DISEASES OF THE STOMACH AND DUODENUM

Gastritis:

Gastritis is a histological diagnosis, although it can sometimes be recognised at endoscopy.

❖ Acute gastritis

Acute gastritis is often erosive and hemorrhagic. Neutrophils are the predominant inflammatory cell in the superficial epithelium. Many cases result from aspirin or NSAID ingestion.

22.38 Common causes of gastritis

Acute gastritis (often erosive and haemorrhagic)
• Aspirin, NSAIDs • *H. pylori* (initial infection) • Alcohol • Other drugs, e.g. iron preparations • Severe physiological stress, e.g. burns, multi-organ failure, CNS trauma • Bile reflux, e.g. following gastric surgery • Viral infections, e.g. CMV, herpes simplex virus in HIV-AIDS (p. 399)
Chronic non-specific gastritis
• *H. pylori* infection • Autoimmune (pernicious anaemia) • Post-gastrectomy
Chronic 'specific' forms (rare)
• Infections, e.g. CMV, tuberculosis • Gastrointestinal diseases, e.g. Crohn's disease • Systemic diseases, e.g. sarcoidosis, graft-versus-host disease • Idiopathic, e.g. granulomatous gastritis
(CMV = cytomegalovirus; NSAIDs = non-steroidal anti-inflammatory drugs)

Clinical features: Acute gastritis often produces no symptoms but may cause dyspepsia, anorexia, nausea or vomiting, and haematemesis or melaena.

Investigations: Many cases resolve quickly and do not merit investigation; in others, endoscopy and biopsy may be necessary to exclude peptic ulcer or cancer.

Treatment: should be directed at the underlying cause. Short-term symptomatic therapy with antacids, and acid suppression using PPIs, prokinetics (domperidone) or antiemetics (metoclopramide) may be necessary.

❖ Chronic gastritis

Chronic gastritis due to Helicobacter pylori infection

This is the *most common cause of chronic gastritis*. The predominant inflammatory cells are lymphocytes and plasma cells. Correlation between symptoms and endoscopic or pathological findings is poor. Most patients are asymptomatic and do not require treatment, but patients with dyspepsia may benefit from H. pylori eradication. (discussed in details later)

Autoimmune chronic gastritis:

This involves the body of the stomach but spares the antrum; it results from autoimmune damage to parietal cells. The histological features are diffuse chronic inflammation, atrophy and loss of fundic glands, intestinal metaplasia and sometimes hyperplasia of enterochromaffin-like (ECL) cells.

Ix: anti intrinsic factor and antipatietal cells Abs may be present. Pernicious anemia may develop.

C/F: usually asymptomatic, clinical features of associated autoimmune diseases (e.g. thyroid diseases ….). the condition is *premalignant*, the risk of developing CA stomach with increase by two to three folds.

Ménétrier's disease

In this rare condition, the gastric pits are elongated and tortuous, with replacement of the parietal and chief cells by mucus-secreting cells of the parietal and chief cells by mucus-secreting cells. The cause is unknown but there is excessive production of TGF-α. As a result, the mucosal folds of the body and fundus are greatly enlarged.

C/F: Most patients are hypochlorhydric. Whilst some patients have upper gastrointestinal symptoms, the majority present in middle or old age with proteinlosing enteropathy due to exudation from the gastric mucosa.

Ix: hypoalbuminemia, Endoscopy shows enlarged, nodular and coarse folds, although biopsies may not be deep enough to show all the histological features.

Rx: ❶ antisecretory drugs, such as PPIs ❷ with or without octreotide, may reduce protein loss ❸H. pylori eradication may be effective ❹unresponsive patients require partial gastrectomy.

Peptic ulcer disease

The term 'peptic ulcer' refers to an ulcer in the lower oesophagus, stomach or duodenum, in the jejunum after surgical anastomosis to the stomach or, rarely, in the ileum adjacent to a Meckel's diverticulum.

Ulcers in the stomach or duodenum may be acute or chronic; both penetrate the muscularis mucosae but the acute ulcer shows no evidence of fibrosis. Erosions do not penetrate the muscularis mucosae.

Gastric and duodenal ulcer

The prevalence of peptic ulcer (0.1–0.2%) is decreasing in many Western communities as a result of widespread use of Helicobacter pylori eradication therapy but it remains high in developing countries.

The male-to female ratio:

for duodenal ulcer: 5: 1 to 2: 1
for gastric ulcer: 2:1 or less.

Chronic gastric ulcer is usually single; 90% are situated on the lesser curve within the antrum or at the junction between body and antral mucosa. Chronic duodenal ulcer usually occurs in the first part of the duodenum and 50% are on the anterior wall. Gastric and duodenal ulcers coexist in 10% of patients and more than one peptic ulcer is found in 10–15% of patients.

Pathophysiology:

