Burning epigastric pain

A 37-year-old executive returns to your clinic for follow-up of **recurrent** upper abdominal pain. He initially presented 3 weeks ago, complaining of an increase in frequency and severity of **burning epigastric pain**, which he has experienced occasionally for more than 2 years. Now the pain occurs three or four times per week, usually when he has an **empty stomach,** and it often awakens him at night. **The pain usually is relieved within minutes by food or over-the-counter antacids**, but then **recurs** within **2 to 3 hours**. He admitted that **stress at work** had recently increased and that because of long working hours, he was drinking more **caffeine** and eating a lot of **take-out foods**. His medical history and review of systems were otherwise unremarkable, and, other than the antacids, he takes no medications.

His physical examination was normal, including **stool** guaiac that was **negative for occult blood**. You advised a **change in diet** and started him on a **proton-pump inhibitor**. His **symptoms resolved completely** with the diet changes and daily use of the medication. Results of laboratory tests performed at his first visit show no anemia, but his **serum *Helicobacter pylori antibody test was positive*.**

What is your diagnosis?
What is your next step?

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What is your diagnosis? Peptic ulcer disease

What is your next step? Triple antibiotic therapy for H pylori infection, and acid suppression.

CFIN n° 4

Dyspepsia

NSAID

War The stomach is a battle ground between the forces of attack (acid, pepsin, *Helicobacter pylori*, bile salts) and defence (mucin secretion, cellular mucus, bicarbonate secretion, mucosal blood flow, cell turnover).[44] Gastric antisecretory agents, eg H_2receptor antagonists (H2RAs), and proton pump inhibitors (PPIs) may only work if you have optimized cytoprotection (antacids and sucralfate work this way). Success may depend on you being not just a brilliant general, but also a tactician, politician, and diplomat. Plan your strategy carefully with the FLOWCHART (fig 1). As in any war, neglecting psychological factors can prove disastrous (see ℞ below). The aim is not outright victory but *maintaining the balance of power* so all may prosper.

Noninvasive test for H pylori

- urea breath test
- Fecal antigen test
- IgG serology

performance of IgG serology is poor in low-prevalence populations, whereas breath and fecal antigen tests have 95% accuracy.

Symptoms Epigastric pain often related to hunger, specific foods, or time of day ± bloating, fullness after meals, heartburn (retrosternal pain + reflux); tender epigastrium. **Alarm symptoms**: **A**naemia (iron deficiency); **l**oss of weight; **a**norexia; **r**ecent onset/progressive symptoms; **m**elaena/haematemesis; **s**wallowing difficulty.

Differential diagnosis of dyspepsia

- Non-ulcer dyspepsia
- Oesophagitis/GORD
- Duodenal/gastric ulcer
- Gastric malignancy
- Duodenitis
- Gastritis (p253)

Functional Dyspepsia →

epigastric pain syndrome and the postprandial distress syndrome. The epigastric pain syndrome consists of intermittent pain or burning in the epigastrium, occurring at least once per week, and the postprandial distress syndrome is marked by the occurrence at least several times per week of bothersome postprandial fullness occurring after normal-sized meals or by early satiety that prevents the person from finishing a regular meal

Table 1. Possible Underlying Causes of Symptoms of Dyspepsia.

Functional dyspepsia
Peptic ulcer disease and infection with *Helicobacter pylori*
Gastroesophageal cancer
Gastroparesis
Gallstones, sphincter of Oddi dysfunction, biliary dyskinesia, or gallbladder cancer
Drugs (e.g., nonsteroidal antiinflammatory drugs, iron, calcium antagonists, angiotensin-converting–enzyme inhibitors, methylxanthines, and glucocorticoids)
Chronic pancreatitis or pancreatic cancer
Parasites (e.g., *Giardia lamblia*, strongyloides, and anisakis)
Hepatocellular carcinoma
Chronic mesenteric ischemia
Crohn's disease
Infiltrative diseases (e.g., eosinophilic gastroenteritis and sarcoidosis)

Functional Dyspepsia

N Engl J Med 2015;373:1853-63.

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excluding from the definition of functional dyspepsia persons with symptoms suggestive of gastroesophageal reflux disease (GERD), such as retrosternal burning pain, regurgitation of acid into the mouth, or the irritable bowel syndrome, which is characterized by lower abdominal pain or discomfort associated with a change in stool form or frequency.[1]

Table 2. Alarm Symptoms of an Underlying Upper Gastrointestinal Cancer.

Age >55 yr with new-onset dyspepsia*
Evidence of overt gastrointestinal bleeding including melena or hematemesis
Dysphagia, especially if progressive, or odynophagia
Persistent vomiting
Unintentional weight loss
Family history of gastric or esophageal cancer
Palpable abdominal or epigastric mass or abnormal adenopathy
Evidence of iron-deficiency anemia after blood testing

* In regions with a high background prevalence rate of gastric cancer, such as Southeast Asia, a lower age threshold should be considered.

