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Keywords Gastric juice/Gastric emzymes/Digestion/Vitamin B12

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In this article...

- Anatomy and functions of the stomach
- Role of gastric enzymes in chemical digestion
- Common conditions affecting the stomach

Gastrointestinal tract 2: the structure and function of the stomach

Key points

In the stomach, cells lining the gastric pits secrete enzymes that break down food proteins

The acidic environment of the stomach favours the neutralisation of most ingested pathogens

The muscles in the stomach wall perform vigorous churning that supports mechanical digestion

Ghrelin, a hormone produced in the stomach, helps to regulate hunger and satiety

Pathologies of the stomach include hiatus hernia, gastric ulcer, pernicious anaemia and stomach cancer

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Abstract After travelling through the mouth, pharynx and oesophagus, ingested food and liquids enter the stomach through the lower oesophageal sphincter. The stomach is both a reservoir for ingested food and a mixing and digestion chamber. It continues the process of mechanical and chemical digestion with the help of a range of gastric enzymes and its various layers of smooth muscle, before funnelling food turned into chyme into the duodenum. This article, the second in a six-part series exploring the gastrointestinal tract, describes the anatomy, function and common pathologies of the stomach.

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Part 1 in our series about the gastrointestinal (GI) tract described the role of the oral cavity in initiating mechanical and chemical digestion, and examined the processes of swallowing and peristalsis, which facilitate the transit of food from the mouth to the stomach. This second article in the series focuses entirely on the role of the stomach in digestion and the regulation of appetite, and discusses common pathologies of the stomach.

Anatomy and functions

The stomach, located in the upper left quadrant of the abdomen, is a J-shaped organ composed predominantly of involuntary smooth muscle. A bolus of food enters the stomach through the lower oesophageal sphincter, which rapidly closes to prevent regurgitation of gastric secretions (see part 1).

Anatomically, the stomach is divided into three main regions:

- Fundic region or fundus – top left, dome-shaped region;
- Stomach body – the expansive main stomach chamber;
- Pyloric region or pylorus – funnel-shaped lower region connecting the stomach and duodenum (Fig 1).

A typical adult human stomach is around 30.5cm long and 15.2cm wide, with an average capacity of around 1.5L. It acts simultaneously as a reservoir for ingested food and a mixing and digestion chamber. The inner mucosal lining of the stomach has prominent folds, the rugae, which allow it to expand to up to 50 times its empty volume (Mahadevan, 2014; Daniels and Allum, 2005).

Gastric pits

The mucosal lining of the stomach contains around 35 million small depressions, the gastric pits (Fig 2), which produce around 2L of gastric juice per day (Jolliffe, 2009).

Gastric pits are lined by secretory cells:

- Mucous (or goblet) cells, which produce copious amounts of mucus, protecting the delicate mucosal lining

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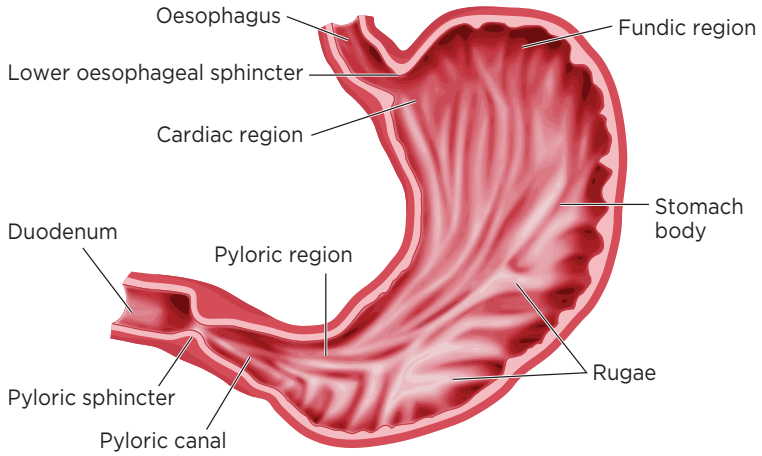
of the stomach. They are found across the mucosal epithelial lining and deeper within each gastric pit, where they are known as mucous neck cells;