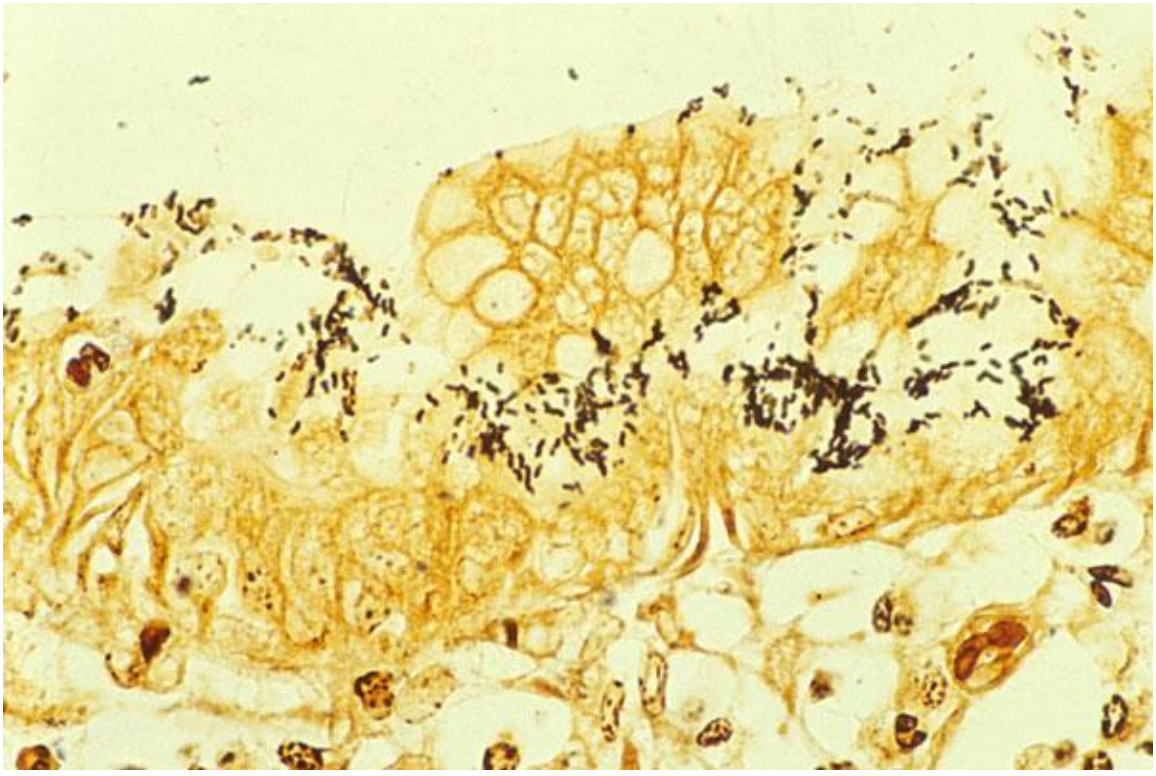
H. pylori

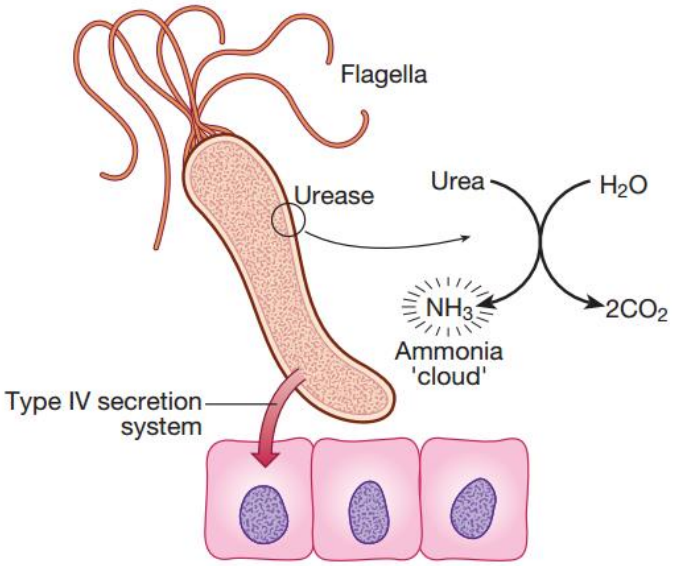
Peptic ulceration is strongly associated with H. pylori infection. The prevalence in developed nations rises with age, and in the UK approximately 50% of people over the age of 50 years are infected. In the developing world, infection is more common, affecting up to 90% of adults. These infections are probably acquired in childhood by person-to-person contact. The vast majority of colonised people remain healthy and asymptomatic and only a minority develop clinical disease.

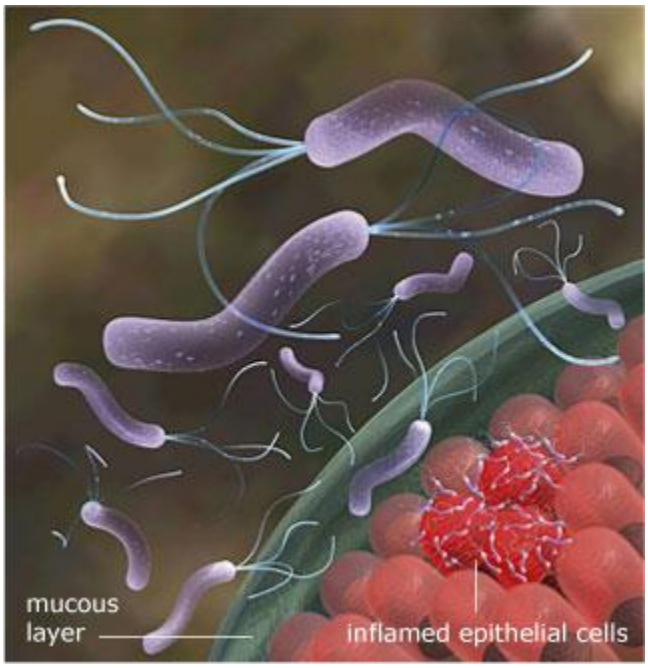
Around 90% of duodenal ulcer patients and 70% of gastric ulcer patients are infected with H. pylori. The remaining 30% of gastric ulcers are caused by NSAIDs and this proportion is increasing in Western countries as a result of H. pylori eradication strategies.

Bacteriology:

H. pylori is Gram-negative and spiral, and has multiple flagella at one end, which make it motile, allowing it to burrow and live beneath the mucus layer adherent to the epithelial surface.



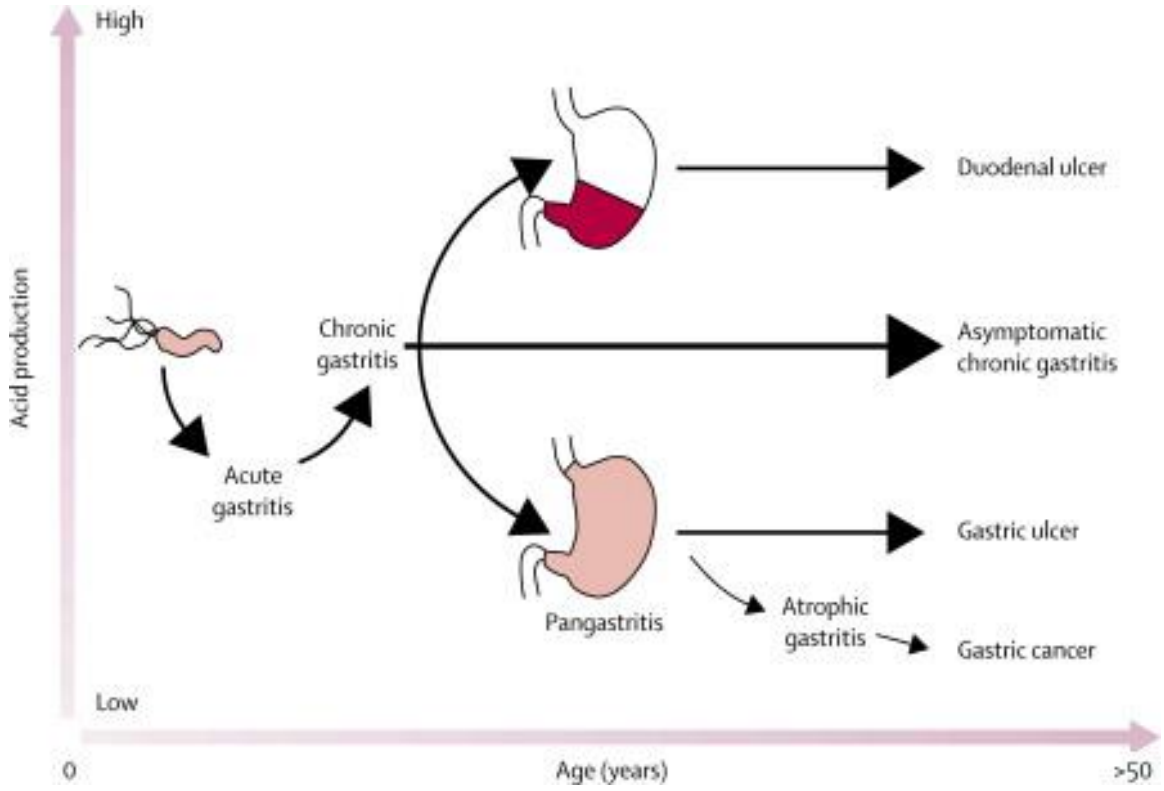




Here the surface pH is close to neutral and any acidity is buffered by the organism's production of the enzyme urease. This produces ammonia from urea and raises the pH around the bacterium and between its two cell membrane layers. H. pylori exclusively colonises gastric-type epithelium and is only found in the duodenum in association with patches of gastric metaplasia. It causes chronic gastritis by provoking a local inflammatory response in the underlying epithelium. This depends on numerous factors, notably expression of bacterial cagA and vacA genes.

In most people, H. pylori causes localised antral gastritis associated with depletion of somatostatin (from D cells) and increased gastrin release from G cells. The subsequent hypergastrinaemia stimulates increased acid production by parietal cells but, in the majority of cases, this has no clinical consequences. In a minority of patients, this effect is exaggerated, leading to duodenal ulceration.

In 1% of infected people, H. pylori causes a pangastritis, leading to gastric atrophy and hypochlorhydria. This allows other bacteria to proliferate within the stomach; these produce mutagenic nitrites from dietary nitrates, predisposing to the development of gastric cancer. The effects of H. pylori are more complex in gastric ulcer patients compared to those with duodenal ulcers. The ulcer probably arises because of impaired mucosal defence resulting from a combination of H. pylori infection, NSAIDs and smoking, rather than excess acid.



