全国高等医药院校规划双语教材

Bailey & Love

外科学

SHORT PRACTICE OF SURGERY

第24版

原著 R.C.G. Russell
Norman S. Williams
Christopher J.K. Bulstrode

主编 陈孝平 刘允怡
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第5卷

腹部外科和小儿外科

人民卫生出版社

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CHAPTER 69

STOMACH AND DUODENUM

LEARNING OBJECTIVES

- To understand the gross and microscopic anatomy and pathophysiology of the stomach in relation to disease
- To be able to decide on the most appropriate techniques to use in the investigation of patients with complaints relating to the stomach and duodenum
- To understand the critical importance of gastritis and *Helicobacter pylori* in upper gastrointestinal disease
- To be able to investigate and treat peptic ulcer disease and its complications
- To be able to recognise the presentation of gastric cancer and understand the principles involved in its treatment
- To know about the causes of duodenal obstruction and the presentation of duodenal tumours

INTRODUCTION

The function of the stomach is to act as a reservoir for ingested food. It also serves to break down foodstuffs mechanically and commence the processes of digestion before these products are passed on into the duodenum.

GROSS ANATOMY OF THE STOMACH AND DUODENUM

Blood supply

Arteries

The stomach is richly endowed with an arterial supply on both lesser and greater curves (Fig. 69.1). On the lesser curve, the left gastric artery, a branch of the coeliac axis, forms an anastomotic arcade with the right gastric artery, which arises from the common hepatic artery. Branches of the left gastric artery pass up towards the cardia. The gastroduodenal artery, which is also a branch of the hepatic artery, passes behind the first part of the duodenum, highly relevant with respect to the bleeding duodenal ulcer. Here it divides into the superior pancreaticoduodenal artery and the right gastroepiploic artery. The superior pancreaticoduodenal artery supplies the duodenum and pancreatic head, and forms an anastomosis with the inferior pancreaticoduodenal artery, a branch of the superior mesenteric artery. The right gastroepiploic artery runs along the greater curvature of the stomach, eventually forming an anastomosis with the left gastroepiploic artery, a branch of the splenic artery. This vascular arcade, however, is often variably incomplete. The fundus of the stomach is supplied by the vasa brevia (or short gastric arteries), which arise from near the termination of the splenic artery.

Veins

In general, the veins are equivalent to the arteries, those along the lesser curve ending in the portal vein and those on the greater curve joining via the splenic vein. On the lesser curve, the coronary vein is particularly important. It runs up the lesser curve towards the oesophagus and then passes left to right to join the portal vein. This vein becomes markedly dilated in portal hypertension.

Lymphatics

The lymphatics of the stomach are of considerable importance in the surgery of gastric cancer and are therefore described in detail in that section.

Nerves

As with all of the gastrointestinal tract, the stomach and duodenum possess both intrinsic and extrinsic nerve supplies. The

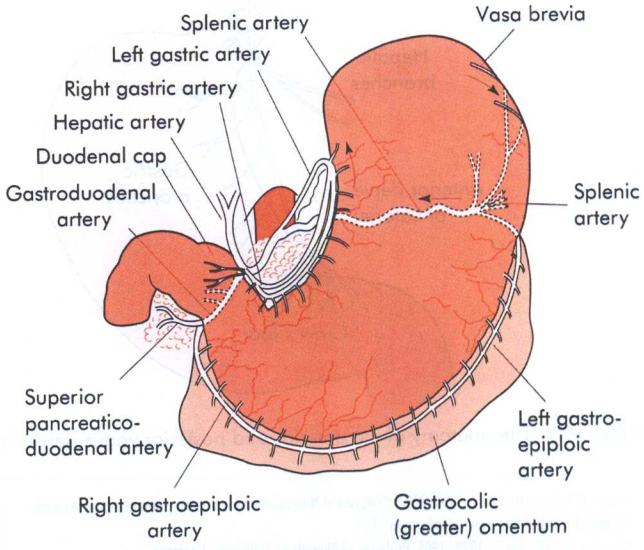

Figure 69.1 The arterial blood supply of the stomach.

intrinsic nerves exist principally in two plexuses, the myenteric plexus of Auerbach and the submucosal plexus of Meissner. Compared with the rest of the gut, the submucosal plexus of the stomach contains relatively few ganglionic cells, as does the myenteric plexus in the fundus. However, in the antrum the ganglia of the myenteric plexus are well developed. The extrinsic supply is derived mainly from the vagus nerves, fibres of which originate in the brainstem. The vagal plexus around the oesophagus condenses into bundles that pass through the oesophageal hiatus (Fig. 69.2), the posterior bundle being usually identifiable as a large nerve trunk. Vagal fibres are both afferent (sensory) and efferent. The efferent fibres are involved in the receptive relaxation of the stomach and the stimulation of gastric motility, as well as having the well-known secretory function. The sympathetic supply is derived mainly from the coeliac ganglia.

MICROSCOPIC ANATOMY OF THE STOMACH AND DUODENUM

The gastric epithelial cells are mucus producing and are turned over rapidly. In the pyloric part of the stomach, and also the duodenum, mucus-secreting glands are found. Most of the specialised cells of the stomach (parietal and chief cells) are found in the gastric crypts (Fig. 69.3). The stomach is also richly endowed with endocrine cells.

Parietal cells

These are in the body (acid-secreting portion) of the stomach and line the gastric crypts, being more abundant distally. They are responsible for the production of hydrogen ions to form hydrochloric acid, which has a pH of around 1. The hydrogen ions are actively pumped by the proton pump, a hydrogen–potassium-ATPase (Sachs), which exchanges intraluminal potassium for hydrogen ions. The potassium ions enter the lumen of the crypts passively, but the hydrogen ions are pumped against an immense concentration gradient (1 000 000:1), explaining the fact that this is an energy-consuming process.

Chief cells

These lie principally proximally in the gastric crypts and produce pepsinogen. Two forms of pepsinogen are described: pepsinogen I and pepsinogen II. Both are produced by the chief cell, but pepsinogen I is produced only in the stomach. The ratio between pepsinogens I and II in the serum decreases with gastric atrophy. Pepsinogen is activated in the stomach to produce pepsin, the active enzyme.

Endocrine cells

The stomach is richly endowed with endocrine cells, which are critical to its function. In the gastric antrum, the mucosa contains G cells, which produce gastrin. Throughout the body of the stomach, enterochromaffin-like (ECL) cells are abundant and produce histamine, a key factor in driving gastric acid secretion. In addition, there are large numbers of somatostatin-producing D cells throughout the stomach, and somatostatin has a negative regulatory role. The peptides and neuropeptides produced in the stomach are discussed later.

Duodenum

The duodenum is lined by a mucus-secreting columnar epithelium. In addition, Brunner's glands lie beneath the mucosa and are similar to the pyloric glands in the pyloric part of the stomach. Endocrine cells in the duodenum produce cholecystokinin and secretin.

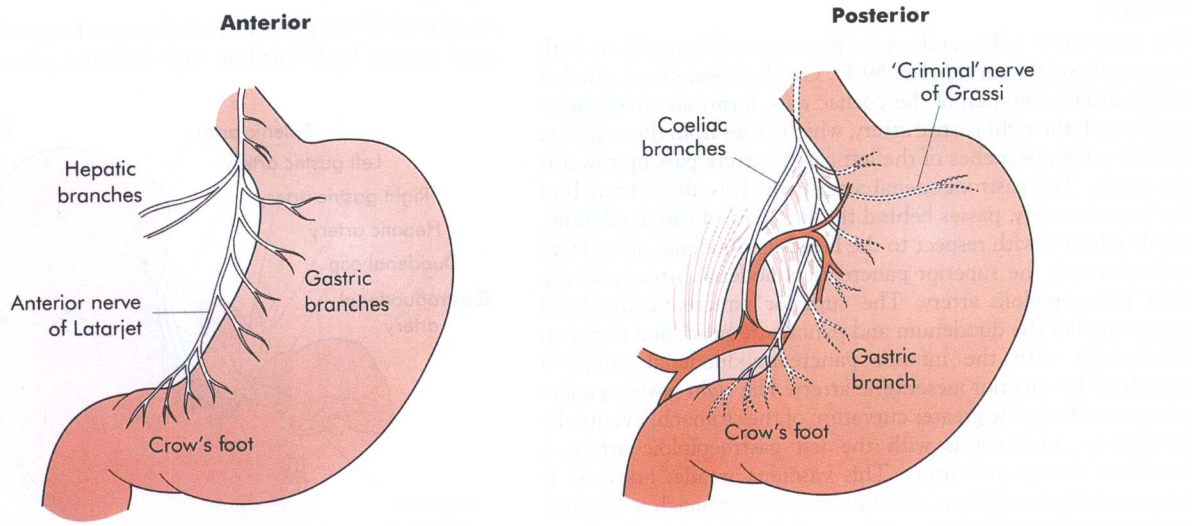

Figure 69.2 The anatomy of the anterior and posterior vagus nerves in relation to the stomach.