- Parietal cells secrete hydrochloric acid (HCl) and intrinsic factor (IF). HCl is a component of gastric juice, which not only supports chemical digestion but also activates the enzyme pepsin. It is produced at high concentrations, giving the stomach a pH of around 2.5-3.5 (Marieb and Hoehn, 2015); this high acidity helps the stomach sterilise ingested food. IF is a small protein that binds to vitamin B12 and transports it across the wall of the intestine into the blood (see part 4);
- Chief cells secrete the inactive enzyme precursor pepsinogen, which is converted into the active enzyme pepsin upon exposure to HCl. Pepsin plays a role in protein digestion and enhances the bacterial killing activity of HCl (Zhu et al, 2006). Chief cells also secrete gastric lipase (Kiela and Ghishan, 2016), which, together with salivary lipase, initiates fat digestion;
- Endocrine cells synthesise various hormones and release them into the blood. As an example, endocrine cells called G cells produce the hormone gastrin, which regulates the secretion of gastric juice. Other endocrine cells called P/D1 cells release the hunger hormone ghrelin, which plays a role in regulating appetite and food intake.

Fig 1. **Regions of the stomach**



Secretion of gastric juice

The secretion of gastric juice occurs in three phases:

- Cephalic phase;
- Gastric phase;
- Intestinal phase (Fry, 2009).

In the cephalic phase, gastric juice secretion is initiated by the sight, smell and taste of food, and is primarily mediated by the parasympathetic nervous system via the vagus nerve, which innervates the stomach wall. When a person is hungry, the mere anticipation of food is enough to stimulate gastric juice secretion (Power and Schulkin, 2008). The cephalic phase accounts for around 30% of gastric juice secretion and prepares the stomach to receive food.

The gastric phase is the longest phase of gastric juice secretion, typically lasting between two and three hours, and is responsible for around 60% of gastric secretion. It begins when food has entered the stomach and the stomach wall is stretched. This prompts the G cells in the gastric pits to release gastrin. Gastrin stimulates the parietal cells to secrete HCl, which creates a pH favourable for protein digestion and the killing of ingested pathogens. Gastrin secretion can also be stimulated by the ingestion of high-protein food, coffee, wine or beer (Papakonstantinou et al, 2016; Stermer, 2002);

Gastric juice secretion continues in the intestinal phase while food is slowly passing from the stomach into the duodenum. The duodenum and jejunum progressively release hormones such as cholecystokinin, secretin and gastric-inhibiting peptide, which gradually reduce the secretion of gastric juice (Daniels and Allum, 2005). The intestinal phase is responsible for around 10% of gastric juice secretion.

Protein digestion

The process of protein digestion starts in the stomach. HCl slowly denatures proteins (for example, actin and myosin from meat), causing structural changes that expose the peptide bonds between adjacent amino acids. This enhances subsequent chemical digestion by proteases (Goodman, 2010). Activated pepsin present in the gastric juice cleaves the initial protein molecules (which can consist of thousands of amino acids) into smaller chains called polypeptides (Fig 3). Pepsin is referred to as an endopeptidase because it acts predominantly by attacking the peptide bonds in the centre of proteins to create polypeptides, which are further broken down in subsequent regions of the GI tract (Vahdatpour et al, 2016; Daniels and Allum, 2005).

Fat digestion

The process of fat digestion starts in the mouth when food is mixed with saliva and exposed to the enzyme salivary lipase. However, salivary lipase functions optimally at a pH of around 4, so it will not work at its maximal efficiency in the mouth because, at 6.2-7.6, the pH of saliva is too high. It works at its maximal efficiency upon reaching the acidic environment of the stomach (see part 1).

In the stomach, fat digestion is amplified by gastric lipase, which is synthesised by the chief cells. Gastric lipase remains stable and active over a broad pH range (2-7); like salivary lipase, however, it functions optimally at a pH of 4-5.4 and so achieves its maximal efficiency in the stomach (Sams et al, 2016).

Together, salivary and gastric lipase attack the Ester bonds of fat molecules, breaking down dietary fat into fatty acids and glycerol (see part 1); however, they are less efficient at digesting fats than the alkaline lipases that will later be released in the small intestine (see parts 3 and 4).