NSAIDs

Treatment with NSAIDs is associated with peptic ulcers due to impairment of mucosal defenses.

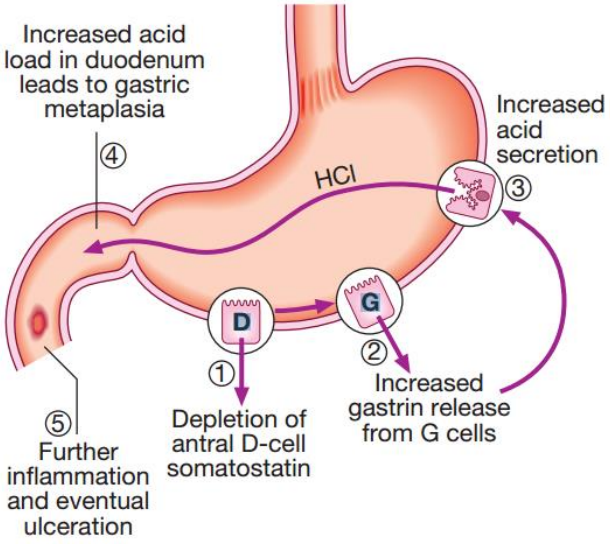
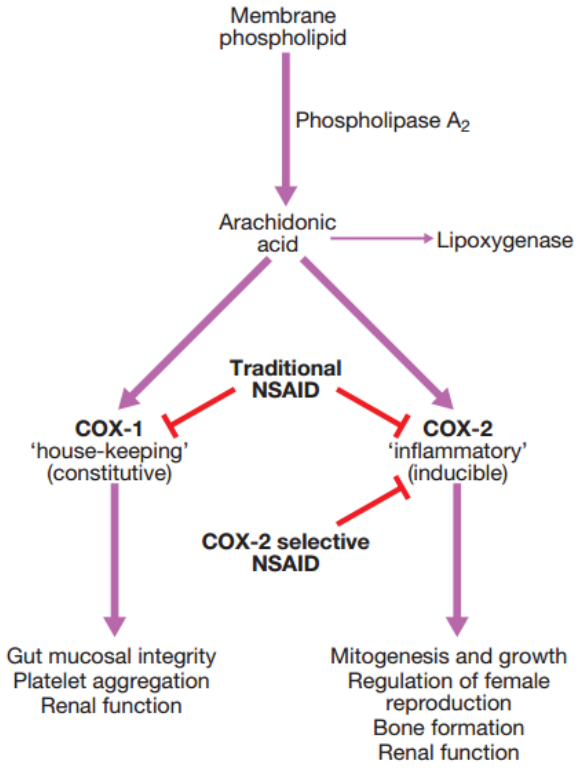


Fig. 22.34 Sequence of events in the pathophysiology of duodenal ulceration.



Smoking

Smoking confers an increased risk of gastric ulcer and, to a lesser extent, duodenal ulcer. Once the ulcer has formed, it is more likely to cause complications and less likely to heal if the patient continues to smoke.

Clinical features: Peptic ulcer disease is a chronic condition with spontaneous relapses and remissions lasting for decades, if not for life. The most common presentation is with

recurrent abdominal pain which has three notable characteristics: ❶ localisation to the epigastrium, ❷ relationship to food and ❸ episodic occurrence.

Occasional vomiting occurs in about 40% of ulcer subjects; persistent daily vomiting suggests gastric outlet obstruction.

In one-third, the history is less characteristic, especially in elderly people or those taking NSAIDs. In them, pain may be absent or so slight that it is experienced only as a vague sense of epigastric unease. Occasionally, the only symptoms are anorexia and nausea, or early satiety after meals. In some patients, the ulcer is completely 'silent', presenting for the first time with anaemia from chronic undetected blood loss, as an abrupt haematemesis or as acute perforation; in others, there is recurrent acute bleeding without ulcer pain. The diagnostic value of individual symptoms for peptic ulcer disease is poor; *the history is therefore a poor predictor of the presence of an ulcer*.

Investigations:

Endoscopy is the preferred investigation. Gastric ulcers may occasionally be malignant and therefore must always be biopsied and followed up to ensure healing. Patients should be tested for H. pylori infection. Some are invasive and require endoscopy; others are noninvasive. They vary in sensitivity and specificity. *Breath tests or faecal antigen tests are best because of accuracy, simplicity and non-invasiveness.*

22.42 Indications for *H. pylori* eradication

Definite
• Peptic ulcer
• Extranodal marginal-zone lymphomas of MALT type
• Family history of gastric cancer
• Previous resection for gastric cancer
• *H. pylori*-positive dyspepsia
• Long-term NSAID or low-dose aspirin users
• Chronic (> 1 yr) PPI users
• Extragastric disorders:
Unexplained vitamin B_{12} deficiency*
Idiopathic thrombocytopenic purpura*
Iron deficiency anaemia* (see text)
Not indicated
• Gastro-oesophageal reflux disease
• Asymptomatic people without gastric cancer risk factors

*If *H. pylori*-positive on testing.

Management:

The aims of management are to relieve symptoms, induce healing and prevent recurrence.

H. pylori eradication is the cornerstone of therapy for peptic ulcers, as this will successfully prevent relapse and eliminate the need for long-term therapy in the majority of patients. H. pylori eradication **All** patients with proven ulcers who are H. pylori-positive should be offered eradication as primary therapy.

❶Triple therapy is based upon a **PPI** taken simultaneously with **two antibiotics** (clarithromycin plus amoxicillin or metronidazole) for 14 days. Success is achieved in 80–90% of patients in developed contries, although compliance, side-effects and antibiotic resistance influence this. Resistance to amoxicillin is rare but rates of metronidazole resistance reach 40% in some countries and, recently, rates of clarithromycin resistance of 20–40% have appeared. Where the latter exceed 15–20% (as expected in our country), a ❷quadruple therapy regimen, consisting of omeprazole (or another PPI), bismuth subcitrate, metronidazole and tetracycline (OBMT) for 10–14 days, is recommended. In areas of low clarithromycin resistance, this regimen should also be offered as second-line therapy to those who remain infected after initial therapy, once compliance has been checked. For those who are still colonised after two treatments, the choice lies between a third attempt of ❸treatment guided by antimicrobial sensitivity testing, ❹rescue therapy (levofloxacin, PPI and clarithromycin) or ❺long-term acid suppression.

H. pylori and NSAIDs are independent risk factors for ulcer disease and *patients requiring long-term NSAID therapy should first undergo eradication therapy to reduce ulcer risk.*

Subsequent co-prescription of a PPI along with the NSAID is advised but is not always necessary for patients being given low-dose aspirin, in whom the risk of ulcer complications is lower.

Prescribing selective COX-2 inhibitors (e.g. meloxicam) is equivalent to prescribing non-selective COX-2 (e.g. ibuprofen) plus PPI.

