STOMACH I

1. What are gastric secretions composed of?

These are both *exocrine* and *endocrine* in nature:

- *Water*
- *Mucus*
- *Ions:* notably hydrochloric acid and bicarbonate
- *Pepsinogen:* enzyme precursor for protein digestion
- *Intrinsic factor:* for the absorption of vitamin B_{12}
- *Hormones:* gastrin is the main one, also histamine from regional mast cells

2. Which gastric cells are involved in these secretions?

Note that these cells are located within the gastric glands, the entrance to which is seen on the surface as *gastric pits:*

- *Parietal cells:* secretion of HCl *and* intrinsic factor. Most frequently in the glands of the fundus
- *Chief cells:* secreting pepsinogen, the precursor of pepsin
- *Mucous cells:* most frequently found in the necks of the gastric glands of the pylorus
- *G-cells:* found in the glands of the pylorus and they secrete the hormone gastrin

3. Why does the stomach secrete acid?

There are three main reasons:

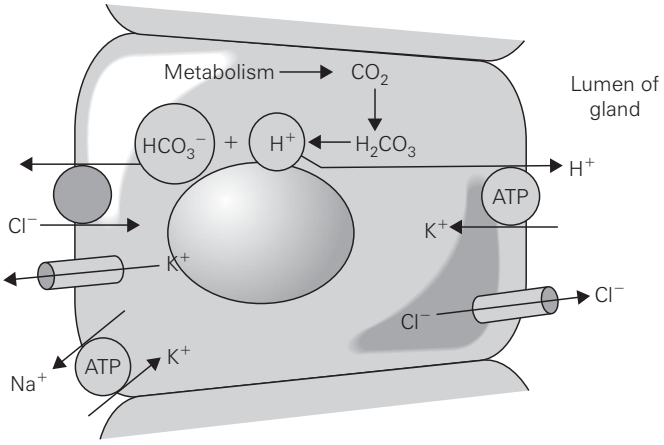
- HCl has some proteolytic activity
- By reducing the gastric pH to 2, it provides the ideal environment for the gastric enzyme pepsin
- Has antibacterial properties and prevents colonisation

4. What is the volume of gastric secretion daily?

1–1.5 L per day.

5. How is hydrochloric acid produced by the parietal cell?

This may be summarised in the diagram below:



From Berne RM, Levy MN. Principles of Physiology, 3rd edition, 2000, London, with permission from Elsevier

- There is the initial active transport of K^+ and Cl^- into the cell
- H^+ that is generated from CO_2 dissolving into the cytoplasm is actively exchanged with K^+ at the H^+-K^+ ATPase. The H^+ enters the gastric lumen
- The HCO_3^- generated through dissociation of H_2CO_3 diffuses back into the plasma in exchange for Cl^-
- Chloride now enters the gastric lumen

6. How is the production of gastric acid controlled?

HCl secretion is stimulated by:

- *ACh:* from parasympathetic vagal neurones that innervate the parietal cells directly
- *Gastrin:* produced by pyloric G-cells

- *Histamine:* produced by mast cells. This stimulates the parietal cells directly and also potentiates parietal cell stimulation by gastrin and neuronal stimulation

HCl secretion is inhibited by:

- *Somatostatin:* from cells in the enteric nervous system
- *Secretin:* produced by the duodenum and inhibits gastrin release
- *CCK:* also inhibits gastrin release

7. Can you name some drugs that inhibit gastric acid secretion?

- *Omeprazole:* one of the proton-pump (H^+-K^+ ATPase) inhibitors
- *Cimetidine, ranitidine:* anti histamines that prevent mast cell stimulation of parietal cells
- *Acetazolamide:* inhibits the enzyme *carbonic anhydrase*, which catalyses the reaction that sees to HCO_3^- generation within the parietal cell

8. How does the stomach protect itself from autodigestion by the acid and pepsin that it produces?

There is copious production of mucus that forms a gel on the surface of the epithelium. Mixed within this is bicarbonate. Together, they ensure that the pH of the environment immediately adjacent to the epithelium is kept at neutral.