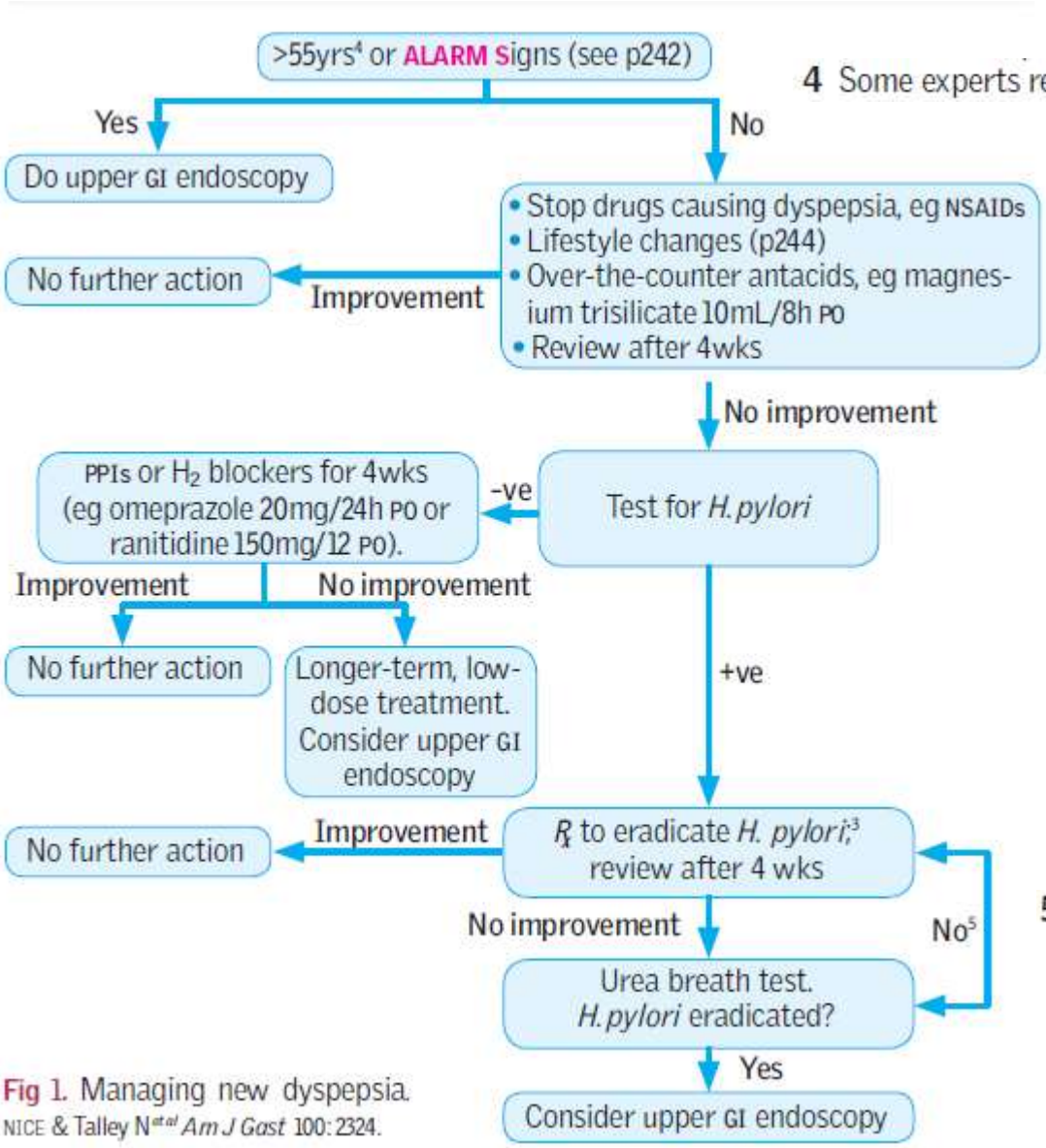


Fig 1. Managing new dyspepsia.
NICE & Talley N[et al] *Am J Gast* 100: 2324.

4 Some experts recommend endoscopy if >45yrs old.

Noninvasive test for H pylori

- urea breath test
- Fecal antigen test
- IgG serology

performance of IgG serology is poor in low-prevalence populations, whereas breath and fecal antigen tests have 95% accuracy.

5 Don't treat +ve cases of *H. pylori* more than twice. If still +ve, do endoscopy.

Why not start everyone on a PPI straight away? Simple measures are safer (more and more PPI SE are reported). Also, PPIs and ranitidine cause false -ve breath tests and antigen tests: stop for >2wks before (>4wks for bismuth and antibiotics).[52] ▶ See NICE.

LFT ..... liver function test

PPI SE reflect lack of gastric acid: gastroenteritis; B_{12}↓ (also osteoporosis, alopecia, photosensitivity; LFT↑).

pneumonia

1 *H. pylori* is the commonest bacterial pathogen found worldwide (>50% of the world population over 40yrs has it).[49] It's a **class I carcinogen** causing gastritis (p253), duodenal/gastric ulcers & gastric cancer/lymphoma (MALT, p356), also associated with coronary artery disease, B_{12} and iron deficiency.

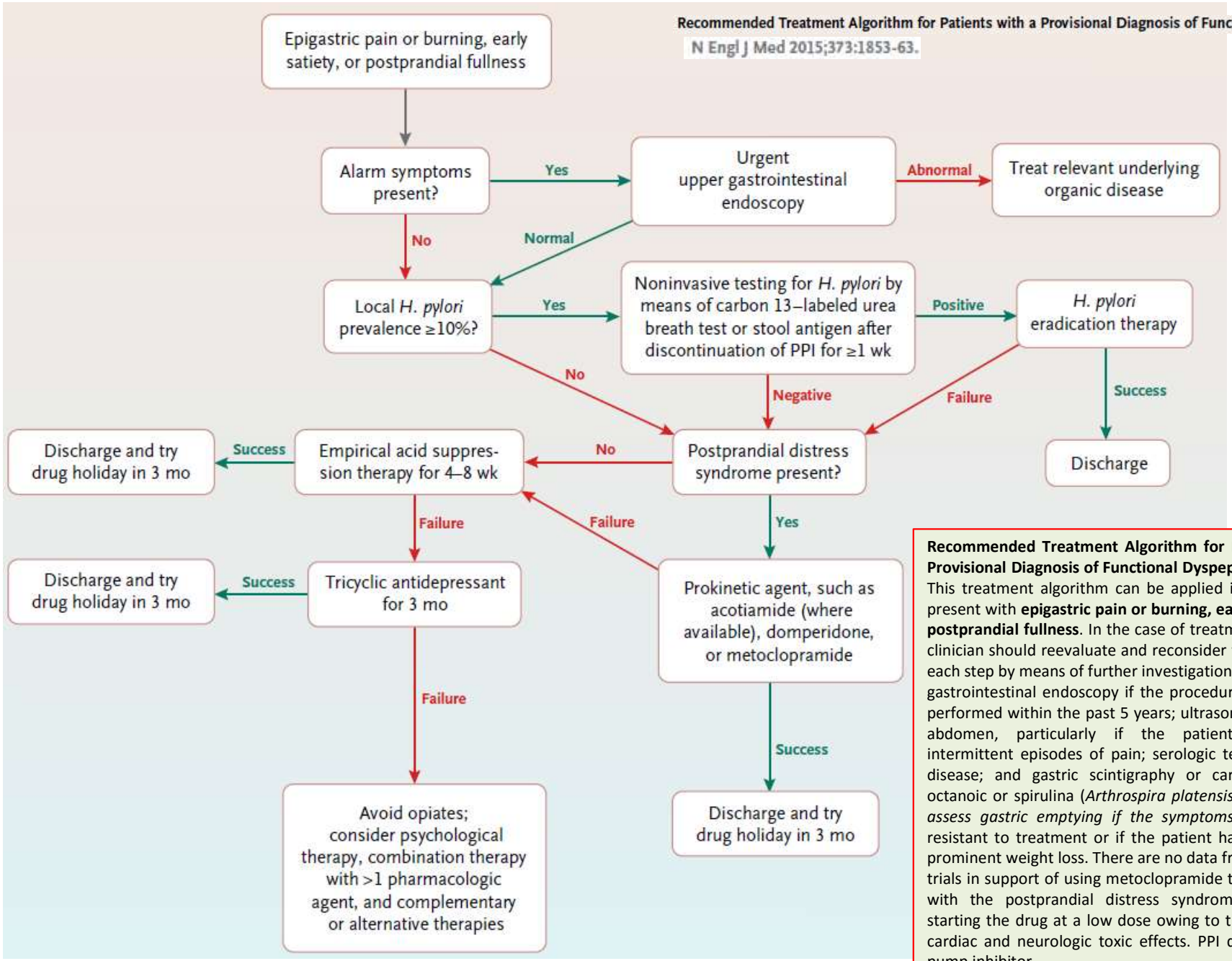
H. pylori[1] (BOX 1). *If ≤55yrs old* test for *H. pylori*; treat if +ve.'Test and treat',[2] eg lansoprazole 30mg/24h PO for 4wks reduces symptoms and recurrence more than acid suppression alone. ►*If ≥55* (and new dyspepsia not from NSAID use and persisting for >4–6wks) or *alarm symptoms*, refer for urgent endoscopy (p256).