22.39 Methods for the diagnosis of *Helicobacter pylori* infection

Test	Advantages	Disadvantages
Non-invasive		
Serology	Rapid office kits available Good for population studies	Lacks specificity Cannot differentiate current from past infection
^{13}C-urea breath tests	High sensitivity and specificity	Requires expensive mass spectrometer
Faecal antigen test	Cheap, specific (> 95%)	Acceptability
Invasive (antral biopsy)		
Histology	Specificity	False negatives Takes several days to process
Rapid urease tests	Cheap, quick, specific (> 95%)	Sensitivity 85%
Microbiological culture	'Gold standard' Defines antibiotic sensitivity	Slow and laborious Lacks sensitivity

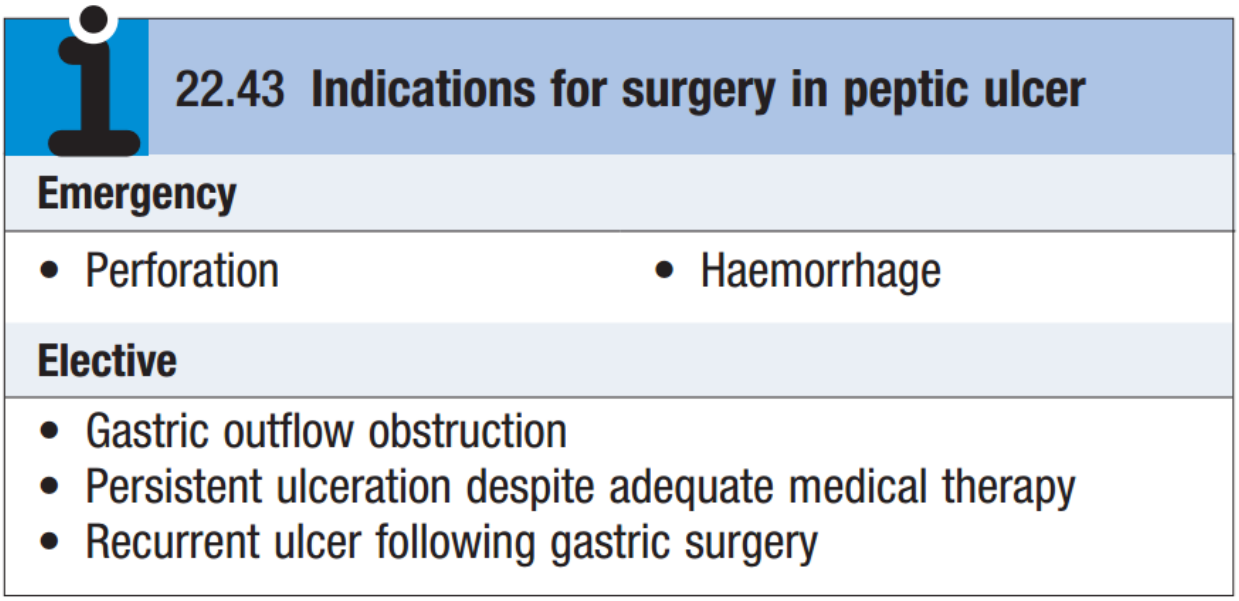
Eradication of the infection has proven benefits in several **extragastric disorders**, including ❶unexplained B12 deficiency and❷ iron deficiency anaemia, once sources of gastrointestinal bleeding have been looked for and excluded. Platelet counts improve and may normalise after eradication therapy in patients with❸ idiopathic thrombocytopenic purpura; the mechanism for this is unclear.

General measures Cigarette smoking, aspirin and NSAIDs should be avoided. *Alcohol in moderation is not harmful and no special dietary advice is required.*

Maintenance treatment Continuous maintenance treatment should not be necessary after successful H. pylori eradication. For the minority who do require it, the lowest effective dose of PPI should be used.

Surgical treatment

Surgery is now rarely required for peptic ulcer disease but it is needed in some cases. The operation of choice for a chronic non-healing gastric ulcer is partial gastrectomy, preferably with a Billroth I anastomosis, in which the ulcer itself and the ulcer-bearing area of the stomach are resected. The reason for this is to exclude an underlying cancer. In an emergency, 'under-running' the ulcer for bleeding or 'oversewing' (patch repair) for perforation is all that is required, in addition to taking a biopsy. For giant duodenal ulcers, partial gastrectomy using a 'Polya' or Billroth II reconstruction may be required.



22.43 Indications for surgery in peptic ulcer

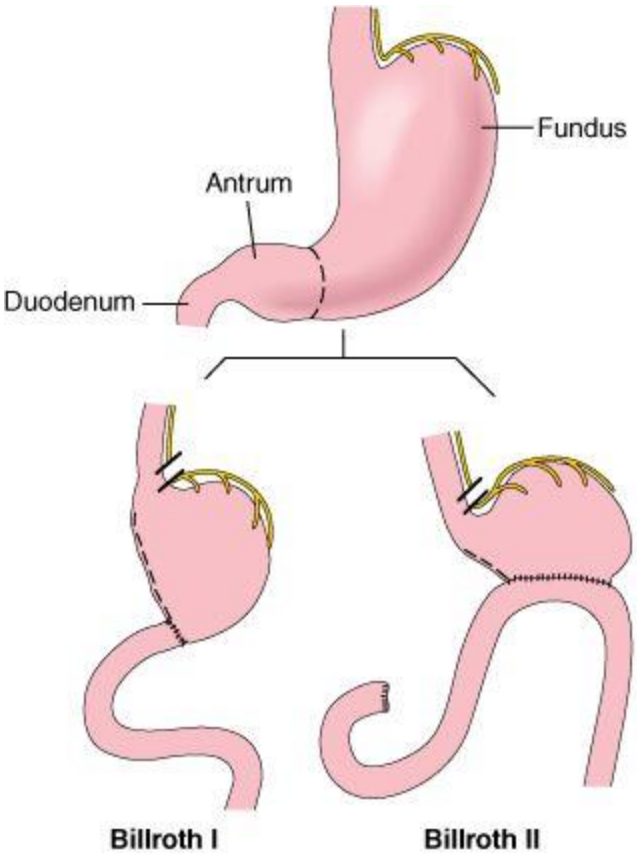
Emergency

- Perforation
- Haemorrhage

Elective

- Gastric outflow obstruction
- Persistent ulceration despite adequate medical therapy
- Recurrent ulcer following gastric surgery

Complications of gastric resection or vagotomy



Up to 50% of patients who undergo gastric surgery for peptic ulcer surgery experience long-term adverse effects. In most cases, these are minor, but in 10% they significantly impair quality of life. ❶**Dumping**. Rapid gastric emptying leads to distension of the proximal small intestine as the hypertonic contents draw fluid into the lumen. This leads to abdominal discomfort and diarrhoea after eating. Autonomic reflexes release a range of gastrointestinal hormones that provoke vasomotor features, such as flushing, palpitations, sweating, tachycardia and hypotension. Patients should therefore avoid large meals with high carbohydrate content. ❷**Chemical (bile reflux) gastropathy.** Duodenogastric bile reflux leads to chronic gastropathy. Treatment with aluminium-containing antacids or sucralfate may be effective. A few patients require revisional surgery with creation of a Roux en Y loop to prevent bile reflux. ❸ **Diarrhoea and maldigestion.** Diarrhoea may develop after any peptic ulcer operation and usually occurs 1–2 hours after eating. Poor mixing of food in the stomach, with rapid emptying, inadequate mixing with pancreaticobiliary secretions, rapid transit and bacterial overgrowth, may lead to malabsorption. Diarrhoea often responds to small, dry meals with a reduced intake of refined carbohydrates. Antidiarrhoeal drugs, such as codeine phosphate (15–30 mg 4–6 times daily) or loperamide (2 mg after each loose stool), are helpful. ❹**Weight loss**. Most patients lose weight shortly after surgery and 30–40% are unable to regain all the weight that is lost. The usual cause is reduced intake because of a small gastric remnant, but diarrhoea and mild steatorrhoea also contribute. ❺**Anaemia**. Anaemia is common many years after subtotal gastrectomy. Iron deficiency is the most common cause; folic acid and B12 deficiency are much less frequent. Inadequate dietary intake of iron and folate, lack of acid and intrinsic factor secretion, mild chronic low grade blood loss from the gastric remnant and recurrent ulceration are responsible. ❻**Metabolic bone** disease. Both osteoporosis and osteomalacia can occur as a consequence of calcium and vitamin D malabsorption. ❼ **Gastric cancer**. An increased risk of gastric cancer has been reported from several epidemiological studies. Surgery itself is an independent risk factor for late development of malignancy in the gastric remnant but the risk is higher in those with hypochlorhydria,

duodenogastric reflux of bile, smoking and H. pylori infection. Although the relative risk is increased, the absolute risk of cancer remains low and endoscopic surveillance is not indicated following gastric surgery.