Leopold Auerbach | 1828–1897. Professor of Neuropathology, Breslau, Germany (now Wroclaw, Poland). Described the myenteric plexus in 1862.
Georg Meissner | 1829–1905. Professor of Physiology, Gottingen, Germany.

George Sachs | Discoverer of the proton pump, Professor of Medicine, CURE, Los Angeles, CA, USA.
Johann Conrad Brunner | 1653–1729. Professor of Anatomy, Heidelberg, Germany, and later at Strasbourg, France.

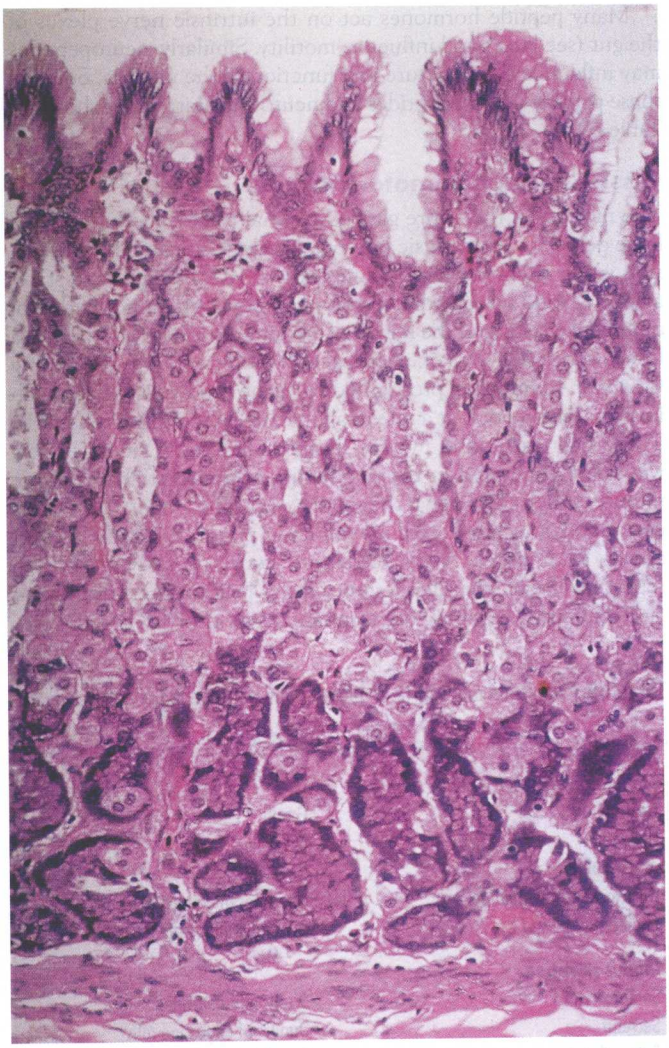

Figure 69.3 The histological appearance of a gastric gland. The mucus-secreting cells are seen at the mucosal surface, the eosinophilic parietal cells superficially in the glands, and the basophilic chief cells in the deepest layer.

Box 69.1
The anatomy and physiology of the stomach

- The stomach acts as a reservoir for food and commences the process of digestion
- Gastric acid is produced by a proton pump in the parietal cells, which in turn is controlled by histamine acting on the H_2-receptors
- The histamine is produced by the endocrine gastric ECL cells in response to a number of factors, particularly gastrin and the vagus
- Proton pump inhibitors abolish gastric acid production, whereas H_2-receptor antagonists only markedly reduce it
- The gastric mucous layer is essential to the integrity of the gastric mucosa

PHYSIOLOGY OF THE STOMACH AND DUODENUM (Box 69.1)

The stomach mechanically breaks up ingested food and, together with the actions of acid and pepsin, forms chyme that passes into the duodenum. In contrast with the acidic environment of the stomach, the environment of the duodenum is alkaline, as a result of the secretion of bicarbonate ions from both the pancreas and the duodenum. This neutralises the acid chyme and adjusts the osmolarity to approximately, which of plasma. Endocrine cells in the duodenum produce cholecystokinin, which stimulates the pancreas to produce trypsin and the gall bladder to contract. Secretin is also produced by the endocrine cells of the duodenum. This hormone inhibits gastric acid secretion and promotes production of bicarbonate by the pancreas.

Gastric acid secretion

The secretion of gastric acid and pepsin tends to run in parallel, although the understanding of the mechanisms of gastric acid secretion is considerably greater than that of pepsin. Numerous factors are involved to some degree in the production of the gastric acid. These include neurotransmitters, neuropeptides and peptide hormones, and several other factors. This complexity need not detract from the fact that there are basic principles that are relatively easily understood (Fig. 69.4). As mentioned above, hydrogen ions are produced by the parietal cell by the proton pump. Although there is a multiplicity of factors that can act on the parietal cell, the most important of these is histamine, which acts via the H_2-receptor. Histamine is produced, in turn, by the ECL cells of the stomach and acts in a paracrine (local) fashion on the parietal cells. These relationships explain why proton pump inhibitors can abolish gastric acid secretion, as they act on the final common pathway secretion, and why H_2-receptor antagonists have such profound effects on gastric acid secretion, even though this is not insurmountable (Fig. 69.4). The ECL cell produces histamine in response to a number of stimuli that include the vagus and gastrin. Gastrin is released by the G cells in response to the presence of the food in the stomach. The production of gastrin is inhibited by acid, hence creating a negative feedback loop. Various other peptides, including secretin, inhibit gastric acid secretion.

Classically, three phases of gastric secretion are described. The *cephalic phase* is mediated by vagal activity, secondary to sensory

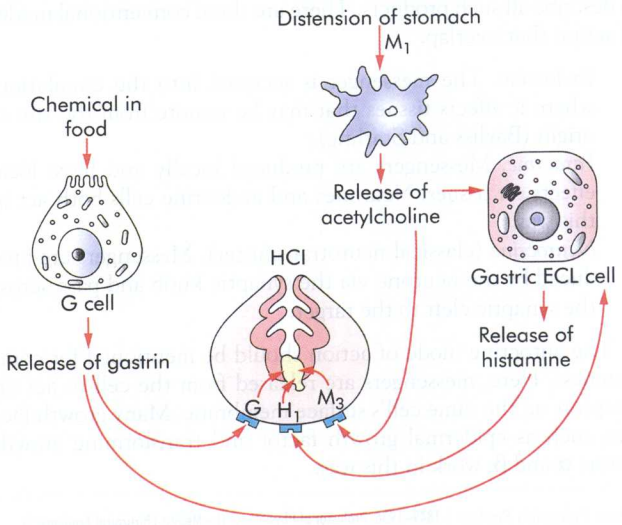

Figure 69.4 The parietal cell in relation to the mechanism of gastric acid secretion. G, gastrin receptor; H, histamine receptor; M, muscarinic receptor.

arousal as first demonstrated by Pavlov. The *gastric phase* is a response to food within the stomach, which is mediated principally, but not exclusively, by gastrin. In the *intestinal phase*, the presence of chyme in the duodenum and small bowel inhibits gastric emptying and, as mentioned above, the acidification of the duodenum leads to the production of secretin, which also inhibits gastric acid secretion, along with numerous other peptides originating from the gut. The stomach also possesses somatostatin-containing D cells. Somatostatin is released in response to a number of factors including acidification. This peptide acts probably on the G cell, the ECL cell and the parietal cell itself to inhibit the production of acid.