^{13}C breath test is the most accurate non-invasive *Helicobacter* test

		Sensitivity		Specificity	
Invasive tests	CLO test		95%		95%
	Histology		95%		95%
	Culture		90%		100%
Non-invasive	^{13}C breath test		95%		95%
	Stool antigen		95%		94%
	Serology		92%		83%

Every breath we exhale leaves our own unique breathprint on the world: nitrogen, oxygen, CO_2, vapour, and ~250 volatile substances that give useful information about our state of health to scientists and lovers—kisses are faster but less reliable than spectrometers, which can inform about GI diseases, asthma, organ rejection, and cancer.[50]

3 *H. pylori* eradication (NICE/*BNF*): **either** PAC500 regimen (full dose PPI, amoxicillin 1g, clarithromycin 500mg) twice daily **or** PMC250 (full dose PPI, metronidazole 400mg, clarithromycin 250mg) twice daily for 7d. PPIs: omeprazole 20mg/12h; lansoprazole: 30mg/12h. **Resistant infections:** tripotassium dicitratobismuthate (De Noltab® 2 twice daily ½h before food[53]) + PPI + 2 antibiotics for 14d. Bismuth causes black stools: warn the patient! NB: you may need to continue the PPI if the ulcer is large or bleeds.[13]

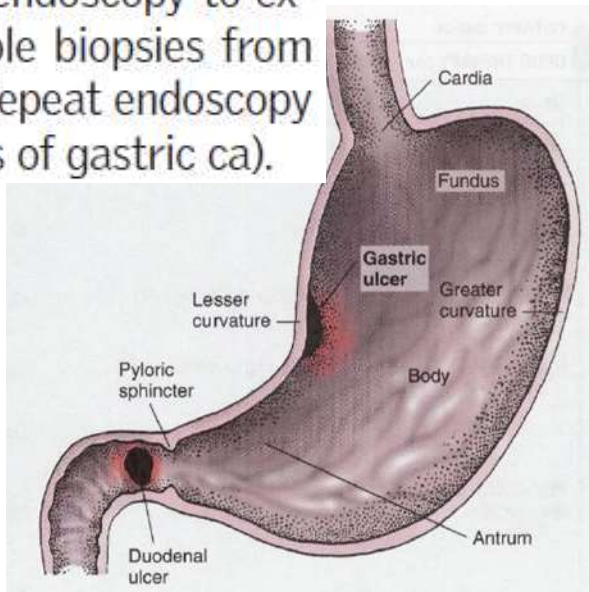


Recommended Treatment Algorithm for Patients with a Provisional Diagnosis of Functional Dyspepsia.
This treatment algorithm can be applied in patients who present with **epigastric pain or burning, early satiation**, or **postprandial fullness**. In the case of treatment failure, the clinician should reevaluate and reconsider the diagnosis at each step by means of further investigations, such as upper gastrointestinal endoscopy if the procedure has not been performed within the past 5 years; ultrasonography of the abdomen, particularly if the patient has severe, intermittent episodes of pain; serologic testing for celiac disease; and gastric scintigraphy or carbon-13–labeled octanoic or spirulina (*Arthrospira platensis) breath test to assess gastric emptying if the symptoms are severe* or resistant to treatment or if the patient has vomiting and prominent weight loss. There are no data from randomized trials in support of using metoclopramide to treat patients with the postprandial distress syndrome; we suggest starting the drug at a low dose owing to the potential for cardiac and neurologic toxic effects. PPI denotes proton-pump inhibitor.

peptic ulcer disease (PUD)

Duodenal ulcer (DU, fig 1 p255) is 4-fold commoner than GU. *Major risk factors:* *H. pylori* (90%); drugs (NSAIDs; steroids; SSRI).[45] *Minor:* ↑Gastric acid secretion; ↑gastric emptying (↓duodenal pH); blood group O; smoking. The role of stress is debated. *Symptoms:* Epigastric pain typically before meals or at night, relieved by eating or drinking milk. 50% are asymptomatic; others experience recurrent episodes. *Signs:* Epigastric tenderness. *Diagnosis:* Upper GI endoscopy (stop PPI 2wks before). Test for *H. pylori*. Measure gastrin concentrations when off PPIs if Zollinger-Ellison syndrome (p730) is suspected. *ΔΔ:* Non-ulcer dyspepsia; duodenal Crohn's; TB; lymphoma; pancreatic cancer (p276). *Follow-up:* None; if good response to R_x (eg PPI).

Gastric ulcers (GU) occur mainly in the elderly, on the lesser curve. Ulcers elsewhere are more often malignant. *Risk factors:* *H. pylori* (~80%); smoking; NSAIDs; reflux of duodenal contents; delayed gastric emptying; stress, eg neurosurgery or burns (Cushing's or Curling's ulcers). *Symptoms:* Asymptomatic or epigastric pain (related to meals ± relieved by antacids) ± weight↓. *Tests:* Upper endoscopy to exclude malignancy (stop PPI >2wks before, see FLOWCHART); multiple biopsies from ulcer rim and base (histology, *H. pylori*) and brushings (cytology). Repeat endoscopy (eg if perforation or bleeding) to check healing (biopsy if suspicious of gastric ca).