Formation of chyme

When food is present, the muscular layer of the stomach wall – known as the muscularis – undergoes regular rhythmic contractions that help mix the food with the gastric secretions to speed up the process of chemical digestion. The muscularis consists of the same circular and longitudinal layers of smooth muscle found in other gut regions (see part 1), but it also possesses an additional inner layer of oblique smooth muscle fibres. These three layers of muscle allow the stomach to perform the vigorous churning motions that

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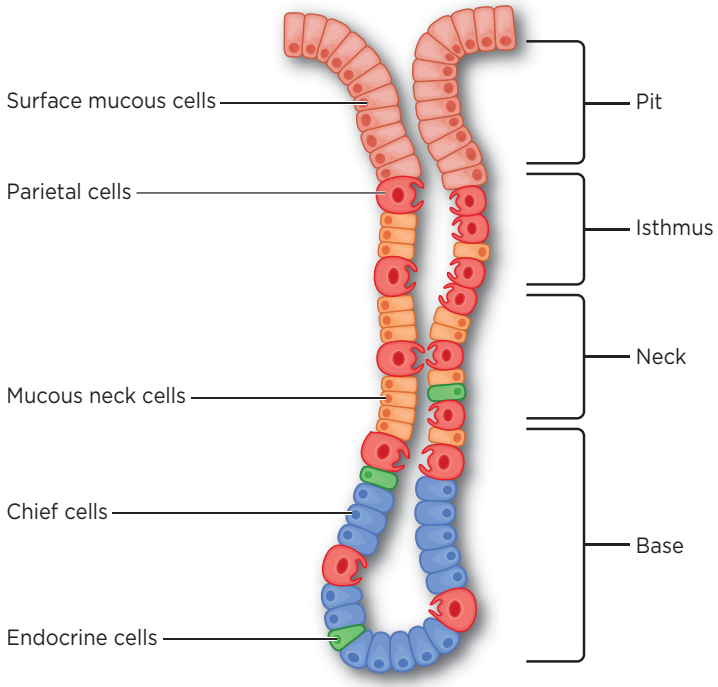
Fig 2. **Structure of gastric pit**



are essential for efficient mechanical digestion. Gradually, most solid pieces of food are mechanically and chemically digested, resulting in a semi-solid, thick and soupy material called chyme (Marieb and Hoehn, 2015).

Depending on the nature of the food consumed, food typically remains in the stomach for 3-6 hours. Meals rich in protein and fat, such as a fried breakfast, tend to stay in the stomach for longer periods, while carbohydrate-rich foods, such as a baked potato or a piece of fruit, tend to pass through much faster (Kong and Singh, 2008; Gentilcore et al, 2006).

Passage of chyme into the duodenum

The pylorus connects the stomach directly to the duodenum, which forms the first segment of the small intestine. At regular intervals – typically every 20 seconds – the pyloric sphincter (a small ring of smooth muscle) dilates to allow small portions of acidic chyme to pass into the duodenum. A slow, gradual release of chyme is essential to allow time for the acidic contents of the stomach to be neutralised by alkaline pancreatic juice before they reach the small intestine; this has a delicate mucosa and would otherwise sustain chemical damage (see part 3).

As the stomach progressively empties, the elastic recoil of its walls allows it to shrink back to its pre-meal volume. An empty stomach will begin to undergo gentle contractions and, if no food is forthcoming, waves of contraction can intensify, sometimes being perceived as hunger pangs (Sanger et al, 2011).

Food absorption

The stomach is not a major area of nutrient absorption. There is minimal absorption of the initial products of protein digestion and it is generally thought that digested fat is not absorbed at in the stomach. However, simple sugars such as glucose, galactose and fructose are readily absorbed, particularly when in high concentration. The stomach is excellent at absorbing water, taking approximately 20 minutes to absorb 50% of the ingested volume of water. Similarly, the ethanol present in alcoholic beverages is rapidly absorbed across the gastric wall into the blood (Daniels and Allum, 2005).