Gastric mucus and the gastric mucosal barrier

The gastric mucous layer is essential to the integrity of the gastric mucosa. It is a viscid layer of mucopolysaccharides produced by the mucus-producing cells of the stomach and the pyloric glands. Gastric mucus is an important physiological barrier to protect the gastric mucosa from mechanical damage, and also the effects of acid and pepsin. Its considerable buffering capacity is enhanced by the presence of bicarbonate ions within the mucus. Many factors can lead to the breakdown of this gastric mucous barrier. These include bile, non-steroidal anti-inflammatory drugs (NSAIDs), alcohol, trauma and shock. Tonometry studies have shown that, of all the gastrointestinal tract, the stomach is the most sensitive to ischaemia following a hypovolaemic insult and also the slowest to recover. This may explain the high incidence of stress ulceration in the stomach.

Peptides and neuropeptides in the stomach and duodenum

As with most of the gastrointestinal tract, the stomach is richly endowed with sources of peptide hormones and neurotransmitters. Previously, nerves and endocrine cells were considered distinct in terms of their products. However, it is increasingly realised that there is enormous overlap within these systems. Many peptides recognised as hormones may also be produced by neurones, hence the term neuropeptides. The term 'messenger' can be used to describe all such products. There are three conventional modes of action that overlap.

1. *Endocrine*. The messenger is secreted into the circulation, where it affects tissues that may be remote from the site of origin (Bayliss and Starling).
2. *Paracrine*. Messengers are produced locally and have local effects on tissues. Neurones and endocrine cells both act in this way.
3. *Neurocrine* (classical neurotransmitter). Messengers are produced by the neurone via the synaptic knob and pass across the synaptic cleft to the target.

The autocrine mode of action should be mentioned for completeness. Here, messengers are released from the cell to act on receptors on the same cell's surface membrane. Many growth factors, such as epidermal growth factor and transforming growth factors α and β, work in this way.

Ivan Petrovich Pavlov | 1849–1936. Professor of Physiology, The Medico-Chirurgical Academy, St Petersburg, Russia.
William Maddock Bayliss | 1860–1924. Physiologist, University College, London, England.
Ernest Henry Starling | 1866–1927. Physiologist, University College, London, England.

Many peptide hormones act on the intrinsic nerve plexus of the gut (see later) and influence motility. Similarly, neuropeptides may influence the structure and function of the mucosa. Some of these peptides, neuropeptides and neurotransmitters are shown in Table 69.1.

Gastroduodenal motor activity

The motility of the entire gastrointestinal tract is modulated to a large degree by its intrinsic nervous system. Critical in this discussion is the migrating motor complex (MMC). In the fasted state, and after food has cleared, in the small bowel there is a period of quiescence lasting in the region of 40 minutes (phase I). There follows a series of waves of electrical and motor activity, also lasting for about 40 minutes, propagated from the fundus of the stomach in a caudal direction at a rate of about three per minute (phase II). These pass as far the pylorus, but not beyond. Duodenal slow waves are generated in the duodenum at a rate of about 10 per minute, which carry down the small bowel. The amplitude of these contractions increases to a maximum in phase III, which lasts for about 10 minutes. This 90-minute cycle of activity is then repeated. From the duodenum, the MMC moves distally at 5–10 cm min^{-1}, reaching the terminal ileum after 1.5 hours.

Table 69.1 Function and source of peptides and neuropeptides in the stomach

Function	Source
Stimulate secretion	
Gastrin	G cells
Histamine	ECL cells
Acetylcholine	Neurones
Gastrin-releasing peptide	Neurones and mucosa
Cholecystokinin (CCK)	Duodenal endocrine cells
Inhibit secretion	
Somatostatin	D cells and neurones
Secretin	Duodenal endocrine cells
Enteroglucagon	Small intestinal endocrine cells
Prostaglandins	Mucosa
Neurotensin	Neurones
GIP	Duodenal and jejunal endocrine cells
PYY	Small intestinal endocrine cells
Stimulate motility	
Acetylcholine	Neurones
5-HT	Neurones
Histamine	ECL cell
Substance P	Neurones
Substance K	Neurones
Motilin	Neurones
Gastrin	G cells
Angiotensin	
Inhibit motility	
Somatostatin	D cells and neurones
VIP	Neurones
Nitric oxide	Neurones and smooth muscle
Noradrenaline	Neurones
Encephalin	Neurones
Dopamine	Neurones

ECL, enterochromaffin-like cells; GIP, gastric inhibitory polypeptide; PYY, peptide YY; VIP, vasoactive intestinal peptide.

Following a meal, the stomach exhibits receptive relaxation, which lasts for a few seconds. Following this, adaptive relaxation occurs, which allows the proximal stomach to act as a reservoir. Most of the peristaltic activity is found in the distal stomach (the antral mill) and the proximal stomach demonstrates only tonic activity. The pylorus, which is most commonly open, contracts with the peristaltic wave and allows only a few millilitres through at a time. The antral contraction against the closed sphincter is important in the milling activity of the stomach. Although the duodenum is capable of generating 10 waves per minute, after a meal it only contacts after an antral wave reaches the pylorus. The coordination of the motility of the antrum, pylorus and duodenum means that only small quantities of food reach the small bowel at a time. Motility is influenced by numerous factors, including mechanical stimulation and neuronal and endocrine influences (Table 69.1).

INVESTIGATION OF THE STOMACH AND DUODENUM (Box 69.2)

Flexible endoscopy

Among all of the methods used to investigate and image the stomach and duodenum, flexible endoscopy is now the 'gold standard'. The original flexible gastroscopes were fibreoptic (Hirschowitz), but now most use a solid-state camera mounted at the instrument's tip (Figs 69.5 and 69.6). The main advantage of the modern instruments is that they do not need the fragile fibreoptic fibre bundle to transmit the image. In addition, as the output is via a monitor rather than an eyepiece, the other members of the endoscopy team see the image. This is useful when taking biopsies or performing interventional techniques, and also facilitates teaching and training.

Flexible endoscopy is more sensitive than conventional radiology in the assessment of the majority of gastroduodenal conditions. This is particularly the case with peptic ulceration, gastritis and duodenitis. In upper gastrointestinal bleeding, endoscopy is far superior to any other investigation and, in most circumstances, is the only imaging required. Although in Japan double-contrast barium meals performed by very experienced radiologists are able to detect quite small gastric cancers, endoscopy is superior in most centres and also allows biopsies to be taken.

Fibreoptic endoscopy is a generally a safe investigation, but it is important that all personnel undertaking this procedure are adequately trained and that resuscitation facilities are always available. Although the morbidity and mortality associated with upper gastrointestinal endoscopy are extremely low, the technique is not without hazard. Careless and rough handling of the endoscope during intubation of a patient may result in perforations of the pharynx and oesophagus. Any other part of the upper gastrointestinal tract may also be perforated. An inadequately performed endoscopy is also dangerous as a serious condition may be overlooked. This is particularly the case in respect of early and curable gastric cancer, the appearances of which may often be extremely subtle and may be missed by inexperienced endoscopists. A more experienced endoscopist will have a higher index of suspicion for any mucosal abnormalities and will take more biopsies. Spraying the mucosa with dye endoscopically may allow better discrimination between normal and abnormal mucosa, so allowing small cancer to be more easily seen. In the future, advances in technology may allow 'optical biopsy' to determine the nature of mucosal abnormalities in real time.

Upper gastrointestinal endoscopy is normally carried out under sedation, usually with incremental doses of a benzodi-

Box 69.2
The investigation of gastric disorders

- Flexible endoscopy is the most commonly used and sensitive technique for investigating the stomach and duodenum
- Great care needs to be exercised in performing endoscopy to avoid complications and missing important pathology
- Axial imaging, particularly multislice CT, is useful in the staging of gastric cancer, although it may be less sensitive in the detection of liver metastases than other modalities
- Endoscopic ultrasound is the most sensitive technique in the evaluation of the 'T' stage of gastric cancer
- Laparoscopy is very sensitive in detecting peritoneal metastases, and laparoscopic ultrasound provides an accurate evaluation of lymph node and liver metastases

Basil I. Hirschowitz | Professor of Medicine, Birmingham, AL, USA.