Lifestyle: Purge stress[46] by creating opportunities for people to move from disease into health through dialogue and reflection on their lives—eg would he/she see benefit in ↓alcohol and tobacco use? Both will help. Avoid any aggravating foods.
H. pylori eradication: Triple therapy[3] is 80–85% effective at eradication.
Drugs to reduce acid: PPIs are effective, eg *lansoprazole* 30mg/24h PO for 4 (DU) or 8 (GU) wks. H_2 blockers have a place (*ranitidine* 300mg each night PO for 8wks).
Drug-induced ulcers: Stop drug if possible. PPIs may be best for treating and preventing GI ulcers and bleeding in patients on NSAID or antiplatelet drugs. Misoprostol is an alternative with different SE.[47] If symptoms persist, re-endoscope, recheck for *H. pylori*, and reconsider differential diagnoses (eg gallstones). *Surgery:* p626.

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PPI SE reflect lack of gastric acid: gastroenteritis; B_{12}↓ (also osteoporosis, alopecia, photosensitivity; LFT↑).

Complications Bleeding ▶▶(p252), perforation ▶▶(p608), malignancy, gastric outflow↓.

Functional (non-ulcer) dyspepsia Treatment is hard. *H. pylori* eradication, only after a +ve result) *may* help, but long-term effects of such a strategy are unknown. Some evidence favours PPIs and psychotherapy. PPI SE aren't negligible![2] Antacids, antispasmodics, H_2 blockers, misoprostol, prokinetic agents, sucralfate, or tricyclics have less evidence.[48] Bismuth preparations are an interesting and ancient option (eg DeNol® 120mg/12h), having healing and anti-*Helicobacter* properties; it's available over-the-counter, avoiding medicalization. It turns stools black.

A rare cause of ulcer is the **Zollinger-Ellison syndrome** (ZES), a condition in which a gastrin-producing tumor (usually pancreatic) causes acid hypersecretion, peptic ulceration, and often diarrhea. This condition should be suspected if patients have ulcers refractory to standard medical therapy, ulcers in unusual locations (beyond the duodenal bulb), or ulcers without a history of NSAID use or *H pylori* infection. About 25% of gastrinomas occur in patients with multiple endocrine neoplasia I (MEN I) syndrome, an autosomal dominant genetic disorder characterized by parathyroid, pancreatic, and pituitary neoplasms. To diagnose Zollinger-Ellison syndrome, the first step is to measure a fasting gastrin level, which may be markedly elevated (>1000 pg/mL), and then try to localize the tumor with an imaging study.

Gastritis

Causes: Alcohol, NSAIDs, *H. pylori*, reflux/hiatus hernia, atrophic gastritis, granulomas (Crohn's; sarcoidosis), CMV, Zollinger–Ellison & Ménétrier's disease (p730 & 720).
Presentation: Epigastric pain, vomiting; haematemesis. *Δ:* Endoscopy + biopsy.
Prevention: Give PPI gastroprotection with NSAIDs; this also prevents bleeding from acute stress ulcers/gastritis so often seen with ill patients (esp. burns) on ITU.
Treatment: Ranitidine or PPI; eradicate *H. pylori* as needed (p243). Triple therapy now often fails: quadruple R_x with bismuth subcitrate may be needed. Troxipide 100mg/8h PO improves gastric mucus. Endoscopic cautery may be needed.

4.1 A 42-year-old overweight but otherwise healthy woman presents with sudden onset of right-upper abdominal colicky pain 45 minutes after a meal of fried chicken. The pain is associated with nausea and vomiting, and any attempt to eat since has caused increased pain. Which of the following is the most likely cause?

A. Gastric ulcer
B. Cholelithiasis
C. Duodenal ulcer
D. Acute hepatitis

4.2 Which of the following is the most accurate statement regarding *H pylori* infection?

A. It is more common in developed than underdeveloped countries.
B. It is associated with the development of colon cancer.
C. It is believed to be the cause of nonulcer dyspepsia.
D. The route of transmission is believed to be sexually transmitted.
E. It is believed to be a common cause of both duodenal and gastric ulcers.

4.3 A 45-year-old man was brought to the ER after vomiting bright red blood. He has a blood pressure of 88/46 mm Hg and heart rate of 120 bpm. Which of the following is the best next step?

A. Intravenous fluid resuscitation and preparation for a transfusion
B. Administration of a proton-pump inhibitor
C. Guaiac test of the stool
D. Treatment for *H pylori*

4.4 Which one of the following patients should be promptly referred for endoscopy?

A. A 65-year-old man with new onset of epigastric pain and weight loss
B. A 32-year-old patient whose symptoms are not relieved with ranitidine
C. A 29-year-old *H pylori*-positive patient with dyspeptic symptoms
D. A 49-year-old woman with intermittent right-upper quadrant pain following meals

4.1 **B.** Right-upper abdominal pain of acute onset that occurs after ingestion of a fatty meal and is associated with nausea and vomiting is most suggestive of biliary colic as a result of gallstones. Duodenal ulcer pain is likely to be diminished with food, and gastric ulcer pain is not likely to have acute severe onset. Acute hepatitis is more likely to produce dull ache and tenderness.

4.2 **E.** Although *H pylori* is clearly linked to gastric and duodenal ulcers and probably to gastric carcinoma and lymphoma, whether it is more common in patients with nonulcer dyspepsia and whether treatment in those patients reduces symptoms are unclear. It is more common in underdeveloped or developing countries.

4.3 **A.** This patient is hemodynamically unstable with hypotension and tachycardia as a consequence of the acute blood loss. Volume resuscitation, immediately with crystalloid or colloid solution, followed by blood transfusion, if necessary, is the initial step to prevent irreversible shock and death. Later, after stabilization, acid suppression and *H pylori* treatment might be useful to heal an ulcer, if one is present.

4.4 **A.** Patient in answer A has "red flag" symptoms: he is older than 45 years and has new-onset symptoms. Patient in answer B may benefit from the reassurance of a negative endoscopic examination. Patient in answer C, however, may benefit from treatment of *H pylori* first. Some studies indicate this approach may be cost-saving overall. This patient could be sent for an endoscopic examination if she does not improve following the therapy.

- The most common causes of duodenal and gastric ulcers are *Helicobacter pylori* infection and use of nonsteroidal anti-inflammatory drugs.
- *Helicobacter pylori* is associated with duodenal and gastric ulcers, chronic active gastritis, gastric adenocarcinoma, and gastric mucosa–associated lymphoid tissue (MALT) lymphoma.
- Treatment of peptic ulcers requires acid suppression with an H_2 blocker or proton-pump inhibitor to heal the ulcer, as well as antibiotic therapy of *Helicobacter pylori* infection, if present, to prevent recurrence.
- Patients with dyspepsia who have "red flag" symptoms (new dyspepsia after the age of 45 years, weight loss, dysphagia, evidence of bleeding or anemia) should be referred for an early endoscopic examination.
- Other patients (patients with dyspepsia who do not have "red flag" symptoms) may be tested for *Helicobacter pylori* and treated first. Antibody tests show evidence of infection but remain positive for life, even after successful treatment. Urea breath tests are evidence of current infection.
- Common treatment regimens for *Helicobacter pylori* infection include a 14-day course of a proton-pump inhibitor in high doses along with antibiotic therapy, which may include clarithromycin, amoxicillin, metronidazole, or tetracycline, along with a bismuth compound.