Hunger and satiety

When the stomach is empty, P/D1 cells of the gastric pits release the peptide hormone ghrelin. Ghrelin is often referred to as the 'hunger hormone', as it circulates in the blood and interacts with receptors in the hypothalamus and other regions of the brain to promote powerful sensations of hunger (Delporte, 2013). Ghrelin levels are highest before the major meals of the day, reaching peak concentration in the blood before breakfast, lunch and dinner (Fig 4). On eating food, the stretching of the stomach wall inhibits the release of ghrelin and the sensation of hunger subsides.

Different hormones are involved in the sensation of satiety (feeling full and satisfied after eating food) (see part 3).

QUICK FACT **2L** Daily volume of gastric juice produced by gastric pits

Common pathologies

Hiatus hernia

The oesophagus passes from the thoracic cavity into the abdominal cavity via an aperture in the diaphragm called the oesophageal hiatus. In some people, the superior portion of the stomach can slide through that opening and become trapped, resulting in a hiatus hernia (HH).

HH is more common in middle and old age, affecting around a third of people over the age of 50 (Bit.ly/BUPAHiatusHernia). Frequency is also higher in overweight people and HH is particularly common in those with a body mass index of >30 (which places them in the obese category). HH may be precipitated by events that force the stomach upwards or the diaphragm downwards, such as bending over, lifting heavy weights, sneezing, vomiting or straining during defecation (Bit.ly/GISHiatusHernia).

Most people who have an HH do not show any obvious symptoms. When symptoms are present, they can be extremely diverse. Indeed, HH is often called 'the great mimic', as many of its presenting symptoms are found in a range of other diseases. Common symptoms include:

- Gastric reflux;
- Bad breath;
- Dysphagia,
- Regurgitation;
- Nausea;
- Chest pain (which is often mistaken for a symptom of angina or myocardial infarction);
- Shortness of breath;
- Palpitations (Bit.ly/NHSHiatusHernia; Schummer, 2017).

Symptoms can usually be managed with antacids and proton pump inhibitors. Another treatment option is surgery, during which the stomach is repositioned and the oesophageal hiatus is reduced to prevent re-herniation.

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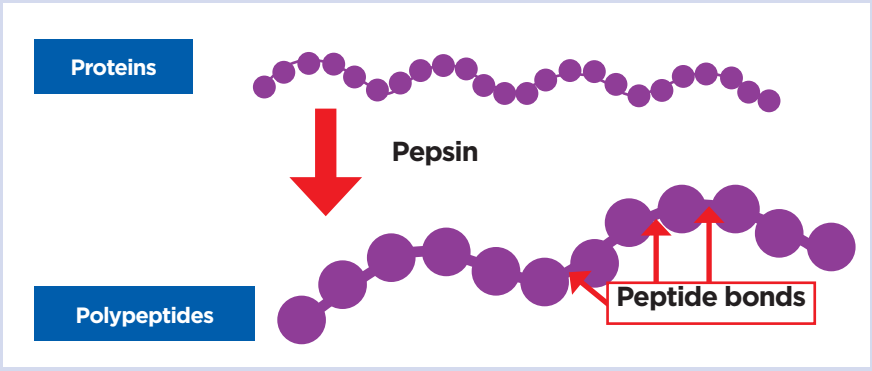
Fig 3. **Action of pepsin**



Gastric ulceration

In a healthy person, the mucus-producing cells of the stomach continually secrete thick, sticky mucus that coats the epithelial lining of stomach. This mucus layer acts as a physical and chemical barrier protecting the delicate tissues of the mucosa and submucosa (see part 1) against autodigestion from the combined effects of HCl and pepsin (Ichikawa and Ishihara, 2011).

Most bacteria cannot survive in the acidic environment of the stomach, but the Gram-negative bacterium *Helicobacter pylori* (*H. pylori*) can, and it will replicate by colonising the mucus layer of the stomach.

H. pylori, which is thought to be carried by around half of the world's population, can irritate the gastric mucosa, leading to gastritis (inflammation of the stomach lining) (Kao et al, 2016). In addition, *H. pylori* can also stimulate the release of gastrin and the production of HCl (Waldum et al, 2016). Elevated stomach acid increases the risk of both gastric and duodenal ulceration, in which gastric juices progressively digest into the mucosal lining of the gut wall, causing intense pain.