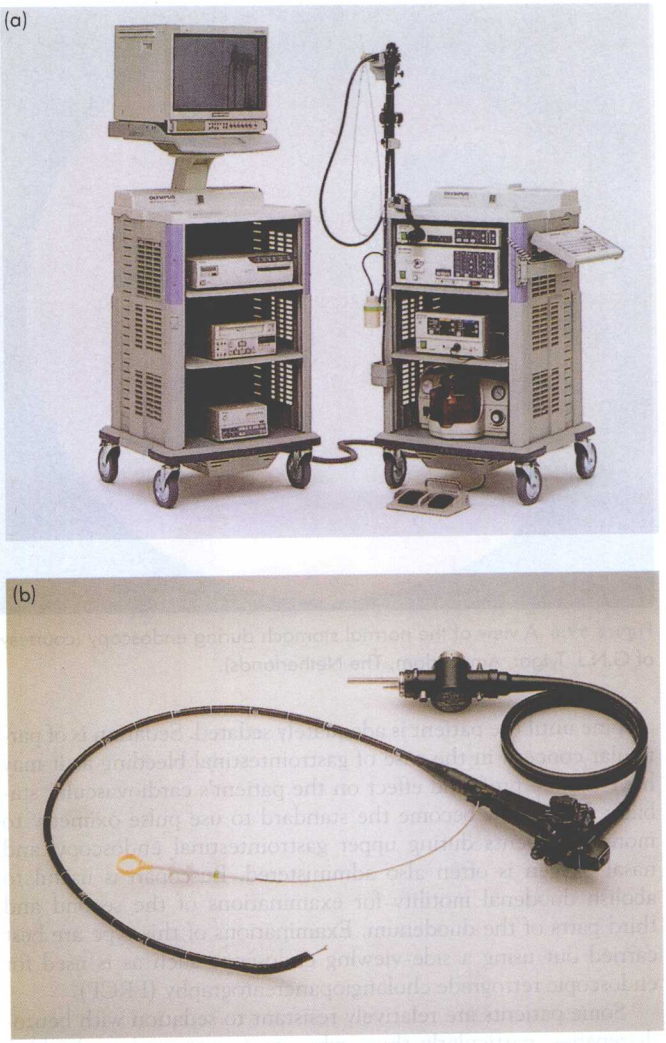

Figure 69.5 A video-gastroscope [courtesy of Keymed (Medical and Industrial Equipment) Ltd]. (a) The camera stack. (b) The gastroscope, and biopsy forceps, in the working channel.

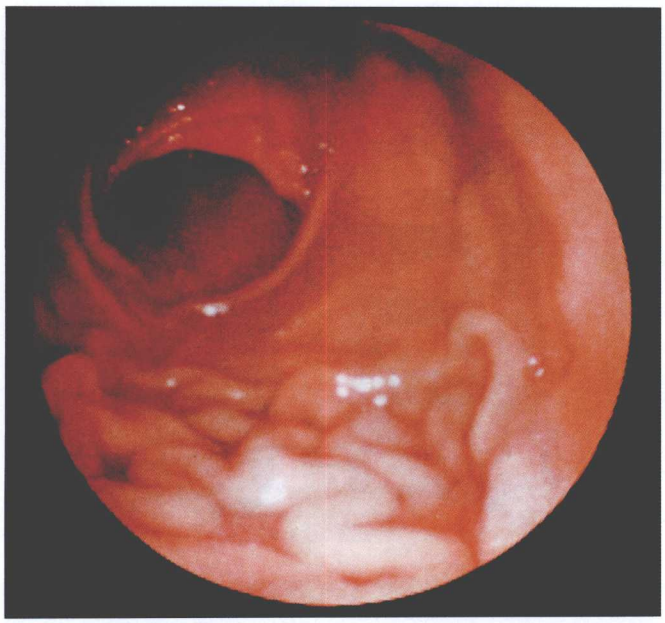

Figure 69.6 A view of the normal stomach during endoscopy (courtesy of G.N.J. Tytgat, Amsterdam, The Netherlands).

azepine until the patient is adequately sedated. Sedation is of particular concern in the case of gastrointestinal bleeding as it may have a more profound effect on the patient's cardiovascular stability. It has now become the standard to use pulse oximetry to monitor patients during upper gastrointestinal endoscopy, and nasal oxygen is often also administered. Buscopan is useful to abolish duodenal motility for examinations of the second and third parts of the duodenum. Examinations of this type are best carried out using a side-viewing endoscope such as is used for endoscopic retrograde cholangiopancreatography (ERCP).

Some patients are relatively resistant to sedation with benzodiazepenes, particularly those who are accustomed to drinking alcohol. Increasing the dose of benzodiazepines in these patients may not result in any useful sedation, but merely make the patient more restless and confused. Such patients are sometimes better endoscoped fully awake using a local anaesthetic throat spray and a narrow-gauge endoscope. Whatever the circumstances, it is important that resuscitation facilities are available including agents that reverse the effects of benzodiazepines, such as flumazenil.

The technology associated with upper gastrointestinal endoscopy is continuing to advance. Instruments which allow both endoscopy and endoluminal ultrasound to be performed simultaneously (see later) are used routinely. Bleeding from the stomach and duodenum can be treated with a number of haemostatic measures. These include injection with various substances, diathermy, heater probes and lasers. These approaches appear to be useful in the treatment of bleeding ulcers, although there are few good controlled trials in this area. There is no good evidence that such interventional procedures at the moment work in patients who are bleeding from very large vessels, such as the gastroduodenal artery or splenic artery, although technology may overcome this problem in future.

Contrast radiology

Upper gastrointestinal radiology is not used as much as in previous years, as endoscopy is a more sensitive investigation for most gastric problems. However, there are a number of circumstances in which the barium meal is of great value and augments the value of endoscopy. These include large hiatus hernias of the rolling type, and chronic gastric volvulus, in which it may be difficult for the endoscopist to determine exactly the anatomy or, indeed, negotiate the deformity to see the distal stomach. Linitus plastica may be missed by even relatively experienced endoscopists, as the mucosal aspect of the stomach may not look particularly abnormal. This condition may be diagnosed more easily by using contrast radiology, although this is of limited value to the patient as the outlook is so poor.

Ultrasonography

Standard ultrasound imaging can be used to investigate the stomach, particularly in patients with neoplasia. Thickening of the gastric wall can be seen in malignancy, some assessment made of local invasion, and liver and peritoneal disease is often detected. However, used conventionally, it is less sensitive than other modalities. In contrast, endoluminal ultrasound and laparoscopic ultrasound are probably the most sensitive techniques available in the preoperative staging of gastric cancer. In endoluminal ultrasound, the transducer is usually attached to the distal tip of the instrument. However, devices have been developed which may be passed down the biopsy channel, albeit with poorer image quality. Five layers (Fig. 69.7) of the gastric wall may be identified on endoluminal ultrasound and the depth of invasion of a tumour can be assessed with exquisite accuracy (90% accuracy for the 'T' component of the staging). Enlarged lymph nodes can also be identified and the technique's accuracy in this situation is about 80%. Finally, it may be possible to identify liver metastases not seen on axial imaging. Laparoscopic ultrasound is also a very sensitive imaging modality to a large measure because of the laparoscopy itself (below). It is one of the most sensitive methods of detecting liver metastases from gastric cancer.

An additional use of ultrasound is in the assessment of gastric emptying. Swallowed contrast is utilised, which is designed to be easily seen using an ultrasound transducer. The emptying of this contrast is then followed directly. The accuracy of the technique is similar to that of radioisotope gastric emptying studies (below).

Computerised tomography scanning and magnetic resonance imaging

The resolution of the computerised tomography (CT) scanners is continuing to improve, and multislice CT is of increasing value in the investigation of the stomach, especially gastric malignancies (Fig. 69.8). The presence of gastric wall thickening associated

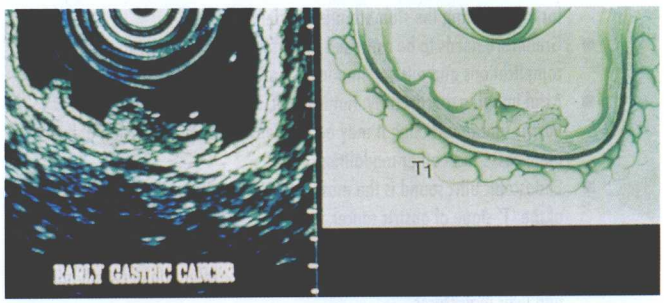

Figure 69.7 Endoscopic ultrasound of the stomach. Five layers can be identified in the normal stomach. A gastric cancer is shown invading the muscle of the gastric wall [courtesy of KeyMed (Medical and Industrial Equipment Ltd)].