Gastro-oesophageal reflux disease (GORD)

GORD is common, and is said to exist when reflux of stomach contents (acid ± bile)[1] causes troublesome symptoms (≥2 heartburn episodes/wk) and/or complications.[54] If reflux is prolonged, it may cause oesophagitis (fig 1), benign oesophageal stricture, or Barrett's oesophagus (fig 2 and p709; it is pre-malignant). Causes: lower oesophageal sphincter hypotension, hiatus hernia (see below), loss of oesophageal peristaltic function, abdominal obesity, gastric acid hypersecretion, slow gastric emptying, overeating,[54] smoking, alcohol, pregnancy, surgery in achalasia, drugs (tricyclics, anticholinergics, nitrates), systemic sclerosis, *Helicobacter pylori*?[2]

Symptoms *Oesophageal:* Heartburn (burning, retrosternal discomfort after meals, lying, stooping or straining, relieved by antacids); belching; acid brash (acid or bile regurgitation); waterbrash (↑↑ salivation: "My mouth fills with saliva"); odynophagia (painful swallowing, eg from oesophagitis or ulceration). *Extra-oesophageal:* Nocturnal asthma, chronic cough, laryngitis (hoarseness, throat clearing), sinusitis.[55]

Complications Oesophagitis, ulcers, benign stricture, iron-deficiency. *Metaplasia→dysplasia→neoplasia:* GORD may induce Barrett's oesophagus (p709; distal oesophageal epithelium undergoes metaplasia from squamous to columnar—this intestinal metaplasia looks velvety, fig 2). 0.6-1.6%/yr of those with low-grade Barrett's progress to oesophageal cancer[56] (higher if 2 histologists concur: diagnosing low-grade dysplasia is tricky: the Prague criteria should be used).[57] Length of lesion matters less than histology. Overall risk of adenocarcinoma in GORD is <1 in 1000/yr. *Histology: Gastric metaplasia:* low risk of malignant change. *Intestinal metaplasia*—2-yrly surveillance. *Low-grade dysplasia*—90% get adenocarcinoma within 6yrs. *High-grade dysplasia:* 50% have adenocarcinoma already.

ΔΔ Oesophagitis from corrosives, NSAIDs, herpes, *Candida*; duodenal or gastric ulcers or cancers; non-ulcer dyspepsia; sphincter of Oddi malfunction; cardiac disease.

Tests Endoscopy if: symptoms for >4wks; persistent vomiting, GI bleeding/iron deficiency; palpable mass; age >55; dysphagia; symptoms despite treatment; relapsing symptoms; weight↓. Barium swallow may show hiatus hernia. 24h oesophageal pH monitoring ± manometry help diagnose GORD when endoscopy is normal.

Treatment *Encourage:* Raising the bed head ± weight loss; smoking cessation; small, regular meals. "Get to know your own disease, and learn tricks that work for you..." *Avoid:* Hot drinks, alcohol, citrus fruits, tomatoes,[58] onions, fizzy drinks, spicy foods, coffee, tea, chocolate, and eating <3h before bed. Avoid drugs affecting oesophageal motility (nitrates, anticholinergics, Ca^{2+} channel blockers—relax the lower oesophageal sphincter) or that damage mucosa (NSAIDs, K^+ salts, bisphosphonates).

Drugs: Antacids, eg ***magnesium trisilicate mixture*** (10mL/8h), or alginates, eg ***Gaviscon Advance***® (10–20mL/8h PO) relieve symptoms. For oesophagitis, try a PPI, eg ***lansoprazole*** 30mg/24h PO.[59] PPIs are better than H_2 blockers. If unresponsive, try twice-daily PPI. Metoclopramide as mono- or adjunctive therapy is discouraged.[60]

Surgery (eg laparoscopic) aims to ↑resting lower oesophageal sphincter pressure. Consider in severe GORD (confirm by pH-monitoring/manometry) if drugs are not working. Atypical symptoms (cough, laryngitis) are less likely to improve with surgery compared to patients with typical symptoms. Options are many, eg Nissen fundoplication, p626; HALO® or Stretta radiofrequency ablation of the gastro-oesophageal junction if high-grade dysplasia (and maybe low-grade too).[61]

4 grades *Los Angeles classification of GORD* Minor diffuse changes (erythema, oedema; friability) are not included, and the term mucosal break (a well-demarcated area of slough/erythema) is used to encompass the old terms erosion & ulceration:[62]

1. ≥1 mucosal break(s) <5mm long not extending beyond 2 mucosal fold tops.
2. Mucosal break >5mm long limited to the space between 2 mucosal fold tops.
3. Mucosal break continuous between the tops of 2 or more mucosal folds but which involves less than 75% of the oesophageal circumference.
4. Mucosal break involving ≥75% of the oesophageal circumference.

1 Bile reflux may be as important as acid; bile is alkaline; it may respond to sucralfate (2g/12h PO), domperidone or metoclopramide. Roux-en-Y diversion may be needed (p624).[63]
2 *H. pylori* eradication may not influence the course of GORD,[64] but may help symptoms.[65]

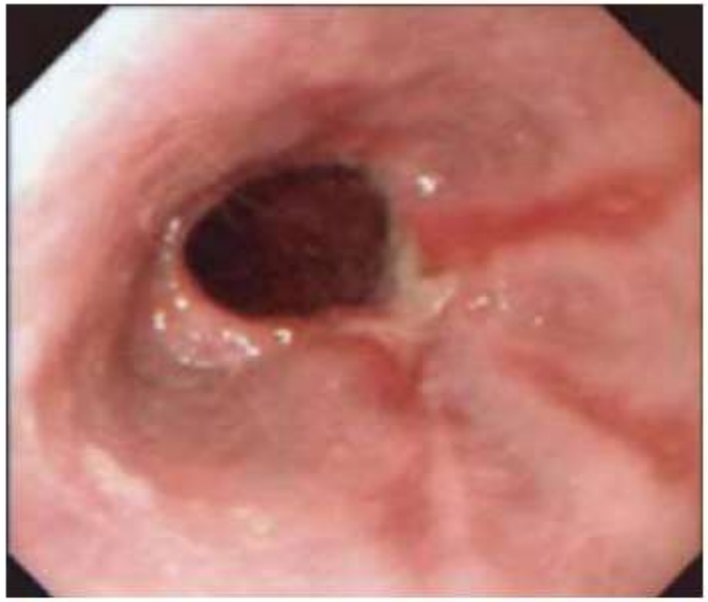


Fig 1. Upper GI endoscopy showing longitudinal mucosal breaks in severe oesophagitis.