Complications of peptic ulcer disease

❶Perforation When perforation occurs, the contents of the stomach escape into the peritoneal cavity, leading to peritonitis. This is more common in duodenal than in gastric ulcers, and is usually found with ulcers on the anterior wall. About one-quarter of all perforations occur in acute ulcers and NSAIDs are often incriminated. Perforation can be the first sign of ulcer, and a history of recurrent epigastric pain is uncommon. The most striking symptom is sudden, severe pain; its distribution follows the spread of the gastric contents over the peritoneum. *The pain initially develops in the upper abdomen and rapidly becomes generalised*; shoulder tip pain is caused by irritation of the diaphragm. The pain is accompanied by shallow respiration due to limitation of diaphragmatic movements and by shock. The abdomen is held immobile and there is generalised 'board-like' rigidity. Bowel sounds are absent and liver dullness to percussion decreases due to the presence of gas under the diaphragm.

After some hours, symptoms may improve, although abdominal rigidity remains. Later, the patient's condition deteriorates as general peritonitis develops.

In at least 50% of cases, an erect chest X-ray shows free air beneath the diaphragm. If not, a water-soluble contrast swallow will confirm leakage of gastroduodenal contents. After resuscitation, the acute perforation should be *treated surgically*, either by simple closure or by converting the perforation into a pyloroplasty if it is large. On rare occasions, a 'Polya' partial gastrectomy is required.

Following surgery, H. pylori should be treated (if present) and NSAIDs avoided. Perforation carries a mortality of 25%, reflecting the advanced age and significant comorbidity of the population that are affected.

❷Gastric outlet obstruction,

22.45 Differential diagnosis and management of gastric outlet obstruction

Cause	Management
Fibrotic stricture from duodenal ulcer (pyloric stenosis)	Balloon dilatation or surgery
Oedema from pyloric channel or duodenal ulcer	PPI therapy
Carcinoma of antrum	Surgery
Adult hypertrophic pyloric stenosis	Surgery

The most common cause is an ulcer in the region of the pylorus. The presentation is with nausea, vomiting and abdominal distension. Large quantities of gastric content are often vomited, and food eaten 24 hours or more previously may be recognised. Physical examination may show evidence of wasting and dehydration. A succussion splash may be elicited 4 hours or more after the last meal or drink.

Visible gastric peristalsis is diagnostic of gastric outlet obstruction. Loss of gastric contents leads to dehydration with low serum chloride and potassium, and raised serum bicarbonate and urea concentrations. This results in enhanced renal absorption of Na+ in exchange for H+ and paradoxical aciduria.

Endoscopy should be performed after the stomach has been emptied by a wide-bore nasogastric tube.

Intravenous correction of dehydration is undertaken and, in severe cases, at least 4 L of **isotonic saline** and 80 mmol of **potassium** may be necessary during the first 24 hours. In some patients, **PPI** drugs heal ulcers, relieve pyloric oedema and overcome the need for surgery. **Endoscopic balloon dilatation** of benign stenoses may be possible in some patients, but in others **partial gastrectomy** is necessary, although this is best done after a 7-day period of **nasogastric aspiration**, which enables the stomach to return to normal size. A gastroenterostomy is an alternative operation but, unless this is accompanied by vagotomy, patients will require long-term PPI therapy to prevent stomal ulceration.

❸Bleeding, discussed elsewhere.

Zollinger–Ellison syndrome

This is a rare disorder characterised by the triad of ❶severe peptic ulceration, ❷gastric acid hypersecretion and a ❸non-β cell islet tumour of the pancreas (‘gastrinoma’). It probably accounts for about 0.1% of all cases of duodenal ulceration. The syndrome occurs in either sex at any age, although it is most common between 30 and 50 years of age.

Pathophysiology: The tumour secretes gastrin, which stimulates acid secretion to its maximal capacity and increases the parietal cell mass three- to sixfold. The acid output may be so great that it reaches the upper small intestine, reducing the luminal pH to 2 or less. Pancreatic lipase is inactivated and bile acids are precipitated. Diarrhoea and steatorrhoea result. Around 90% of tumours occur in the pancreatic head or proximal

duodenal wall. At least half are multiple, and tumour size can vary from 1 mm to 20 cm. Approximately one-half to two-thirds are malignant but are often slow-growing. Adenomas of the parathyroid and pituitary glands (multiple endocrine neoplasia, MEN type 1) are present in 20–60% of patients.

Clinical features: The presentation is with severe and often multiple peptic ulcers in unusual sites, such as the post-bulbar duodenum, jejunum or oesophagus. There is a poor response to standard ulcer therapy. The history is usually short; bleeding and perforations are common. Diarrhoea is seen in one-third or more of patients and can be the presenting feature.

Investigations:

❶Hypersecretion of acid under basal conditions, with little increase following pentagastrin, may be confirmed by gastric aspiration.

❷Serum gastrin levels are grossly elevated (10- to 1000-fold). If possible, PPIs should be stopped for one week as it increase the level of gastrin.

❸Injection of the hormone secretin normally causes no change or a slight decrease in circulating gastrin concentrations, but in Zollinger–Ellison syndrome produces a paradoxical and dramatic increase in gastrin.

❹Tumour localisation is best achieved by EUS and radio-labelled somatostatin receptor scintigraphy.

Management

❶Surgery: Some 30% of small and single tumours can be localised and resected but many tumours are multifocal. Some patients present with metastatic disease and, in these circumstances, surgery is inappropriate.

❷PPI: In the majority of these patients, continuous therapy with omeprazole or other PPIs can be successful in healing ulcers and alleviating diarrhoea, although double the normal dose is required.

❸Octreotide: The synthetic somatostatin analogue, octreotide, given by subcutaneous injection, reduces gastrin secretion and is of value.

Prognosis: overall 5-year survival is 60–75% and all patients should be monitored for the later development of other manifestations of MEN 1.

Functional disorders

Functional dyspepsia

This is defined as chronic dyspepsia in the absence of organic disease. Other commonly reported symptoms include early satiety, fullness, bloating and nausea. 'Ulcer-like' and 'dysmotility-type' subgroups are often reported, but there is overlap between these and with irritable bowel syndrome.

Pathophysiology: The cause is poorly understood but probably covers a spectrum of mucosal, motility and psychiatric disorders.

Clinical features: Patients are usually young (< 40 years) and women are affected twice as commonly as men. Abdominal discomfort is associated with a combination of other 'dyspeptic' symptoms, the most common being nausea, satiety and bloating after meals. Morning symptoms are characteristic and pain or nausea may occur on waking. Direct enquiry may elicit symptoms suggestive of irritable bowel syndrome. *Peptic ulcer disease must be considered, whilst in older subjects intra-abdominal malignancy is a prime concern.* There are no diagnostic signs, apart perhaps from inappropriate tenderness on abdominal palpation. *Symptoms may appear disproportionate to clinical well-being and there is no weight loss*. Patients often appear anxious. A drug history should be taken and the possibility of a depressive illness should be considered. Pregnancy should be ruled out in young women before radiological studies are undertaken. Alcohol misuse should be suspected when early morning nausea and retching are prominent.

Investigations: The history will often suggest the diagnosis. ❶All patients should be checked for H. pylori infection and patients over the age of 55 years should undergo ❷endoscopy to exclude mucosal disease. While an ❸ultrasound scan may detect gallstones, these are rarely responsible for dyspeptic symptoms.