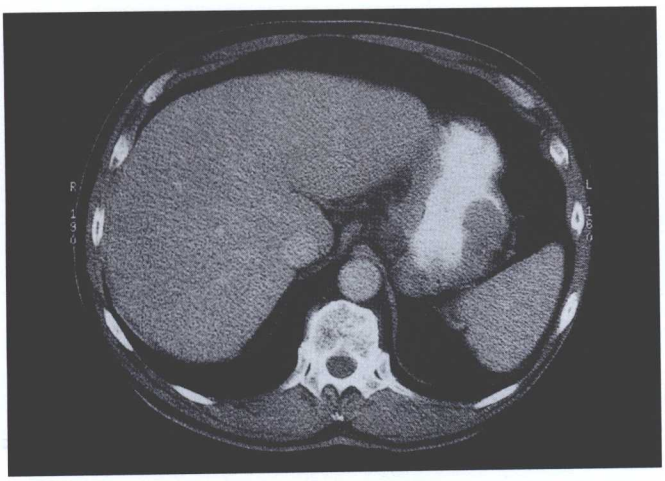

Figure 69.8 A computerised tomography (CT) scan of the abdomen, showing a gastric cancer arising in the body of the stomach.

with a carcinoma of any reasonable size can be easily detected by CT, but the investigation lacks sensitivity in detecting smaller and curable lesions. It is much less accurate in 'T' staging than endoluminal ultrasound. Lymph node enlargement can be detected and, based on the size and shape of the nodes, it is possible to be reasonably accurate in detecting nodal involvement with tumour. However, as with all imaging techniques, it is limited. Microscopic tumour deposits in lymph nodes cannot be detected when the node is not enlarged and, in contrast, lymph nodes may undergo reactive enlargement but not contain tumour. These problems apply to all imaging techniques.

The detection of small liver metastases is improving, although in general terms metastases from gastric cancer are less easy to detect using CT than those, for instance, from colorectal cancer. This is because metastases from gastric cancer may be of the same density as liver and may not handle the intravenous contrast any differently. At present, magnetic resonance imaging (MRI) scanning does not offer any specific advantage in assessing the stomach, although it has a higher sensitivity for the detection of gastric cancer liver metastases than conventional CT imaging.

Laparoscopy

This technique is now well used in the assessment of patients with gastric cancer. Its particular value is in the detection of peritoneal disease, which is difficult by any other technique, unless the patient has ascites or bulky intraperitoneal disease. Its main limitation is in the evaluation of posterior extension but other techniques are available to evaluate posterior invasion, especially CT and endoluminal ultrasound. Usually laparoscopy is combined with peritoneal cytology unless laparotomy follows immediately.

Gastric emptying studies

These are useful in the study of gastric dysmotility problems, particularly those that follow gastric surgery. The principle of the examination is that a radioisotope-labelled liquid and solid meal are ingested by the patient and the emptying of the stomach is followed on a gamma camera. This allows the proportion of activity in the remaining stomach to be assessed numerically, and it is possible to follow liquid and solid gastric emptying independently (Fig. 69.9).

Angiography

Angiography is used most commonly in the investigation of upper gastrointestinal bleeding that is not identified using endoscopy. Therapeutic embolisation may also be of value in the treatment of bleeding in patients in whom surgery is difficult or inadvisable.

Other gastric investigations

In the past, measurement of gastric acid secretion was commonly performed, but these tests are now seldom used as gastric acidity can be completely abolished pharmacologically. Gastric motility may be measured in some specialist units. Plasma gastrin may be measured as part of the investigation of patients with suspected gastrinoma.

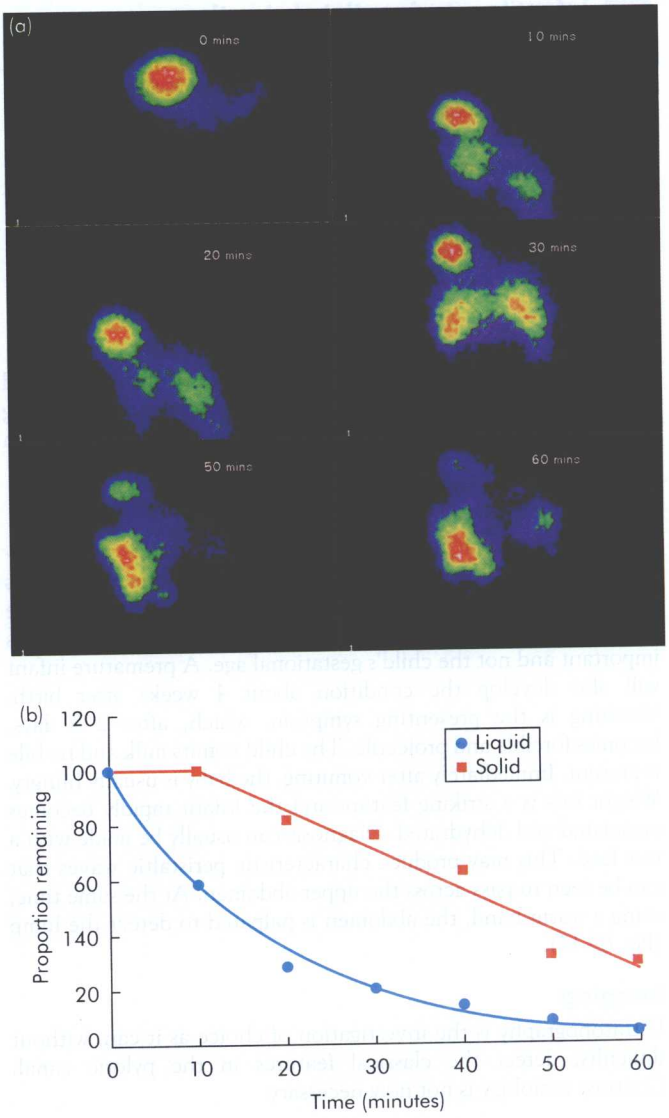

Figure 69.9 Dual-phase solid and liquid gastric emptying. The use of two isotopic labels allows the liquid and solid phases of the emptying to be followed separately. (a) Image acquisition. (b) Gastric emptying curves in a normal individual showing typical lag period in solid phase before linear emptying (courtesy of Dr V. Lewington, Southampton, England).

PAEDIATRIC DISORDERS

Hypertrophic pyloric stenosis of infancy (Box 69.3)

Aetiology

The incidence of this condition is approximately three cases per 1000 births. It is four times as common in males as in females and the aetiology is unknown. It may be that the condition is analogous to achalasia of the oesophagus, in which there is a failure of the pylorus to relax, leading to the muscular hypertrophy. In some cases, there seems to be a familial association. In such families, the mother is found to have suffered from the condition in 50% of cases, and 10% of male siblings and 2% of female siblings are affected.

Box 69.3
Infantile gastric outlet obstruction

- Occurs in 3 per 1000 babies and four times as many boys as girls
- It most commonly presents at 4 weeks of age and vomiting of milk without bile staining is the most obvious clinical feature
- Ultrasound is the investigation of choice
- Ramstedt's operation (pyloromyotomy) is the procedure of choice
- Duodenal atresia presents with bile-stained vomiting in the neonate but the diagnosis is often made antenatally by ultrasound
- Duodenoduodenostomy is the treatment of choice

Pathology

The classical feature is that the musculature of the pylorus and adjacent antrum is grossly hypertrophied, the hypertrophy being maximum in the pylorus itself. The mucosa is compressed such that only a probe can be inserted.

Clinical features

Characteristically, it is a first-born male child that is most commonly affected. The condition is most commonly seen 4 weeks after birth, ranging from the third week to, on rare occasions, the seventh. Inexplicably, it is the time following birth that seems important and not the child's gestational age. A premature infant will also develop the condition about 4 weeks after birth. Vomiting is the presenting symptom, which, after 2–3 days, becomes forcible and projectile. The child vomits milk and no bile is present. Immediately after vomiting, the baby is usually hungry. Weight loss is a striking feature and the infant rapidly becomes emaciated and dehydrated. Diagnosis can usually be made with a test feed. This may produce characteristic peristaltic waves that can be seen to pass across the upper abdomen. At the same time, using a warm hand, the abdomen is palpated to detect the lump (Fig. 69.10).

Imaging

Ultrasonography is the investigation of choice as it can, without difficulty, detect the classical features in the pyloric canal. Contrast radiology is not now necessary.