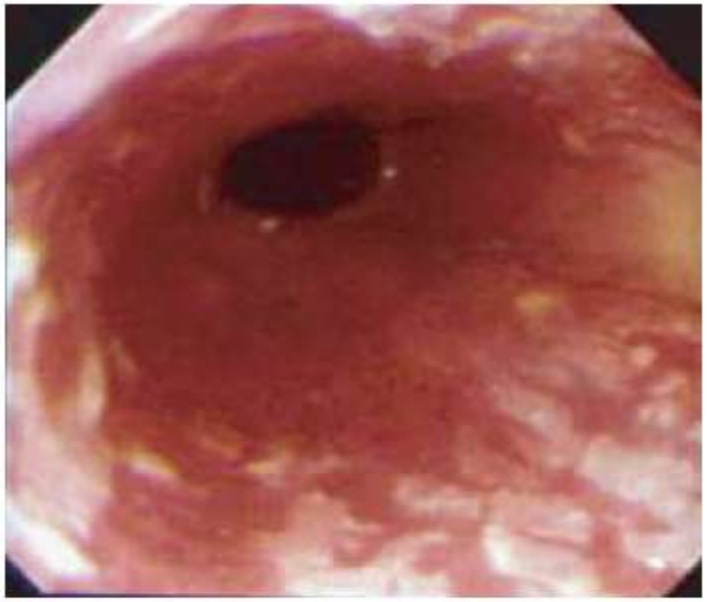


Fig 2. Barrett's oesophagus.

Figs 1 & 2 ©Dr A Mee.

Hiatus hernia

Sliding hiatus hernia (80%) is where the gastro-oesophageal junction slides up into the chest—see fig 3. Acid reflux often happens as the lower oesophageal sphincter becomes less competent in many cases.

Rolling hiatus hernia (20%) is where the gastro-oesophageal junction remains in the abdomen but a bulge of stomach herniates up into the chest alongside the oesophagus—see figs 3 and 4. As the gastro-oesophageal junction remains intact, gross acid reflux is uncommon.

Clinical features Common: 30% of patients >50yrs, especially obese women. 50% have symptomatic gastro-oesophageal reflux.

Imaging Barium swallow is the best diagnostic test; upper GI endoscopy visualizes the mucosa (?oesophagitis) but cannot reliably exclude a hiatus hernia.

Treatment Lose weight. Treat reflux symptoms. Surgery indications: intractable symptoms despite aggressive medical therapy, complications (see opposite). It is advised to repair rolling hiatus hernia prophylactically (even if asymptomatic) as it may strangulate, which needs prompt surgical repair (which has a high mortality and morbidity rate).

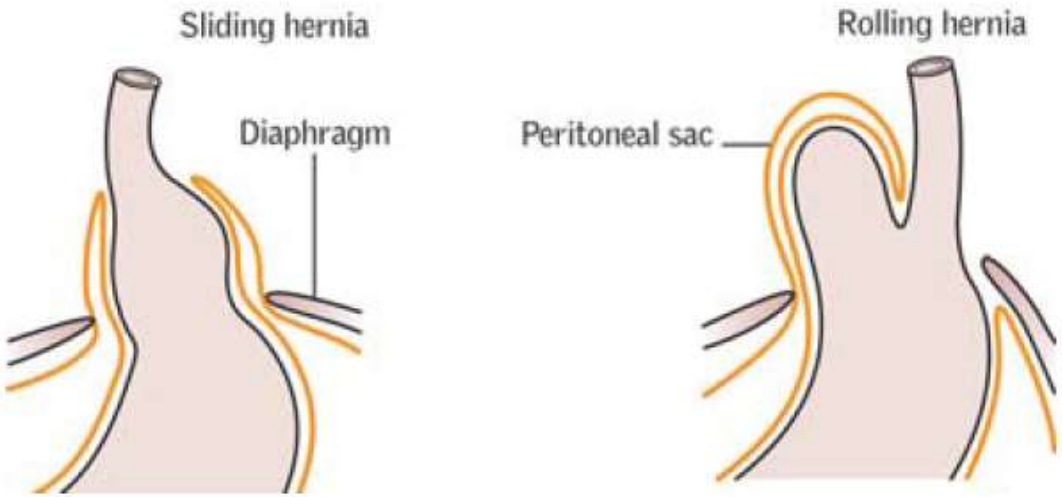


Fig 3. Hiatus hernia—sliding and rolling.

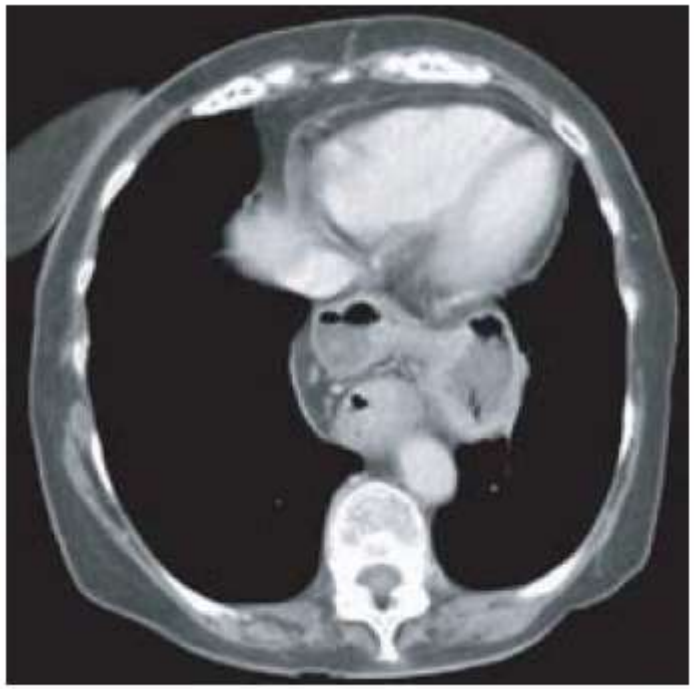


Fig 4. CT chest (IV contrast) showing the rolling components of a hiatus hernia anterior to the oesophagus. Between the oesophagus and the vertebral column on the left-hand side is the aorta. ©Dr S Golding.

