC FACTOR AND ITS COBALAMIN COMPLEX
Intrinsic Factor

1. Glycoprotein of Mol. Wt. 55,000 which binds Vitamin B$_{12}$ (cobalmin).

3. Produced by parietal cells.

4. After binding B$_{12}$ it binds receptors on ileal absorptive cells and is internalized by endocytosis.

4. Absent in pernicious anemia.
Sequential Steps in the Absorption of Cobalamin (Vit B$_{12}$)

MECHANISMS CONTRIBUTING TO GASTRIC CYTOPROTECTION
GASTRIC MOTILITY

1. Proximal – Receptive relaxation as stomach fills (Fundus)

2. Distal – Propulsive mixing and grinding (Antrum)

3. Pylorus – Regulates outflow
Entry of Food is Preceded by Gastric Relaxation

- **Esophagus**
- **LES**
- **Fundus**

Graph shows a peak in pressure in the **Esophagus** indicating relaxation, followed by a decreased pressure in the **LES** and **Fundus**.
Antral Peristalsis

Fig. 4-9 Granger, D, et al. Clinical Gastrointestinal Physiology. W.B. Saunders, Philadelphia, PA; 1985: 84.
John Williams


Stomach Emptying

- inhibition
- nerves & hormones

Duodenum

- fatty acids
- acidity
- osmolarity
- volume
- amino acids

% Emptyed

- Dextrose
- Liver
- Spheres

Hours

- 1
- 2
- 3
- 4

400 ml 1% Dextrose
50g cubed liver
40 plastic spheres
Additional Source Information

for more information see: http://open.umich.edu/wiki/CitationPolicy

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Slide 6 – Source Undetermined
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Slide 8 – Source Undetermined
Slide 9 – Source Undetermined
Slide 11 – Fig. 9 Johnson, L. *Essential Medical Physiology*. Raven Press, New York, NY; 1992: 484.
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Slide 34 – Fig. 4-9 Granger, D, et al. Clinical Gastrointestinal Physiology. W.B. Saunders, Philadelphia, PA; 1985: 84.
Slide 35 – Jim Sherman
Slide 36 – (Left) John Williams