Differential diagnosis

The common conditions from which pyloric stenosis must be differentiated are gastro-oesophageal reflux, feeding problems, urinary tract infection and raised intracranial pressure. The condition cannot normally be confused with duodenal atresia or intestinal obstruction because of the absence of bile in the milk vomit.

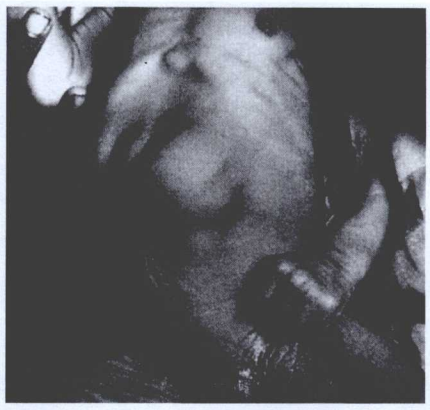

Figure 69.10 Visible persitalsis in an infant with hypertrophic pyloric stenosis. This was induced by a test feed.

Treatment

Following diagnosis, the first concern is to correct the metabolic abnormalities. Essentially this is the same situation that pertains in adults, with the patient being dehydrated, with low sodium, chloride and potassium, and a metabolic alkalosis. The child should be rehydrated with dextrose–saline and potassium (2.5% dextrose plus 0.45% sodium chloride plus 1 g of potassium chloride per 500 ml of fluid). This will restore the infant's clinical condition and return electrolytes to normal. Following this, operation is required. Conservative treatment has little place in the management of this condition, as with appropriate surgical treatment recovery is virtually 100%.

Ramstedt's operation

In preparing the child for operation it is important that the stomach is emptied and washed out with saline, and that hypothermia is avoided. To achieve this, the patient is encased in cotton wool, allowing exposure of the upper abdomen. Operation is performed under general anaesthesia, although it is possible to perform the procedure under a local anaesthetic. The skin is opened through a transverse incision placed in the upper abdomen over the right rectus sheath, which is opened in the same line. The rectus muscle is then split along the line of its fibres and the posterior rectus sheath is opened in the line of the skin incision. The hypertrophied pylorus is delivered and rotated so that its superior surface comes into view (Fig. 69.11). Thus, the least vascular portion can be selected for incision. To ascertain the distal limit of the hypertrophy, the surgeon invaginates the duodenum with the index finger. The incision is made through the serosa only and from this point along the whole length of the pylorus and, importantly, the distal antrum. The hypertrophied pylorus has the consistency of an unripe pear, hence splitting the muscle coats can be accomplished by blunt dissection (Fig. 69.11). On separating the edges with artery forceps, the pyloric mucosa bulges into the cleft which has been made in the muscle. Great care is taken not to penetrate

Wilhelm Conrad Ramstedt | 1867–1963. Surgeon, Rafael Clinic, Munster, Germany. Performed his first pylorotomy in 1911.

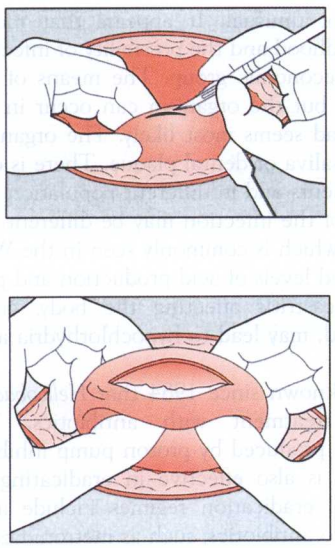

Figure 69.11 Ramstedt's operation, showing the mucosa bulging into the incision in the hypertrophied muscle.

the mucosa. When this injury occurs, it is almost always in dividing the most distal part of the constricting fibres, which are in the vicinity of the duodenal fornix. To be sure that there is no perforation, some air is squeezed from the stomach into the duodenum. If a perforation has occurred, it is closed and a piece of omentum placed over the closure. Haemostasis should be meticulous.

After operation, the nasogastric tube can be removed and feeding commenced on the morning after operation. If the infant manages to feed without difficulty he or she can be discharged early from hospital. If the mucosa is inadvertently opened, it is wise to delay feeding for 48 hours and to retain the child in hospital longer.

Complications of operation

Postoperative pyrexia is common and usually treated with paracetamol elixir. Wound disruption is rare and is more liable to occur in emaciated subjects. The incidence of wound infection is around 5%, and 1% will suffer wound disruption.

Duodenal atresia

This occurs at the point of fusion between the foregut and midgut, and therefore lies in the neighbourhood of the ampulla of Vater. There is a diaphragm, which is usually complete, across the duodenum at this point (Fig. 69.12) and the condition is frequently accompanied by other defects. The diagnosis is now made antenatally, in most cases through the use of ultrasound. This shows the characteristic appearance of a dilated stomach and first part of the duodenum (double bubble). The child vomits from birth and the vomitus is bile stained. The differential diagnosis includes high intestinal obstruction. Occasionally, however, the diaphragm may be proximal to the ampulla, and in these circumstances the condition can be confused with pyloric stenosis, although in pyloric stenosis vomiting does not start from birth. Treatment is performing a duodenoduodenostomy in which the dilated proximal duodenum is anastomosed to the atrophic distal

Abraham Vater | 1684–1751. Professor of Anatomy and Biology, Wittenburg, Germany.

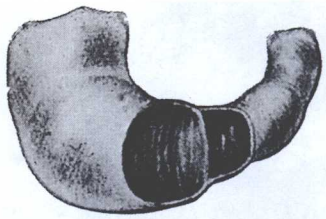

Figure 69.12 Congenital septum of duodenal obstruction at the commencement of the third part of the duodenum. The proximal gut is enormously dilated (after W.E. Ladd).

duodenum (Ladd). The disparity in luminal size can produce delays in emptying and some surgeons have advocated the use of a transanastomotic tube. However, this has been demonstrated to delay emptying and is not now commonly used.

HELICOBACTER PYLORI

Over the last 20 years, this organism has proved to be of overwhelming importance in the aetiology of a number of common gastroduodenal diseases such as chronic gastritis, peptic ulceration and gastric cancer. The organism had unquestionably been observed by a number of workers since Bircher's first description in 1874, but it was not until 1980 that Warren and Marshall, with enthusiasm but perhaps a lack of caution, ingested the organism to confirm that Koch's postulates could be fulfilled with respect to the gastritis that they succeeded in causing in themselves. Eradication therapy was then employed with mixed success. The organism is spiral shaped and is fastidious in its requirements, being difficult to culture outside the mucous layer of the stomach.

One of the characteristics of the organism is its ability to hydrolyse urea, resulting in the production of ammonia, a strong alkali. The effect of ammonia on the antral G cells is to cause the release of gastrin via the previously described negative-feedback loop. This is probably responsible for the modest, but inappropriate, hypergastrinaemia in patients with peptic ulcer disease, which, in turn, may result in gastric acid hypersecretion. The organism's obligate urease activity is utilised by various tests used to detect the presence of the organism, including the ^{13}C and ^{14}C breath tests and the CLO test (a commercially available urease test kit), which is performed on gastric biopsies. The organism can also be detected histologically (Fig. 69.13), using the Giemsa or the Ethin–Starey silver stains, and cultured using appropriate media. Previous or current infection with the organism may also be detected serologically.

Infection leads to the disruption of the gastric mucous barrier by the enzymes produced by the organism, and the inflammation induced in the gastric epithelium is the basis of many of the associated disease processes. The association of the organism with chronic (type B) gastritis is not in doubt as Koch's postulates have

William Edwards Ladd | 1880–1967. Professor of Child Surgery, Harvard, Boston, MA, USA.
C.S. Warren | Perth, Australia, now Chicago, IL, USA. Credited with awakening the current interest in *Helicobacter*.
Barry Marshall | Perth, Australia, now Charlottesville, VA, USA. Credited with awakening the current interest in *Helicobacter*.
Robert Koch | 1843–1910. Professor of Hygiene and Bacteriology, Berlin, Germany. Stated his 'postulates' in 1882. The postulates define the conditions that must be met before an organism can be shown to be the causal agent for a particular disease.