Stomach ulcers may also be triggered by the long-term use of non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin or ibuprofen. NSAIDs not only act as gastric irritants, but also suppress the production of prostaglandins, which protect the gastric mucosa by stimulating the production of mucus and bicarbonate (Drini, 2017; Cohen, 1987). As erosion of the gastric mucosa extends deeper, blood vessels in the wall of the stomach are damaged, which can result in significant bleeding and progressive anaemia.

Often, patients with gastric ulceration will vomit blood-stained gastric juices that resemble coffee grounds or produce sticky, black and tarry stools known as melaena. Both are indicative of significant blood loss (Bit.ly/NHSStomachUlcer). If untreated, gastric ulcers can progressively worsen: gastric juices further erode the wall of the stomach until, eventually, perforation occurs.

A perforated gastric ulcer is a medical emergency, as gastric juices and undigested food can now leak into the abdominal cavity, causing widespread visceral organ damage and inflammation. Perforated ulcers are characterised by peritonitis (extensive inflammation of the peritoneal membranes) and intense pain. Surgery is immediately required to wash out the abdominopelvic cavity and repair the perforation. Many patients with perforated ulcers enter a state of septic shock and do not recover (Rohit et al, 2017).

To promote ulcer healing, proton pump inhibitors, such as omeprazole are usually the first-line treatment option. If these are not well tolerated, histamine 2 (H2) receptor antagonists such as ranitidine can be prescribed. Both classes of medications are effective at reducing the production of HCl in the stomach. If *H. pylori* infection is present, triple therapy involving two antibiotics (clarithromycin plus either amoxicillin or metronidazole) and a proton pump inhibitor can be prescribed to eradicate infection. If NSAIDs are the cause, they can be discontinued (Bit.ly/NICEPeptic).

Not all gastric and duodenal ulcers are attributable to *H. pylori* infection, as stress and lifestyle can also play a role (see part 3).

Vitamin B12 deficiency and pernicious anaemia

The production of healthy erythrocytes (red blood cells) requires dietary vitamin B12 (also known as cobalamin). Foods such as red meat, liver, fish and yeast extract are excellent sources of vitamin B12 (National Institutes of Health, 2018). Vitamin B12 cannot be directly absorbed in the gut – first, it needs to bind to IF, which is produced by the parietal cells of the gastric pits. IF then helps transport vitamin B12 across the gut wall into the blood (Marieb and Hoehn, 2015).

A lack of vitamin B12 can result in megaloblastic anaemia. Fewer erythrocytes are produced, they take on an abnormally large appearance (hence the name megaloblasts) and they are less efficient at transporting oxygen. The most common cause of vitamin B12 deficiency and megaloblastic anaemia is pernicious anaemia (PA), an autoimmune disease that becomes more common with age, affecting around 1.9% of the over-60s (Andres and Serraj, 2012).

"Pernicious anaemia is the most common cause of vitamin B12 deficiency and megaloblastic anaemia"

The exact cause of PA is poorly understood. The disease is characterised by the production of autoantibodies that bind to a person's own cells and tissues, and initiate the destruction of the parietal cells that synthesise IF. Other autoantibodies may also be generated that bind to IF and block its ability to facilitate the absorption of vitamin B12 (Bit.ly/PASPerniciousAnaemia).

PA produces symptoms that are very similar to those of iron-deficiency anaemia, such as tiredness, breathlessness, pale skin and tachycardia. It is also associated with depression and cognitive changes. Once diagnosed, PA can be effectively treated with regular intramuscular injections of vitamin B12. The implications of regular vitamin B12 injections and the absorption of vitamin B12 in the ileum will be discussed in part 4.

In some patients, the binding of autoantibodies to the parietal cells of the stomach can trigger a chronic inflammation of the gastric mucosa resulting in gastritis. Gastritis associated with PA needs to be carefully assessed and monitored, as it is associated with an increased risk of stomach cancer (Murphy et al, 2015).