Management: The most important elements are ❶explanation and reassurance. Possible psychological factors should be explored and the concept of psychological influences on gut function should be explained. ❷Idiosyncratic and restrictive diets are of little benefit, but smaller portions and fat restriction may help. ❸Up to 10% of patients benefit from H. pylori eradication therapy and this should be offered to infected patients. Eradication also removes a major risk factor for gastric cancer but at the cost of a small risk of side effects and worsening symptoms of underlying gastro esophageal reflux disease. Drug treatment is not especially successful but merits trial. ❹Antacids, such as hydrotalcite, are sometimes helpful. ❺Prokinetic drugs, such as metoclopramide (10 mg 3 times daily) or domperidone (10–20 mg 3 times daily), may be given before meals if nausea, vomiting or bloating is prominent. Metoclopramide may induce extrapyramidal side effects, including tardive dyskinesia in young subjects. ❻H2-receptor antagonist drugs may be tried if night pain or heartburn is troublesome. ❼Low-dose tricyclic agents, such as amitriptyline, are of value in up to two-thirds. Symptoms that can be associated with an identifiable cause of stress resolve with appropriate counselling. Some patients have major psychological disorders that result in persistent or recurrent symptoms and need ❽behavioural or other formal psychotherapy.

Functional causes of vomiting

Psychogenic retching or vomiting may arise in anxiety. *It typically occurs on wakening or immediately after breakfast and only rarely later in the day*. The disorder is probably a reaction to facing up to the worries of everyday life; in the young, it can be due to school phobia. Early morning vomiting also occurs in pregnancy, alcohol misuse and depression. Although functional vomiting may occur regularly over long periods, there is little or

no weight loss. Children, and less often adults, sometimes suffer from acute and recurrent disabling bouts of vomiting for days at a time. The cause of this **cyclical vomiting syndrome** is unknown. *Characteristically the patient has no nausea or vomiting between the episodes*. In all patients, it is essential to exclude other common causes. Treatment: ❶Tranquillisers and ❷antiemetic drugs (metoclopramide 10 mg 3 times daily, domperidone 10 mg 3 times daily, prochlorperazine 5–10 mg 3 times daily) have only a secondary place in management. ❸Antidepressants in full dose may be effective

Gastroparesis

Defective gastric emptying without mechanical obstruction of the stomach or duodenum can occur as a primary event, due to inherited or acquired disorders of the gastric pacemaker, or can be secondary to disorders of autonomic nerves (particularly diabetic neuropathy) or the gastroduodenal musculature (systemic sclerosis, myotonic dystrophies and amyloidosis).

Drugs such as opiates, calcium channel antagonists and those with anticholinergic activity (tricyclics, phenothiazines) can also cause gastroparesis.

Clinical features: ❶Early satiety and ❷recurrent vomiting are the major symptoms; ❸abdominal fullness and a ❹succussion splash may be present on examination. Endoscopic findings may include loss or decrease gastric motility, food residues may be seen after prolonged fasting.

Treatment: is based upon ❶small, frequent, low-fat meals and ❷the use of metoclopramide and domperidone. In severe cases, nutritional failure can occur and ❸long-term jejunostomy feeding or total parenteral nutrition is required. ❹Surgical or endoscopic insertion of a gastric neurostimulator has been successful in some cases, especially those complicating diabetic autonomic neuropathy.

Tumours of the stomach

Gastric carcinoma

Gastric carcinoma is the fourth leading cause of cancer death worldwide, but there is marked geographical variation in incidence. It is most common in China, Japan, Korea (incidence 40/100 000 males), Eastern Europe and parts of South America (20/100 000). Rates in the UK are 12/100 000 for men. In most countries, the incidence is 50% lower in women. In both sexes, it rises sharply after 50 years of age. Studies of Japanese migrants to the USA have revealed a much lower incidence in second generation migrants, confirming the importance of environmental factors. The overall prognosis is poor, with less than 30% surviving 5 years, and the *best hope for improved survival lies in more efficient detection of tumours at an earlier stage.*

Pathophysiology: Infection with *H. pylori plays a key pathogenic role*. It is associated with chronic atrophic gastritis, gastric mucosal atrophy and with gastric cancer. It has been estimated that H. pylori infection may contribute to the occurrence of gastric cancer in 60–70% of cases and that acquisition of infection at an early age may be important. Although H. pylori infection is common in Africa, gastric cancer is uncommon and this enigma may be explained by lower life expectancy in this part of the world. Although the majority of H. pylori-infected individuals have normal or increased acid secretion, a few become hypo- or achlorhydric and these people are

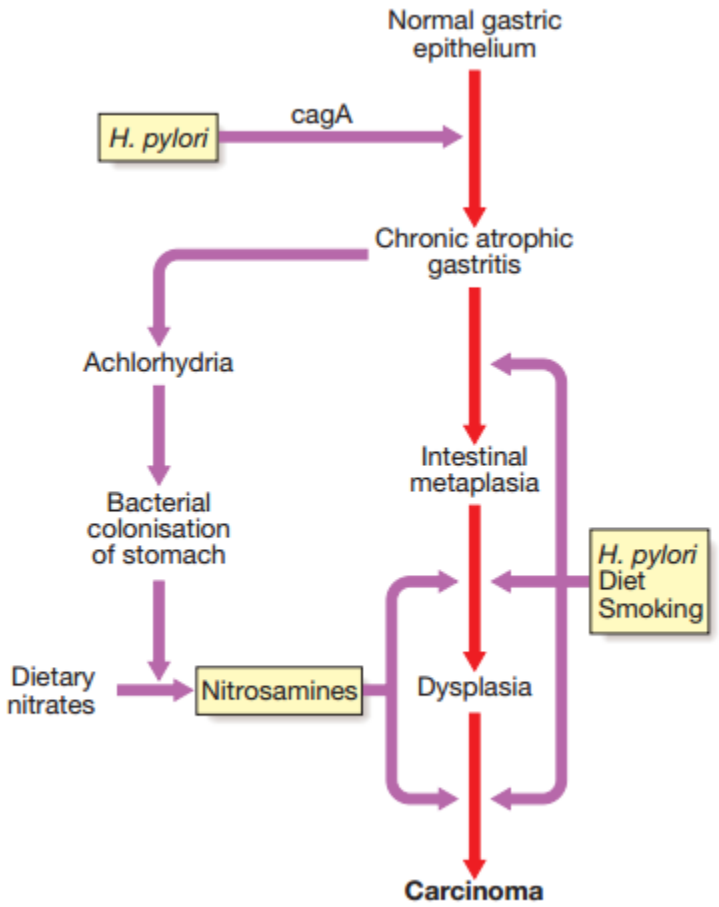
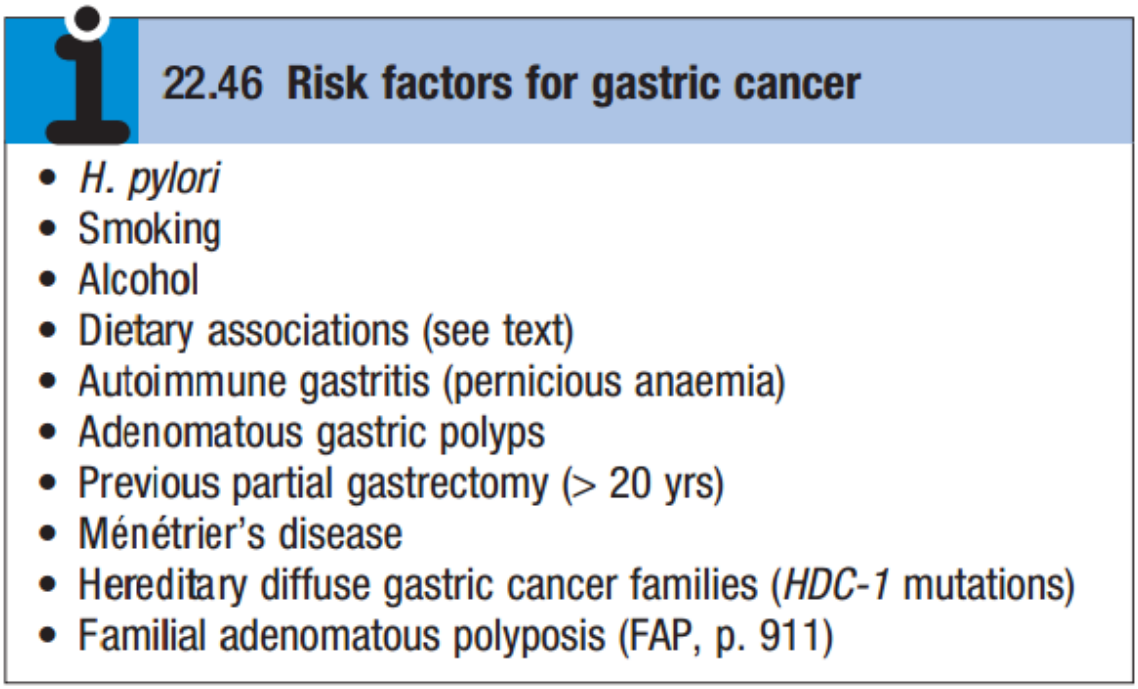