9. Describe the phases of gastric acid secretion.

- *Cephalic phase:* initiated by the thought, smell and taste of food. Leads to vagal activation that stimulates HCl and gastrin secretion
- *Gastric phase:* initiated by the presence of food in the stomach particularly protein rich food. There is, again, both an increase in the level of HCl *and* gastrin

- *Intestinal phase:* initially, the presence of amino acid and food in the duodenum stimulate acid production. Later there is inhibition following the release of secretin and CCK

10. Summarise, then, the actions of gastrin.

- Stimulates gastric acid secretion
- Stimulates exocrine pancreatic secretions
- Stimulates gastric motility

STOMACH II – APPLIED PHYSIOLOGY

1. Describe briefly the sources of gastric innervation.

- *Extrinsic supply:* from the sympathetic and parasympathetic systems
- *Intrinsic supply:* from the enteric nervous system

2. What is the autonomic supply?

- *Sympathetic:* from the cœliac plexus. Reduces gastric motility
- *Parasympathetic:* from the vagus nerve – causing increased motility

3. What is the storage capacity of the stomach?

1–2 L.

4. How does the stomach accommodate this volume without painful distension?

It undergoes the process of *receptive relaxation*. This is a vagally mediated reflex where the fundus and the body relax when distending with food.

5. Apart from receptive relaxation, name some other important gastric reflexes.

- *Peristalsis:* the *basic electrical rhythm* of the stomach generates *slow waves* that pass from inflow to outflow segments, propelling food
- *Retropulsion:* when chyme is pushed backwards and forwards in the lumen. This helps to break up boluses
- *Emptying*
- *Vomiting reflex*

6. List the hormones which stimulate gastric emptying.

- *Gastrin:* released from the gastric G-cells

- *CCK:* from the duodenum
- *Secretin:* also from the duodenum

7. What happens to the stomach during the process of vomiting? Outline the steps.

- The process begins with a deep inspiration
- This is followed by closure of the glottis
- There is diffuse contraction of the abdominal and thoracic muscles. This elevates the pressures of both compartments. The intra-abdominal pressure may rise to 800 mmHg
- Simultaneously, there is relaxation of the lower oesophageal sphincter
- There is a large retrograde contraction of the stomach, forcing the contents into the oesophagus following relaxation of the cricopharyngeus muscle
- There is generalised activity of the vasomotor centres, producing pallor and sweating. Also it is accompanied by tachycardia and palpitations
- Note that this process is coordinated by the *vomiting centre* of the medulla, and the chemoreceptor trigger zone (CRTZ)

8. Where is the CRTZ located, and what is its anatomic significance?

This is found in the area postrema in the floor of the 4th ventricle. Its position is significant because it lies outside of the BBB, and so can be influenced directly by noxious stimuli and drugs (such as opiates).

9. Briefly outline the physiological effects of pyloric stenosis.

- Persistent vomiting leads to dehydration which may lead to acute renal failure
- There is progressive metabolic alkalosis, which is perpetuated by the normal compensatory mechanisms

10. Describe how metabolic alkalosis develops in pyloric stenosis.

- Gastric secretions are rich in H^+ and Cl^-, both of which are lost
- There is a reduction of pancreatic exocrine secretions due to the reduced acid load at the duodenum. This therefore leads to retention of bicarbonate-rich pancreatic secretion, worsening the alkalosis already caused by loss of protons
- Volume depletion maintains the alkalosis by leading to bicarbonate absorption over chloride
- In order to maintain electrochemical neutrality, in response to loss of chloride, there is increased renal uptake of bicarbonate, further worsening the alkalosis

11. Describe some of the physiological effects of a total gastrectomy.

In simple terms, this leads to a complete loss of parietal cells leading to no gastric acid, together with no intrinsic factor nor pepsin:

- *No IF:* leads to vitamin B_{12} deficiency, manifest as a megaloblastic anaemia
- *Achlorhydria:* promotes iron deficiency
- *Dumping syndrome:* gastrectomy leads to the rapid transfer of hypertonic chyme into the small bowel. This leads to transfer of fluid from the extracellular space into the bowel. The immediate effect of this is abdominal distension, vomiting and diarrhoea. The fall in the circulating volume leads to the physiological shock response, with tachycardia, sweating and narrow pulse pressure
- *Hypokalaemia*: Vomitus contains around 10 $mmol L^{-1}$ of potassium, which is lost. Further potassium is lost from the kidney as protons are exchanged for potassium. Also, the increased aldosterone secreted by the adrenal cortex in response to fluid loss exacerbates renal potassium loss