Stomach cancer

Stomach cancer accounts for approximately 2% of new cancers in the UK, with around 6,700 new cases identified each year; incidence is greatest in older people, with a peak incidence at 85-89 years of age, and men are at greater risk than women (Bit.ly/CRUKStomachCancerFigs).

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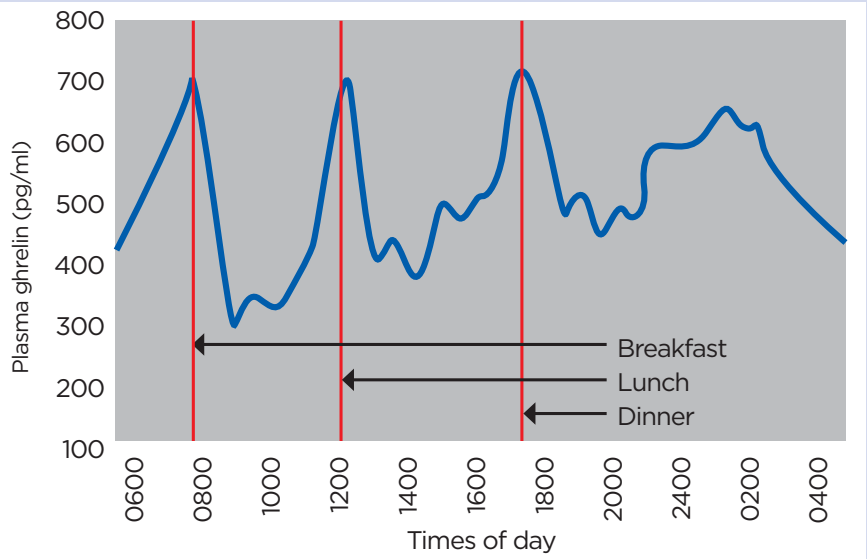
Fig 4. **Ghrelin release throughout the day**



Source: Adapted from Cummings et al, 2001

The development of stomach cancer appears to be multifactorial and many risk factors have been identified, including smoking, obesity, a high-salt diet, alcohol consumption, a history of PA and having a low socioeconomic status. *H. pylori* infection is a major risk factor: the World Health Organization recognises *H. pylori* as a carcinogen and *H. pylori* infection increases the risk of stomach cancer by up to six times (Zali et al, 2011).

Most people do not experience significant symptoms until the disease is fairly advanced. When symptoms are present, they are diverse and may include:

- Heartburn and indigestion;
- Loss of appetite;
- Feeling full after a small amount of food;
- Weight loss;
- Feeling tired and breathless (anaemia due to blood loss);
- Nausea and vomiting;
- Pain in the abdominal area (Bit.ly/ACSStomachCancer).

Stomach cancer is usually treated by surgery, often followed by radio- and chemotherapy. Even with treatment, the outlook is poor, with only around one in five people surviving longer than 10 years after diagnosis (Bit.ly/CRUKStomachCancerFigs). Since total or partial gastrectomy will remove the parietal cells that produce IF, patients with stomach cancer who undergo surgery will lose the ability to efficiently absorb vitamin B12 and will, therefore, require regular intramuscular injections of vitamin B12 to avoid developing PA. **NT**

- Our six-part series on the anatomy and physiology of the GI tract continues next month with part 3, dedicated to the duodenum, pancreas and biliary tract

CLINICAL SERIES **Gastrointestinal tract series**

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Part 2:	The stomach	Jul
Part 3:	The duodenum, liver and pancreas	Aug
Part 4:	The jejunum and ileum	Sep
Part 5:	The large intestine	Oct
Part 6:	Gut microbes	Nov

