Peptic Ulcer Disease

Peptic ulcer disease is defined as: 'a set of disorders characterized by well circumscribed mucosal defects, founds only in portions of the gastrointestinal tract that are exposed to the acid and pepsin component of gastric juice. The ulcers can be erosions (not involving full thickness of mucosa) acute (full thickness of mucosa) of chronic (penetration depth varies, but muscularis mucosae is breached, and there is scarring at the ulcers base)

The stomach is a saclike organ, located between the oesophagus and the small intestine. Its functions are to store, dissolve, and partially digest the macromolecules in food and to regulate the rate at which the stomachs contents empty into the small intestine. The glands lining the stomach wall secrete hydrochloric acid, a strong acid, and several protein digesting enzymes collectively known as pepsin. Considering the high concentration of acid and pepsin secreted by the stomach, is would expected that the contents would lead to the breakdown of the stomach wall.

⇓

PROTECTION OF STOMACH WALL

⇓

The surface of the mucosa is lined with cells secreting a mucus that is of alkaline pH. The alkalinity is due to the presence of bicarbonate anions. This forms a protective layer over the luminal surface. The protein content and the alkalinity of the mucus result in the neutralisation of hydrogen ions on the epithelium surface.	**The tight junctions between the epithelial cells reduces the diffusion of hydrogen ions to the underlying layers of the stomach wall such as the mucosa.**	**Epithelial cells are constantly being replaced due to action in the gastric pits. Thus damage to the cells is not cumulative over prolonged periods of time.**

⇓

AETIOLOGY

⇓

Peptic ulcers can result due to a number of factors, the main including: high acid secretion, high pepsin secretion, reflux of duodenal content into the stomach and infection by *Helicobacter pylori*. Others include exposure to stress, Non-steroidal anti inflammatory drugs (NSAID's) such as asprin; cigarettes and alcohol.

⇓

PATHOLOGY

⇓

Sodium Taurocholate derived from the bile is present in the reflux of duodenal content. (Which can be due to reduction in pyloric sphincter tone) This decreases bicarbonate secretion and thus	**Increased acid secretion can be due to increased mass of parietal cells and an increase in the sensitivity of these cells to gastrin.. Increased pepsinogen secretion correlates with increased acid secretion since acidification is required to activate the pepsinogen. The increased acid concentration increases the concentration gradient**	***Helicobacter pylori* colonise in and beneath the layer of mucus protecting the gastric mucosa. It is found that *H. pylori* produces a variety of toxic substances such as ammonia, urease, mucinase, haemolysin and cytotoxins. All of these toxins are able to contribute to the**

reduces the pH gradient across the mucus layer. This effect is also caused by asprin. The degradation of the mucus layer, facilitates the decomposition of it by pepsin.	allowing an increased rate of back-diffusion of the acid through the mucus. Upon reaching the mucosa, the acid is able to corrode the layer, damaging the cells. The increased pepsin degrades the protective mucus layer, facilitating this process. Pepsin is a proteolytic enzyme and will hydrolyse any polypeptides that it may encounter, thus destroying the cells.	direct injury of the mucosa. Some, such as urease, can stimulate inflammation, thus reducing the mucosal integrity. It is thought that infection by *H. pylori* is a possible prerequisite, rather than a cause of peptic ulcer disease.

⇓

The overall effect of each of the factors is to reduce the effectiveness of the defence mechanisms. As a result of each of the problems, the gastric juice is able to come into direct contact with the stomach wall. The acid and pepsin content comes into contact with the epithelial layer of the mucosa and, by autodigestion, breaks down the layer of cells. This process of autodigestion continues throughout the mucosa. As a result there is inflammation due to the primary immune response, thus an ulcer results. Usually the ulcers are found in the duodenal bulb or the wall of the stomach.

⇓

COMPLICATIONS

⇓

Haemorrhage – This occurs with chronic ulcers as well as erosions. The acid gastric juice causes the ulcer by autodigestion and inflammatory response. The autodigestion of the stomach wall may include the destruction of blood vessels. This causes there to be bleeding points – haemorrhage. Such a complication can manifest as iron-deficiency anaemia and can be detected by haematemesis (vomiting of blood) and occult blood in stools.	Perforation – The gastric juice can cause the autodigestion of the stomach wall such that the ulcer erodes through the full thickness of the stomach wall. Such perforation allows the contents of the stomach or duodenum to enter the peritoneal cavity, causing peritonitis. This is when the peritoneum becomes acutely inflamed which results in very severe pain, and rigidity of the abdomen due to the irritation.	Pyloric Stenosis – Chronicity in inflammatory disorders is associated with scarring. In the presence of a chronic peptic ulcer, fibrous tissue (scarring) results. If the ulcer is in the prepyloric region, the fibrous tissue may cause the narrowing of the pylorus, resulting in pyloric stenosis in which the outflow of the stomach is obstructed, resulting in persistent vomiting.	Development of malignant tumour – The development of an 'ulcer cancer' is rare. That is: a carcinoma that has developed at the margins of a pre-existing chronic peptic ulcer. The prognosis and signs of such carcinoma will depend on degree of advancement.

⇓

TREATMENT

⇓

There are several types of treatments which act in different ways to treat peptic ulcers, before they lead to complications

Antibiotics – Antibiotics are used to treat the *H. pylori*	H_2 Receptor Antagonist – Such	Chelates and Complexes – Examples include: Tripotassium	Prostaglandin analogues – Prostaglandin deficiency	Proton-pump inhibitors – They act by

infection. A combination of three antibiotics is usually used. The three most common are: amoxycillin, clarithromycin and metronidazole. They act to inhibit the growth and replication of the bacteria on the mucosa. All of them are used in different proportions, usually with an acid suppressant for the best results of treatment of the infection.	**drugs heal peptic ulcers by reducing gastric acid output as a result of histamine hydrogen receptor blockade. Examples of hydrogen receptor antagonists include: cimetidine, famotidine, nizatidine, ranitidine.**	**dicitratobismuthate, a bismuth chelate which acts by absorbing pepsin, enhancing local prostaglandin synthesis and stimulating bicarbonate secretion. It also has a toxic effect on *H. pylori*. Another is sucralfate, which is a complex which can form complex gels with mucus which decreases the degradation of mucus by pepsin and reduces the diffusion of hydrogen ions through it.**	**may contribute to ulcer formation. Misoprostol is a stable prostaglandin analogue. It inhibits gastric acid secretion which occurs in response to food, histamine and caffeine by a direct action on the parietal cells. It maintains or increases blood flow to the mucosa, and increases the secretion of mucus and bicarbonate.**	**irreversibly inhibiting the proton pump, the terminal step in the acid secretory pathway. Thus they reduce the secretion of gastric acid. They are effective short-term treatments. Examples include: omeprazole, esomeprazole and lansoprazole.**

The treatments above all follow from the pathology of the disease, and understanding of the pathology is necessary when choosing the type of drug used to treat the ulcers.