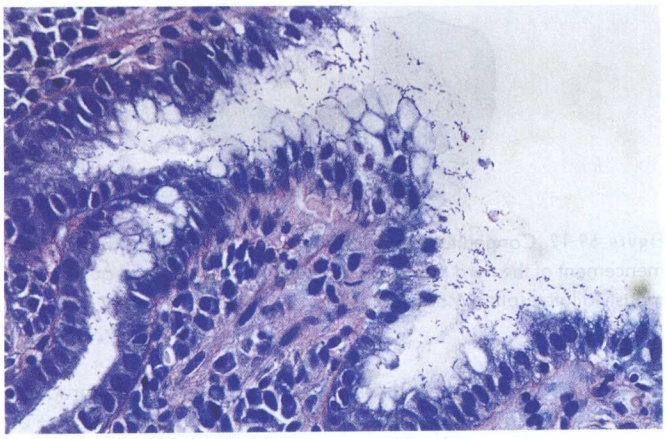

Figure 69.13 Antral mucosa showing colonisation with *Helicobacter pylori* (modified Giemsa stain).

been fulfilled, most notably by Marshall and Warren. Some strains of *H. pylori* produce cytotoxins, notably the Cag A and Vac A products, and the production of cytotoxins seem to be associated with the ability of the organism to cause gastritis, peptic ulceration and cancer (Crabtree). The effect of the organism on the gastric epithelium is to incite a classical inflammatory response that involves the migration and degranulation of acute inflammatory cells, such as neutrophils, and also the accumulation of chronic inflammatory cells, such as macrophages and lymphocytes.

It is evident how *H. pylori* infection results in chronic gastritis and also how this may progress to gastric ulceration, but for a while it remained an enigma as to how the organism could be involved in duodenal ulceration, as the normal duodenum is not colonised. As mentioned above, the production of ammonia does increase the level of circulating gastrin and it has been shown subsequently that eradication of the organism in patients with duodenal ulcer disease will reduce the acid levels to normal. However, the overlap in gastric acid secretion between normal subjects and those with duodenal ulcers is considerable and the modestly increased acid levels in patients with *Helicobacter*-associated antral gastritis are insufficient to explain the aetiology of duodenal ulceration.

The explanation can probably be found in the phenomenon of duodenal gastric metaplasia. Gastric metaplasia is the normal response of the duodenal mucosa to excess acidity. It can be thought of in the same way as any other metaplasia in the gastrointestinal tract: an attempt by the mucosa to resist an injurious stimulus. Although normal duodenal mucosa cannot be infected with *H. pylori*, gastric metaplasia in the duodenum is commonly infected and this infection results in the same inflammatory process that is observed in the gastric mucosa (Wyatt and Dixon). The result is duodenitis, which is almost certainly the precursor of duodenal ulceration.

Infection with *H. pylori* may be the most common human infection. The incidence of infection within a population increases with age, and in many populations infection rates of 80–90% are not unusual. It appears that most infection is acquired in childhood and the possibility of infection is inversely related to socioeconomic group. The means of spread has not been identified, but the organism can occur in the faeces and faecal–oral spread seems most likely. The organism is not normally found in saliva or dental plaque. There is evidence in different environments and in different population groups that the manifestations of the infection may be different. Predominantly antral gastritis, which is commonly seen in the West, results initially in increased levels of acid production and peptic ulcer disease, whereas gastritis affecting the body, common in the developing world, may lead to hypochlorhydria and gastric neoplasia.

It has been known since 1984 that *Helicobacter* infection is amenable to treatment with antibiotics. The profound hypochlorhydria produced by proton pump inhibitors combined with antibiotics is also effective in eradicating the organism. Commonly used eradication regimes include a proton pump inhibitor and two antibiotics, such as metronidazole and amoxycillin. Very high eradication rates, in the region of 90%, can be achieved with combinations that include the antibiotic clarithromycin, although it may be that in the future antibiotic resistance will become a problem. Reinfection following successful eradication appears rare but incomplete eradication is a more important clinical problem.

At present, eradication therapy is recommended for patients with duodenal ulcer disease, but not for patients with non-ulcer dyspepsia or in asymptomatic patients who are infected. However, recent data show that a proportion of patients with non-ulcer dyspepsia do respond to treatment. *H. pylori* is now classed by the World Health Organisation as a class 1 carcinogen and it may be that the further epidemiological studies on the risk of gastric cancer change the current advice on treatment.

GASTRITIS (Box 69.4)

The understanding of gastritis has increased markedly following elucidation of the role of *H. pylori* in chronic gastritis.

Box 69.4
Gastritis

- The spiral bacterium ***Helicobacter pylori*** is critical in the development of type B gastritis, peptic ulceration and gastric cancer
- Infection appears to be acquired mainly in childhood and the infection rate is inversely associated with socioeconomic status
- Eradication, recommended specifically in patients with peptic ulcer disease, can be achieved in up to 90% of patients with a combination of a proton pump inhibitor and antibiotics, and reinfection is uncommon
- Erosive gastritis is usually related to the use of NSAIDs
- Type A gastritis is an autoimmune process and is associated with the development of gastric cancer

Type A gastritis

This is an autoimmune condition in which there are circulating antibodies to the parietal cell. This results in the atrophy of the parietal cell mass, hence hypochlorhydria and ultimately achlorhydria. As intrinsic factor is also produced by the parietal cell there is malabsorption of vitamin B_{12}, which, if untreated, may

Jean Crabtree | Biologist, Leeds, England.
Michael Frederick Dixon | Professor of Gastro-intestinal Pathology, University of Leeds, Leeds, England.
Judith Irene Wyatt | Histopathologist, St James's University Hospital, Leeds, England.

result in pernicious anaemia. In type A gastritis, the antrum is not affected and the hypochlorhydria leads to the production of high levels of gastrin from the antral G cells. This results in chronic hypergastrinaemia. This, in turn, results in hypertrophy of the ECL cells in the body of the stomach, which are not affected by the autoimmune damage. Over time it is apparent that microadenomas develop in the ECL cells of the stomach, sometimes becoming identifiable tumour nodules. Very rarely, these tumours can become malignant. Patients with type A gastritis are predisposed to the development of gastric cancer, and screening such patients endoscopically may be appropriate.

Type B gastritis

There are abundant epidemiological data to support the association of this type of gastritis with *H. pylori*. Most commonly, type B gastritis affects the antrum, and it is these patients who are prone to peptic ulcer disease. *Helicobacter*-associated pangastritis is also a very common manifestation of infection, but gastritis affecting the corpus alone does not seem to be associated. However, there are some data to suggest that *Helicobacter* may be involved in the initiation of the process. Patients with pangastritis seem to be most prone to the development of gastric cancer.

Intestinal metaplasia is associated with chronic pangastritis with atrophy. Although intestinal metaplasia *per se* is common, intestinal metaplasia associated with dysplasia has significant malignant potential and, if this condition is identified, the patient should be regularly screened endoscopically.

Reflux gastritis

This is caused by enterogastric reflux and is particularly common after gastric surgery. Its histological features are distinct from other types of gastritis. Although commonly seen after gastric surgery, it is occasionally found in patients with no previous surgical intervention or who have had a cholecystectomy. Bile chelating or prokinetic agents may be useful in treatment and as a temporising measure to avoid consideration of revisional surgery. Operation for the condition should be reserved for the most severe cases.

Erosive gastritis

This is caused by agents that disturb the gastric mucosal barrier; NSAIDs and alcohol are common causes. The NSAID-induced gastric lesion is associated with inhibition of the cyclo-oxygenase type 1 (Cox 1) receptor enzyme, hence reducing the production of cytoprotective prostaglandins in the stomach. Fortunately, many of the beneficial anti-inflammatory activities of NSAIDs are mediated by Cox 2, and the use of specific Cox 2 inhibitors should reduce incidence of side-effects.

Stress gastritis

This is a common sequel of serious illness or injury and is characterised by a reduction in the blood supply to superficial mucosa of the stomach. Although common, this is not usually recognised unless stress ulceration and bleeding supervene, in which case treatment can be extremely difficult. The condition also sometimes follows cardiopulmonary bypass. Prevention of the stress bleeding from the stomach is much easier than treating it, and hence the routine use of H_2 antagonists with or without barrier agents, such as sucralfate, in patients who are on intensive care. These measures have been shown to reduce the incidence of bleeding from stress ulceration.

Ménétrier's disease

This is an unusual condition characterised by gross hypertrophy of the gastric mucosal folds, mucus production and hypochlorhydria. The condition is premalignant and may present with hypoproteinaemia and anaemia. There is no treatment other than a gastrectomy. The disease seems to be caused by overexpression of transforming growth factor alpha (TGF-α). Like epidermal growth factor (EGF), this peptide also binds to the EGF receptor. The histological features of Ménétrier's disease may be reproduced in transgenic mice overexpressing TGF-α (Coffey).