Fig. 22.36 Gastric carcinogenesis: a possible mechanism.

thought to be at greatest risk. Chronic inflammation with generation of reactive oxygen species and depletion of the normally abundant antioxidant ascorbic acid are also important. There is strong evidence that H. pylori eradication, especially if achieved before irreversible pre-neoplastic changes have developed, reduces the risk of cancer development in high-risk populations and is cost-effective. Diets rich in salted, smoked or pickled foods and the consumption of nitrites and nitrates may increase cancer risk. Carcinogenic N-nitroso-compounds are formed from nitrates by the action of nitrite-reducing bacteria which colonise the achlorhydric stomach. Diets lacking fresh fruit and vegetables, as well as vitamins C and A, may also contribute. Other risk factors are listed in Box 22.46.



22.46 Risk factors for gastric cancer

- *H. pylori*
- Smoking
- Alcohol
- Dietary associations (see text)
- Autoimmune gastritis (pernicious anaemia)
- Adenomatous gastric polyps
- Previous partial gastrectomy (> 20 yrs)
- Ménétrier's disease
- Hereditary diffuse gastric cancer families (*HDC-1* mutations)
- Familial adenomatous polyposis (FAP, p. 911)

No predominant genetic abnormality has been identified, although cancer risk is increased two- to threefold in first-degree relatives of patients, and links with blood group A have been reported. Rarely, gastric cancer may be inherited in an autosomal dominant manner in association with mutations of the E-cadherin (CDH1) gene.

Virtually all tumours are adenocarcinomas arising from mucus-secreting cells in the base of the gastric crypts. Most develop upon a background of chronic atrophic gastritis with intestinal metaplasia and dysplasia. Cancers are either '**intestinal'**, arising from areas of intestinal metaplasia with histological features reminiscent of intestinal epithelium, or '**diffuse'**, arising from normal gastric mucosa. Intestinal carcinomas are more common and arise against a background of chronic mucosal injury. Diffuse cancers tend to be poorly differentiated and occur in younger patients.

In the developing world, 50% of gastric cancers develop in the antrum; 20–30% occur in the gastric body, often on the greater curve; and 20% are found in the cardia.

In Western populations, however, proximal gastric tumours are becoming more common than those arising in the body and distal stomach. This change in disease pattern may be a reflection of changes in lifestyle or the decreasing prevalence of H. pylori in the West.

Diffuse submucosal infiltration by a scirrhous cancer (*linitis plastica*) is uncommon. Early gastric cancer is defined as cancer confined to the mucosa or submucosa. It is more often recognised in Japan, where widespread screening is practised. Some cases can be cured by endoscopic mucosal or submucosal resection The majority of patients (> 80%) in the West, however, present with advanced gastric cancer.

Clinical features: Early gastric cancer is usually ❶asymptomatic but may be discovered during endoscopy for investigation of dyspepsia. Two-thirds of patients with advanced cancers have ❷weight loss and 50% have ❸ulcer-like pain. ❹Anorexia and nausea occur in one-third, while ❺early satiety, ❻haematemesis, ❼melaena and ❽dyspepsia alone are less common. ❾Dysphagia occurs in tumours of the gastric cardia which obstruct the gastro-oesophageal junction. ❿Anaemia from occult bleeding is also common.

Examination may reveal no abnormalities but signs of ❶weight loss, ❷anaemia and a ❸palpable epigastric mass are not infrequent. ❹ Jaundice or ascites signify metastatic spread. Occasionally, tumour spread

occurs to the supraclavicular lymph nodes (**Troisier's sign**), umbilicus (**Sister Joseph's nodule**) or ovaries (**Krukenberg tumour**).

Paraneoplastic phenomena, such as acanthosis nigricans, thrombophlebitis (Trousseau's sign) and dermatomyositis, occur rarely. Metastases arise most commonly in the liver, lungs, peritoneum and bone marrow.

Investigations: ❶Upper gastrointestinal endoscopy is the investigation of choice and should be performed promptly in any dyspeptic patient with 'alarm features'. Multiple biopsies from the edge and base of a gastric ulcer are required. ❷Barium meal is a poor alternative since any abnormalities must be followed by endoscopy and biopsy. Once the diagnosis is made, further imaging is necessary for staging and assessment of resectability. ❸ CT will provide evidence of intraabdominal spread or liver metastases. Even with these techniques, ❹laparoscopy with peritoneal washings is required to determine whether the tumour is resectable, as it is the only modality that will reliably detect peritoneal spread

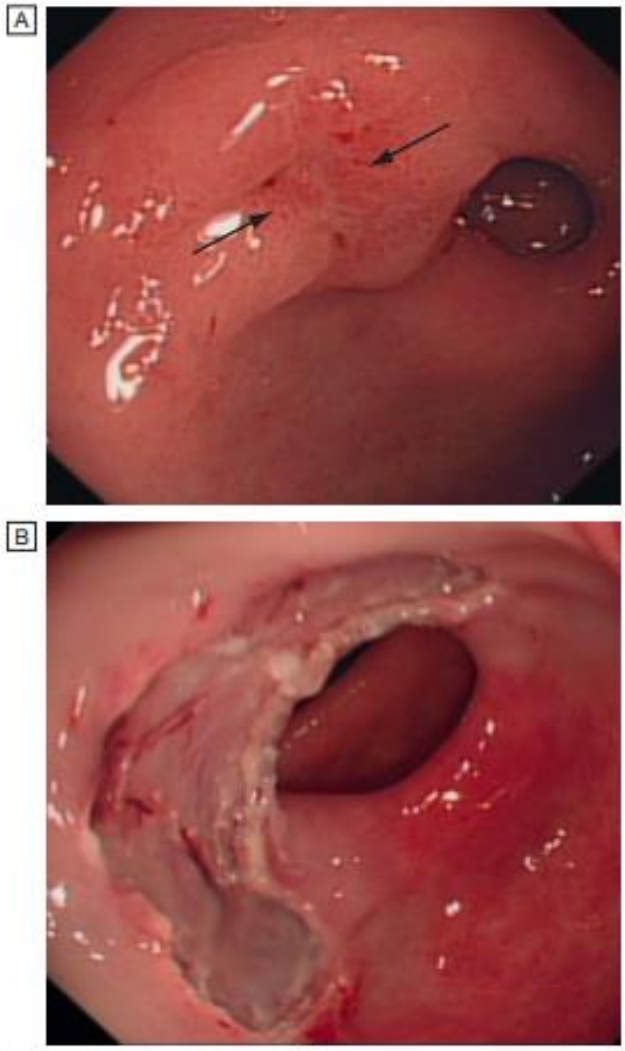


Fig. 22.37 Gastric carcinoma. A Endoscopic image of a small superficial pre-pyloric cancer (arrows). B Appearance after endoscopic mucosal resection (EMR). The tumour has been completely removed.