Inibitori della Pompa Protonica (uso ≥12 mesi)	
Perchè?	Nonostante l'uso sia regolato da note ministeriali dell'AIFA (48/1) sono ampiamente utilizzati anche per indicazioni non registrate, talvolta inappropriate ed ingiustificate. Vi sono patologie come la dispepsia, la MRGE (soprattutto NERD: *malattia da reflusso non erosiva*) e la gastroprotezione, per le quali i dati di letteratura non sono univoci con conseguenti raccomandazioni non uniformi. Nella Dispepsia i PPI non risultano più efficaci rispetto al placebo e pertanto non sono indicati; è comunque mandatorio in tali pazienti (> 50 aa) escludere preliminarmente una patologia organica ® EGDS. L'ASA nella prevenzione primaria cardiovascolare ha mostrato un incremento del rischio assoluto per ulcera e sanguinamento grave molto modesto (0,1% e 0,6%). Non esistono evidenze conclusive per raccomandare l'uso di PPI per la prevenzione primaria del danno gastrointestinale da steroidi, da anticoagulanti orali, da eparine, da bifosfonati e da chemioterapici (anche se in associazione). Gli H2-antagonisti, pur essendosi dimostrati superiori al placebo nella terapia della MRGE e nella gastroprotezione primaria (follow-up 1 anno), presentano vantaggi modesti in relazione al fenomeno della tachifilassi che ne invalida l'impiego long-term. L'infezione da Helicobacter Pylori và ricercata e trattata in tutti i pazienti con ulcera peptica, in quelli che richiedono terapie con PPI > 6 settimane o che devono intraprendere una terapia antiaggregante con ASA. Dosi standard dei vari PPI producono gradi comparabili di guarigione e remissione delle patologie acido-correlate e pertanto non esistono evidenze che mostrino differenze di efficacia antisecretiva e sicurezza tra le varie molecole disponibili anche in termini di interazione farmacologica. L'utilizzo protratto dei PPI (+360 gg), inoltre, è associato ad un aumentato rischio di effetti avversi di rilevanza clinica significativa che vengono di seguito riportati: ▪ frattura d'anca ▪ incremento recidiva ischemica miocardica nel pz in tratt con Clopidrogel ▪ interazioni farmacologiche avverse nel paziente politrattato ▪ miopatia ▪ infezione enteriche (Clostridium d., SIBO) ▪ infezioni respiratorie ▪ poliposi gastrica ▪ carcinoma gastrico (NET) e del colon

	▪ nefrite interstiziale ▪ colite microscopica (Tauseef Ali, David N.R., William M.T. Long-term Safety Concerns with Proton Pump Inhibitors. Am J of Med, 2009; Lodato F. et al. Adverse effects of proton pump inhibitors. Best Practice & Clinical Gastroenterol, 2010 (24); 193-201; Batuwitage BT, Kingham JHC, Morgan NE, Bardett RL. Inappropriate prescribing of proton pump inhibitors in primary care. Postgrad Med J 2007;93:66-8)
Quando appropriato?	DISPEPSIA. ▪ Mai (New Zealand Guidelines Group "*Management of Dyspepsia and Heartburn*"– Evidence Based best practice Guideline www.nzgg.org.nz , 2004) MALATTIA DA REFLUSSO GASTRO-ESOFAGEO La terapia continuativa con dosi standard è consigliabile nei pazienti con: ▪ Esofagite severa (grado C e D) documentato alla EGDS ▪ Esofago di Barrett ▪ Frequenti recidive della sintomatologia, tipica o atipica, con associata esofagite documentata ad un controllo endoscopico successivo nonostante la terapia con PPI (*utile in questo caso la gestione in collaborazione con lo specialista gastroenterologo*) (University of Michigan Health System, "*Management of Gastroesophageal Reflux Disease (GERD): Guidelines for Clinical Care", 2010; De Vault KR, Castell DO. Updated Guidelines for the diagnosis and treatment of Gastroesophageal reflux disease* Am J Gastroenterol 2007; 100: 190-200) ULCERA PEPTICA Nei casi infrequenti di ulcera peptica (gastrica/duodenale) HP-negativa e nella quale un controllo endoscopico successivo abbia documentato la mancata guarigione nonostante terapia con PPI GASTROPROTEZIONE Prevenzione primaria del danno gastrointestinale da FANS/ASA All'interno dei criteri fissati dalla nota 1, risulta razionale una valutazione caso per caso in relazione al rischio di base del paziente. Prevenzione secondaria del danno gastrointestinale da FANS/ASA Nei pazienti H. pylori negativi con precedente ulcera peptica complicata (Sung JJ., Lau JY, Ching JY, et al. Continuation of Low-Dose Aspirin Therapy in Peptic Ulcer Bleeding. A Randomized Trial. Ann Intern Med. 2010;152:1-9)

Carcinoma of the stomach

Incidence of adenocarcinoma at the gastro-oesophageal junction is increasing in the West, though incidence of distal and body gastric carcinoma has fallen sharply. It remains a tumour notable for its gloomy prognosis and non-specific presentation.

Associations

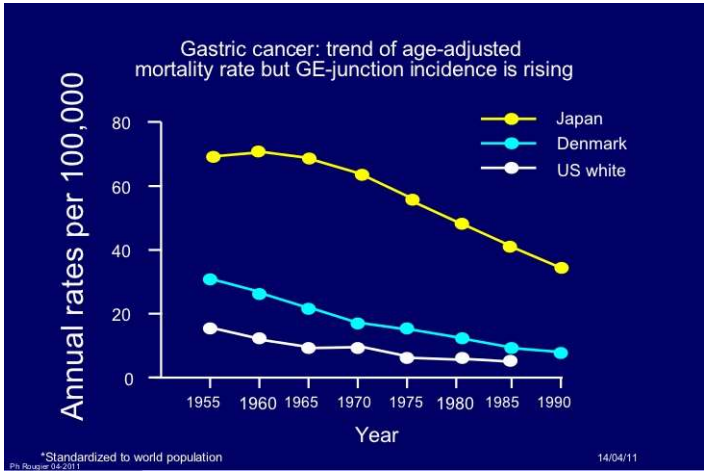
- Pernicious anaemia
- Blood group A
- *H. pylori* (p242)
- Atrophic gastritis
- Adenomatous polyps
- Lower social class
- Smoking
- Diet (high nitrate, high salt, pickling, low vitamin C)
- Nitrosamine exposure

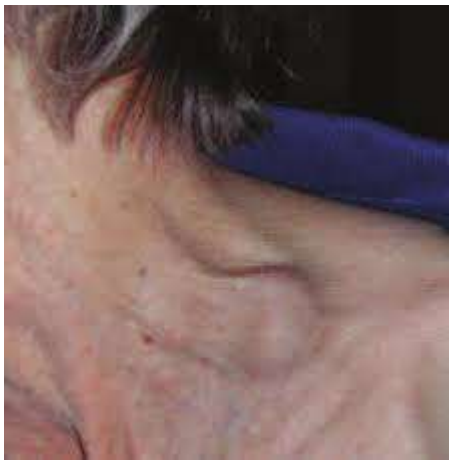
Incidence 23/100,000/yr in the UK, but there are unexplained wide geographical variations; it is especially common in Japan, as well as Eastern Europe, China, and South America. ♂:♀≈2:1.