References

Andres E, Serraj K (2012) Optimal management of pernicious anemia. *Journal of Blood Medicine;* 3, 97-103.
Cohen MM (1987) Role of endogenous prostaglandins in gastric secretion and mucosal defense. *Clinical and Investigative Medicine;* 10: 3, 226-231.
Cummings DE et al (2001) A preprandial rise in plasma ghrelin levels suggests a role in meal initiation in humans. *Diabetes;* 50: 8, 1714-1719.
Daniels IR, Allum WH (2005) The anatomy and physiology of the stomach. In: Fielding JWL, Hallissey MT (eds) *Upper Gastrointestinal Surgery.* London: Springer Verlag.
Delporte C (2013) Structure and physiological actions of ghrelin, *Scientifica;* 2013: 518909.
Drini M (2017) Peptic ulcer disease and non-steroidal anti-inflammatory drugs. *Australian Prescriber;* 40: 3, 91-93.
Fry C (2009) Secretions of the salivary glands and stomach. *Surgery;* 27: 12, 503-506.
Gentilcore D et al (2006) Effects of fat on gastric emptying of and the glycemic, insulin, and incretin responses to a carbohydrate meal in type 2 diabetes. *Journal of Clinical Endocrinology and Metabolism;* 91: 6, 2062-2067.
Goodman BE (2010) Insights into digestion and absorption of major nutrients in humans. *Advances in Physiology Education;* 34: 2, 44-53.
Ichikawa T, Ishihara K (2011) Protective effects of gastric mucus. In: Tonino P (ed) *Gastritis and Gastric Cancer – New Insights in Gastroprotection, Diagnosis and Treatments.* London: IntechOpen.
Jolliffe DM (2009) Practical gastric physiology. *Continuing Education in Anaesthesia, Critical Care and Pain;* 9: 6, 173-177.
Kao CY et al (2016) *Helicobacter pylori* infection: an overview of bacterial virulence factors and pathogenesis. *Biomedical Journal;* 39: 1, 14-23.
Kiela PR, Ghishan FK (2016) Physiology of intestinal absorption and secretion. *Best Practice and Research – Clinical Gastroenterology;* 30: 2, 145-159.
Kong F, Singh RP (2008) Disintegration of solid foods in human stomach. *Journal of Food Science;* 73: 5, R67-R80.
Mahadevan V (2014) Anatomy of the stomach. *Surgery;* 32: 11, 571-574.
Marieb EN, Hoehn K (2015) *Human Anatomy and Physiology*. London: Pearson
Murphy G et al (2015) Cancer risk following pernicious anemia in the US elderly population. *Clinical Gastroenterology and Hepatology;* 13: 13, 2282-2289.
National Institutes of Health (2018) *Vitamin B12: Fact Sheet for Health Professionals.* Bit.ly/NIHVitB12
Papakonstantinou E et al (2016) Acute effects of coffee consumption on self-reported gastrointestinal symptoms, blood pressure and stress indices in healthy individuals. *Nutrition Journal;* 15: 26.
Power ML, Schulkin J (2008) Anticipatory physiological regulation in feeding biology: cephalic phase responses. *Appetite;* 50: 2-3, 194-206.
Rohit DK et al (2017) Clinical study and management of peritonitis secondary to perforated peptic ulcer. *International Surgery Journal;* 4: 8, 2721-2726.
Sams L et al (2016) Relevant pH and lipase for in vitro models of gastric digestion. *Food and Function;* 7: 1, 30-45.
Sanger GJ et al (2011) The hungry stomach: physiology, disease, and drug development opportunities. *Frontiers in Pharmacology;* 18: 1, 145.
Schummer W (2017) Hiatal hernia mimicking heart problems. *BMJ Case Reports;* 2017: bcr-2017-220508.
Stermer E (2002) Alcohol consumption and the gastrointestinal tract. *Israel Medical Association Journal;* 4: 3, 200-202.
Vahdatpour S et al (2016) The systematic review of proteins digestion and new strategies for delivery of small peptides. *Electronic Journal of Biology;* 12: 3.
Waldum HL et al (2016) *Helicobacter pylori* and gastric acid: an intimate and reciprocal relationship. *Therapeutic Advances in Gastroenterology;* 9: 6, 836-844.
Zali H et al (2011) Gastric cancer: prevention, risk factors and treatment. *Gastroenterology and Hepatology from Bed to Bench;* 4: 4, 175-185.
Zhu H et al (2006) Bacterial killing in gastric juice – effect of pH and pepsin on *Escherichia coli* and *Helicobacter pylori*. *Journal of Medical Microbiology;* 55: Pt9, 1265-1270.

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