Management

Surgery: Resection offers the only hope of cure, and this can be achieved in about 90% of patients with early gastric cancer. For the majority of patients with locally advanced disease, **total gastrectomy with lymphadenectomy is the operation of choice**, preserving the spleen if possible. Proximal tumours involving the oesophago-gastric

junction also require a **distal oesophagectomy**. Small, distally sited tumours can be managed by a **partial gastrectomy with lymphadenectomy and either a Billroth I or a Roux en Y reconstruction**. More extensive lymph node resection may increase survival rates but carries greater morbidity. Even for those who cannot be cured, *palliative resection may be necessary when patients present with bleeding or gastric outflow obstruction.*

Prognosis: Following surgery, recurrence is much more likely if serosal penetration has occurred, although complete removal of all macroscopic tumour combined with lymphadenectomy will achieve a 50–60% 5-year survival. Recent evidence suggests that perioperative chemotherapy improves survival rates.

Palliative treatment

In patients with inoperable tumours, survival can be improved and palliation of symptoms achieved with **chemotherapy** using 5-fluorouracil and cisplatin, ECF or other platinum and taxane-based regimens. The **biological agent** trastuzumab may benefit some patients whose tumours over-express HER2. **Endoscopic laser ablation or Argon Plasma Coagulation** for control of dysphagia or recurrent bleeding benefits some patients. Carcinomas at the cardia or pylorus may require **endoscopic dilatation or insertion of expandable metallic stents** for relief of dysphagia or vomiting. A **nasogastric tube** may offer temporary relief of vomiting due to gastric outlet obstruction.

Gastric lymphoma

This is a rare tumour accounting for less than **5%** of all gastric malignancies. The stomach is, however, the most common site for extranodal non-Hodgkin lymphoma and 60% of all primary gastrointestinal lymphomas occur at this site. *Lymphoid tissue is not found in the normal stomach but lymphoid aggregates develop in the presence of H. pylori infection.* Indeed, H. pylori infection is closely associated with the development of a low grade lymphoma (classified as extranodal marginal zone lymphomas of MALT type). **EUS** plays an important role in staging these lesions by accurately

defining the depth of invasion into the gastric wall. The clinical presentation is similar to that of gastric cancer, and endoscopically the tumour appears as a **polypoid or ulcerating mass**. While initial <u>treatment</u> of **<u>low-grade</u>** lesions confined to the superficial layers of the gastric wall consists of ❶ H. pylori eradication and close observation, 25% contain t(11: 18) chromosomal translocations. In these cases, additional ❷radiotherapy or ❸chemotherapy is usually necessary. **<u>High-grade</u>** B-cell lymphomas should be treated by a ❹combination of rituximab, chemotherapy, surgery and radiotherapy. The choice depends on the site and extent of tumour, the presence of comorbid illnesses, and other factors, such as symptoms of bleeding and gastric outflow obstruction.

22.48 How to insert a nasogastric tube

Equipment

- 8–9F 'fine-bore' tube for feeding or 16–18F 'wide-bore' tube for drainage
- Lubricant jelly
- Cup of water and straw for sipping
- Adhesive tape
- pH (not litmus) paper
- Sickness bowl and tissues
- Catheter drainage bag and clamp (for drainage)

Technique

- A clear explanation and a calm patient are essential
- Establish a 'stop signal' for the patient to use, if needed
- Ask the patient to sit semi-upright
- Examine the nose for deformity or blockage to determine which side to use
- Measure the distance from ear to xiphoid process via the nose and mark the position on the tube
- Advance the lubricated tube tip slowly along the floor of the nasal passage to the oropharynx
- Ask the patient to sip water and advance the tube 2–3 cm with each swallow
- Stop, withdraw and retry if the patient is distressed or coughing, as the tube may have entered the larynx
- Advance until the mark on the tube reaches the tip of the nose and secure with tape
- Aspirate the contents and check pH (gastric acid confirmed if pH < 5). If in doubt, perform a chest X-ray to confirm tube position (usually necessary with feeding tubes)
- Attach the catheter drainage bag, if necessary, and clamp

Aftercare

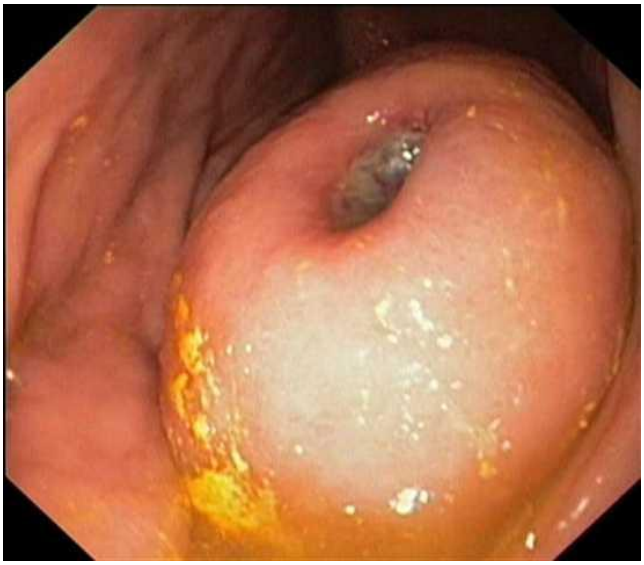
- Flush the tube daily after feeding or drug dosing
- Check position regularly and look for signs of displacement
- Check with the pharmacist what drugs, if any, can be safely given via the tube

The prognosis depends on the stage at diagnosis. Features predicting a favourable prognosis are stage I or II disease, small resectable tumours, tumours with low grade histology, and age below 60 years.

Other tumours of the stomach

Gastrointestinal stromal cell tumours (GIST), arising from the interstitial cells of Cajal, are occasionally found at upper gastrointestinal endoscopy. They are differentiated from other mesenchymal tumours by expression of

the c-kit proto-oncogene, which encodes a tyrosine kinase receptor. These tumours are usually benign and *asymptomatic*, but may occasionally be responsible for *dyspepsia*, *ulceration* and gastrointestinal *bleeding*. Endoscopically the lesion seen as subepithelial mass with occasional umbilication (see the figure)



Small lesions (< 2 cm) are usually followed up by endoscopy, while larger ones require surgical resection.

Very large lesions should be treated pre-operatively with imatinib (a tyrosine kinase inhibitor) to reduce their size and make surgery easier.

Imatinib can also be used for palliation of metastatic GISTs.

Polyps, a variety of polyps occur. ❶ Hyperplastic polyps and ❷ fundic cystic gland polyps are common and of no consequence. ❸ Adenomatous polyps are rare but have malignant potential and should be removed endoscopically. Occasionally, ❹ gastric carcinoid tumours are seen in the fundus and body in patients with long-standing pernicious anaemia. These benign tumours arise from ECL or other endocrine cells, and are often multiple but rarely invasive. Unlike carcinoid tumours arising elsewhere in the gastrointestinal tract, they usually run a benign and favourable course. However, large (> 2 cm) carcinoids may metastasise and should be removed.

Rarely, small nodules of ❺ ectopic pancreatic exocrine tissue are found. These 'pancreatic rests' may be mistaken for gastric neoplasms and usually cause no symptoms. EUS is the most useful investigation.