Complications of peptic ulcers

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Abstract

Peptic ulcer disease, defined as the breakdown of the epithelial mucosal barrier of the stomach and/or duodenum, remains a cause of significant morbidity and mortality. Major aetiological factors include *Helicobacter pylori* infection and non-steroidal anti-inflammatory drug use. Epigastric pain, heartburn, reflux symptoms and nausea are common in patients with peptic ulceration. The diagnosis is most often established following upper gastrointestinal endoscopy. The introduction of acid-reducing pharmacological agents and *H. pylori* eradication regimes are the mainstay of current treatment. Surgical management is generally reserved for the management of the complications of peptic ulcer disease, such as acute haemorrhage, intestinal perforation and gastric outflow obstruction. Surgery in these circumstances is often challenging and may require a high level in expertise. This review will discuss the main aetiological agents involved in the development of peptic ulcer disease and describe the underlying pathogenesis. The diagnosis and management of uncomplicated peptic ulcer disease will then be outlined. Finally, the management of peptic ulcer complications will be detailed, with particular reference to the surgical aspects of care.

Keywords Complications; *Helicobacter pylori*; management; pathophysiology; peptic ulcer disease; perforation

Introduction

Peptic ulcer disease is defined as the breakdown of the defensive epithelial mucosal barrier of the stomach and/or duodenum characterized by inflammation and ulcer formation. Peptic ulceration, and its associated complications, has reduced in incidence since the introduction of effective acid suppressant therapy and the identification and treatment of *Helicobacter pylori* infection. However, peptic ulcer disease remains an important clinical burden; approximately 1 in 1000 patients are diagnosed with the condition every year in Western societies with appreciable associated morbidity. Diagnosis is usually made by endoscopic examination of the upper gastrointestinal tract (oesophago-gastro-duodenoscopy – OGD) and the majority of peptic ulcers are treated medically. Therapeutic endoscopy, interventional radiology and surgery are usually reserved for the management of complications of peptic ulcer disease: such as bleeding, perforation and outflow obstruction. This review will describe the main aetiological factors implicated in the development of peptic ulcer disease and outline the underlying pathogenesis associated with the development of ulceration. Investigation and treatment of peptic ulcer disease will be discussed with special emphasis on the recognition and management of the complications of peptic ulcer disease.

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Conflict of interest: none.

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Conflict of interest: none.

Aetiology and pathophysiology of peptic ulceration

Factors implicated in the development and progression of peptic ulceration are listed in Table 1. Of these, *H. pylori* infection and non-steroidal anti-inflammatory drugs (NSAIDS) play the biggest role.

Helicobacter pylori infection

H. pylori was discovered in 1983 when the bacterium was identified in many patients with active peptic ulceration. This landmark discovery challenged previous perceptions that peptic ulcer disease was primarily a condition of excessive acid secretion to one of an infective aetiology. Over half the world's population is thought to be currently infected with *H. pylori*; however, only approximately 5–10% of individuals will develop ulceration with most remaining asymptomatic. This variation in pathogenicity is partly explained by *H. pylori* genotype subtypes that produce strains of differing virulence. Subtype CagA (cytotoxin-associated gene A) and certain VacA (vacuolating cytotoxin A) code for major pathogenic proteins and are associated with increased pathogenicity. *H. pylori* infection is the most common aetiological factor associated with peptic ulceration and is present in approximately 95% of gastric and 70% of duodenal ulceration. Most *H. pylori* infections involve the gastric antral mucosa. The bacterium induces local irritation resulting in an inflammatory response within the mucosa leading to epithelial damage. To aid survival, *H. pylori* produces a urease enzyme, which converts urea to ammonia and carbon dioxide, and in turn buffers gastric acid and protects the organism from the hostile gastric environment. This local alkali environment is thought to have an inhibitory effect on somatostatin producing antral D cells, thus reducing somatostatin production and preventing the inhibition of gastrin secretion by antral G cells. Unregulated gastrin production results in hypergastrinaemia, parietal cell hyperplasia and increased gastric acid secretion[1] (Figure 1). There is also evidence that *H. pylori* infection can disrupt neural pathways controlling acid secretion and impair the inhibitory reflex that reduces acid production. Furthermore, the resulting increased acid production by the stomach reduces the pH within the duodenum, which in turn promotes gastric metaplasia that can then be further colonized by *H. pylori*.

Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs are a major aetiological factor associated with peptic ulceration in the Western world. It is estimated that approximately 1–2% of patients taking NSAIDs will develop clinically significant ulceration.[2] NSAIDs, including acetylsalicylic acid (ASA), may cause peptic injury by both local and systemic mechanisms. Some NSAIDs (for example, diclofenac and aspirin) are acidic and exert a direct local cytotoxic affect on mucosal epithelial cells, as well as potentially inhibit epithelial cell proliferation. Most NSAIDs, however, act via a systemic effect

Factors associated with the development and progression of peptic ulcer disease

Infective	*Helicobacter pylori* infection
	Cytomegalovirus
	Herpes simplex virus
Drugs	Non-steroidal anti-inflammatory drugs
	Acetylsalicylic acid (Aspirin)
	Corticosteroids
Increased acid production	Zollinger-Ellison syndrome (gastrinoma)
Post surgical	Anastomotic marginal following gastric surgery
Malignancy	Adenocarcinoma
	Lymphoma
Autoimmune	Crohn's disease
Stress	Secondary to burns (Curling's ulcer), head injury (Cushing's ulcer), trauma, sepsis and multiple organ failure
Life style	Alcohol intake
	Smoking
Idiopathic	

Table 1

through suppression of gastric prostaglandin synthesis via inhibition of the enzyme cyclooxygenase-1 (COX-1), and to a lesser extent COX-2. Prostaglandins act in a number of ways to protect the gastrointestinal tract against peptic mucosal injury, including stimulating mucus production that acts as a mechanical barrier protecting the intestinal epithelium from direct contact from acid and cytotoxic compounds. Prostaglandin also stimulates bicarbonate production that reduces luminal acid concentration, increases mucosal blood flow thus aiding damage repair and, at higher concentrations, the inhibition of acid secretion as well as down regulation of a number of inflammatory mediators associated with mucosal injury.[3]

Clinical features

Patients with uncomplicated peptic ulcer disease most commonly report abdominal pain. Approximately 80% of patients with endoscopically confirmed peptic ulceration will report epigastric pain, often in association with symptoms of 'dyspepsia' (bloating, belching, heartburn, nausea and reflux).[4] Pain secondary to gastric ulceration is classically described as worsened by eating, whereas pain arising from duodenal ulceration is typically relieved with intake of food or acid-neutralizing agents and worse at times of fasting ('hunger pangs'). In clinical practice, this distinction is not always readily apparent. Chronic ulcers may be asymptomatic, a finding particularly common in patients taking analgesic NSAIDs. Complications from peptic ulcer disease are decreasing in incidence with the introduction of acid suppression therapy and *H. pylori* eradication. The most frequent complication is bleeding from vessel erosion resulting in features of gastrointestinal blood loss – specifically, haematemesis, melaena and, at times, potentially life threatening hypovolemic shock. In some situations the bleeding may be occult and iron deficiency anaemia is noted. Patients can also present with a

Pathways involved in the pathophysiology of *Helicobacter pylori* infection associated peptic ulcer disease

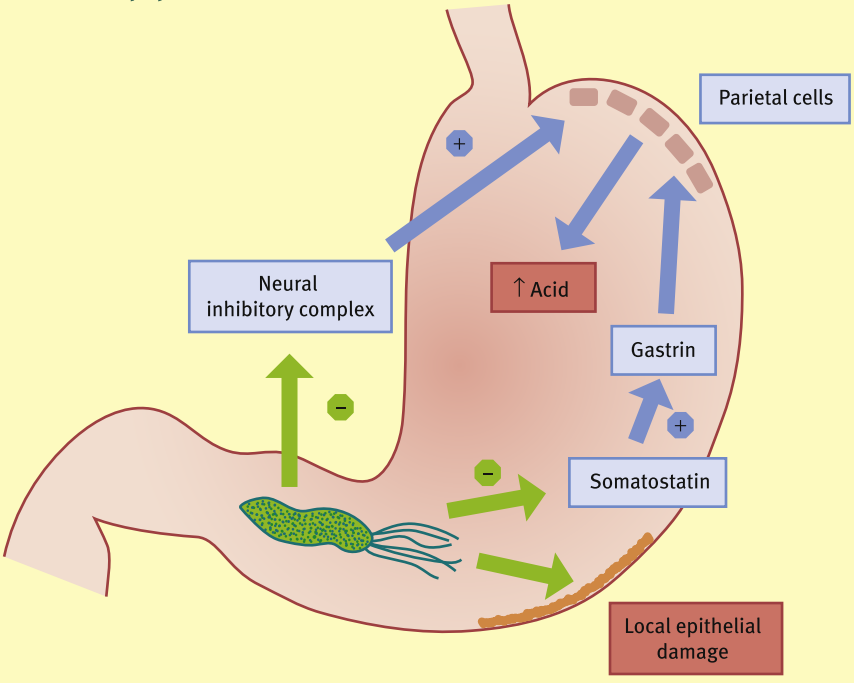

Figure 1