Lymphocytic gastritis

This type of gastritis is seen rarely. It is characterised by the infiltration of the gastric mucosa by T cells and is probably associated with *H. pylori* infection. The pattern of inflammation resembles that seen in coeliac disease or lymphocytic colitis.

Other forms of gastritis

Eosinophilic gastritis appears to have an allergic basis, and is treated with steroids and cromoglycate. Granulomatous gastritis is seen rarely in Crohn's disease and also may be associated with tuberculosis. Acquired immunodeficiency syndrome (AIDS) gastritis is secondary to infection with cryptospiridiosis. Phlegmonous gastritis is a rare bacterial infection of the stomach found in patients with severe intercurrent illness. It is usually an agonal event.

PEPTIC ULCER (Box 69.5)

Although the name 'peptic' ulcer suggests an association with pepsin, this is essentially unimportant as in the absence of acid, for instance in type A gastritis with atrophy, peptic ulcers do not occur. All peptic ulcers can be healed by using proton pump inhibitors, which can render a patient virtually achlorhydric.

Common sites for peptic ulcers are the first part of the duodenum and the lesser curve of the stomach, but they also occur on

Box 69.5
Peptic ulceration

- Most peptic ulcers are caused by *H. pylori* or NSAIDs and changes in epidemiology mirror changes in these principal aetiological factors
- Duodenal ulcers are more common than gastric ulcers, but the symptoms are indistinguishable
- Gastric ulcers may become malignant and an ulcerated gastric cancer may mimic a benign ulcer
- Gastric antisecretory agents and *H. pylori* eradication therapy are the mainstay of treatment, and elective surgery is not now commonly performed
- The long-term complications of peptic ulcer surgery may be difficult to treat
- The common complications of peptic ulcers are perforation, bleeding and stenosis
- The treatment of the perforated peptic ulcer is primarily surgical, although some patients may be managed conservatively

Pierre Ménétrier | 1859–1935. French physician.
Robert Coffey | Professor of Medicine, Nashville, TN, USA.
Burrill Bernard Crohn | 1884–1956. Gastroenterologist, Mount Sinai Hospital, New York, NY, USA. Described regional ileitis in 1932.

the stoma following gastric surgery, the oesophagus and even in a Meckel's diverticulum, which contains ectopic gastric epithelium. In general, the ulcer occurs at a junction between different types of epithelia, the ulcer occurring in the epithelium least resistant to acid damage.

In the past, much distinction has been made between acute and chronic peptic ulcers, but this difference can sometimes be difficult to determine clinically. It is probably best to consider that there is a spectrum of disease from the superficial gastric and duodenal ulceration, frequently seen at endoscopy, to deep chronic penetrating ulcers. This does not minimise the importance of acute stress ulceration. These ulcers can both perforate and bleed.

For many years, the cause of peptic ulceration remained an enigma. When comparing groups of patients with duodenal and pre-pyloric peptic ulcers with normal subjects, gastric acid levels are higher, but the overlap is very considerable. Patients with gastric ulceration have relatively normal levels of gastric acid secretion. As peptic ulceration will occur in the presence of very high acid levels, such as those found in patients with a gastrinoma (Zollinger–Ellison syndrome), and as all ulcers can be healed in the absence of acid it is clear that acid is important. In patients with a gastrinoma it may be the only aetiological factor, but this is not the case in the majority of patients. As with many diseases, genetic factors may be involved to a limited degree and social stress has also been implicated, falsely (Asher).

It is now widely accepted that infection with *H. pylori* is the most important factor in the development of peptic ulceration. The other factor of major importance at present is ingestion of NSAIDs. Cigarette smoking predisposes to peptic ulceration and increases the relapse rate after treatment, with either gastric antisecretory agents or, in the past, elective surgery. Multiple other factors may be involved in transition between the superficial and the deep penetrating chronic ulcer, but they are of lesser importance.

Duodenal ulceration

Incidence

There have been marked changes in the last two decades in the demography of patients presenting with duodenal ulceration in the West. First, even before the introduction of H_2-receptor antagonists, the incidence of duodenal ulceration and the frequency of elective surgery for the condition were falling. This trend has continued and now, in the West, dyspeptic patients presenting with a duodenal ulcer at gastroscopy are uncommon. In part, this may relate to the widespread use of gastric antisecretory agents and eradication therapy for patients with dyspepsia. Second, the peak incidence is now in a much older age group than previously and, although it is still more common in men, the difference is less marked. These changes (Susser) mirror the changes, at least in part, in the epidemiology of *H. pylori* infection. Thus, the age group in whom *H. pylori* infection was prevalent in the earlier part of the twentieth century are now elderly but still suffer from the complications of peptic ulceration. This probable relationship with *H. pylori* can also be seen in relation to gastric ulceration and, indeed, gastric cancer. Similarly, the incidence of perforation and bleeding duodenal ulcers in young and middle-aged patients appears to be falling but, in contrast, there is currently a marked increase in the numbers of elderly and often infirm patients suffering these complications. This trend can be explained not only by the *H. pylori* cohort effect but also by the increased use of NSAIDs in the elderly. In Eastern Europe, the disease remains common and, from having been uncommon in some developing nations, it is now observed more frequently. Again, the relationship with *H. pylori* appears convincing.

Johann Friedrich Meckel (The Younger) | 1781–1833. Professor of Anatomy and Surgery, Halle, Germany. Described the diverticulum in 1809.
Robert Milton Zollinger | b.1903. Professor of Surgery, Ohio State University, Columbus, OH, USA.
Edwin Homer Ellison | b.1918. Professor of Surgery, Marquette University, Milwaukee, WI, USA.
Zollinger and Ellison described this condition in a joint paper in 1955 when they were both working at the Ohio State University.
Richard Asher | 1912–1969. Physician, the Central Middlesex Hospital, London, England. Ridiculed the concept that the stress of modern living caused peptic ulceration by pointing out that the same claim was made for syphilis! It is an interesting coincidence that both diseases have strong aetiological associations with spiral organisms.
Mervyn Susser | Epidemiologist, Columbia, New York, NY, USA.

Pathology

Most occur in the first part of the duodenum (Figs 69.14 and 69.15). A chronic ulcer penetrates the mucosa and into the

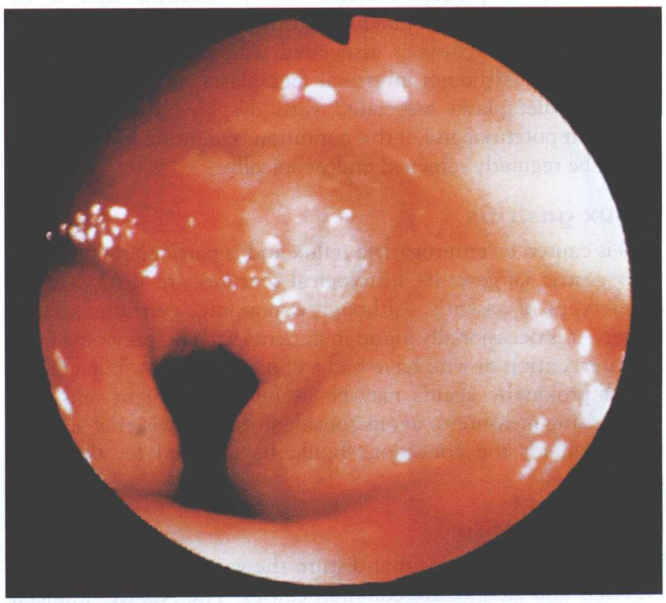

Figure 69.14 Duodenal ulcer at gastroduodenoscopy (courtesy of Dr G.N.J. Tytgat, Amsterdam, The Netherlands).

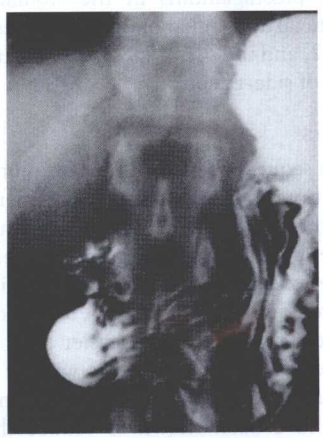

Figure 69.15 Duodenal ulcer shown by barium meal.