Pathology Borrmann classification: i) Polypoid ii) Excavating iii) Ulcerating and raised iv) Diffusely infiltrative. Some are confined to mucosa and submucosa— 'early' gastric carcinoma.

Presentation *Symptoms:* Often non-specific. Dyspepsia (p59; for >1 month and age ≥50yrs demands investigation), weight ↓, vomiting, dysphagia, anaemia. *Signs* suggesting incurable disease: epigastric mass, hepatomegaly; jaundice, ascites (p606); large left supraclavicular (Virchow's) node (=Troisier's sign); acanthosis nigricans (p564). Most patients in the West present with locally advanced (inoperable) or metastatic disease. *Spread* is local, lymphatic, blood-borne, and transcoelomic, eg to ovaries (Krukenberg tumour).

Tests Gastroscopy + multiple ulcer edge biopsies. ►*Aim to biopsy all gastric ulcers as even malignant ulcers may appear to heal on drug treatment*. Endoscopic ultrasound (EUS) can evaluate depth of invasion; CT/MRI helps staging. Staging laparoscopy is recommended for locally advanced tumours. Cytology of peritoneal washings can help identify peritoneal metastases.[133]





Treatment See p624 for a description of surgical resections. Partial gastrectomy may suffice for distal tumours. If more proximal, total gastrectomy may be needed. Combination chemotherapy (eg *epirubicin*, *cisplatin* and *5-fluorouracil*) appears to increase survival in advanced disease.[134] If given perioperatively in operable disease it improves survival compared to surgery alone.[135] Endoscopic mucosal resection is used for early tumours confined to the mucosa.[136] Surgical palliation is often needed for obstruction, pain, or haemorrhage. In locally advanced and metastatic disease, chemotherapy increases quality of life and survival.[137] Targeted therapies are likely to have an increasing role, eg *trastuzumab* for HER-2 positive tumours.

5yr survival <10% overall, but nearly 20% for patients undergoing radical surgery. The prognosis is much better for 'early' gastric carcinoma.

Carcinoma of the oesophagus

Incidence Australia <5/100,000/yr; UK <9; Brittany >50; Iran >100. *Risk factors:* Diet, alcohol excess, smoking, achalasia, Plummer-Vinson syn. (p240), obesity, diet ↓ in vit A&C, nitrosamine exposure, reflux oesophagitis ± Barrett's oesophagus (p708). ♂:♀≈5:1.

Site 20% occur in the upper part, 50% in the middle, and 30% in the lower part. They may be squamous cell (proximal) or adenocarcinomas (distal; incidence rising).

Presentation Dysphagia; weight↓; retrosternal chest pain. *Signs from the upper third of the oesophagus:* Hoarseness; cough (may be paroxysmal if aspiration pneumonia). *ΔΔ:* See Dysphagia, p240.

Tests Oesophagoscopy with biopsy is the investigation of choice ± EUS, CT/MRI for staging (fig 1), or laparoscopy if significant infra-diaphragmatic component. *Staging:* See TABLE.

Treatment Survival rates are poor with or without treatment. If localized T1/T2 disease, radical curative oesophagectomy may be tried. Pre-op chemotherapy (*cisplatin + 5-FU*) for localized disease may improve survival, but causes some morbidity.[138] Surgery alone may be preferable.[139] If surgery is not indicated, then chemoradiotherapy may be better than radiotherapy alone.[140] Palliation in advanced disease aims to restore swallowing with chemo/radiotherapy, stenting, and laser use.

TNM staging in oesophageal cancer

(See also p527)

Spread of oesophageal cancer is direct, by submucosal infiltration and local spread—or to nodes, or, later, via the blood.

T_{is}	Carcinoma *in situ*	Nx	Nodes cannot be assessed
T1	Invading lamina propria/submucosa	N0	No node spread
T2	Invading muscularis propria	N1	Regional node metastases
T3	Invading adventitia	M0	No distant spread
T4	Invasion of adjacent structures	M1	Distant metastasis

. Estimated 10 most common cancer cases in the United States in males and females (all races).

Rank	Males Total Cases = 855,220 (percent)	Females Total Cases = 810,320 (percent)
1	Prostate (27)	Breast (29)
2	Lung and bronchus (14)	Lung and bronchus (13)
3	Colon and rectum (8)	Colon and rectum (8)
4	Urinary bladder (7)	Uterine corpus (6)
5	Melanoma (5)	Thyroid (6)
6	Lymphoma (5)	Lymphoma (5)
7	Kidney and renal pelvis (5)	Melanoma (4)
8	Oral cavity and pharynx (4)	Kidney and renal pelvis (3)
9	Leukemia (4)	Pancreas (3)
10	Liver and intrahepatic bile duct (3)	Leukemia (3)
	Other sites (18)	Other sites (20)

Data from the American Cancer Society, 2013.

TABLE 2-2 LEADING CAUSES OF DEATH WORLDWIDE, 2010

Disease or Injury	Deaths (Millions)	Percent of Total Deaths	Disease or Injury	Deaths (Millions)	Percent of Total Deaths
World			**High-income countries[b]**		
1 Ischemic heart disease	7.3	13.3	1 Ischemic heart disease	1.6	17.9
2 Cerebrovascular disease	5.9	11.1	2 Cerebrovascular disease	0.9	9.9
3 COPD	2.9	5.5	3 Lung cancer	0.5	5.6
4 Lower respiratory infections	2.8	5.3	4 Lower respiratory infections	0.4	4.7
5 Lung cancer	1.5	2.9	5 COPD	0.4	4.5
6 HIV/AIDS	1.5	2.8	6 Alzheimer's and other dementias	0.4	4.0
7 Diarrheal diseases	1.4	2.7	7 Colon and rectum cancers	0.3	3.3
8 Road injury	1.3	2.5	8 Diabetes	0.2	2.6
9 Diabetes	1.3	2.4	9 Other cardiovascular and circulatory diseases	0.2	2.5
10 Tuberculosis	1.2	2.3	10 Chronic kidney disease	0.2	2.0
Developing countries[a]			**Sub-Saharan Africa**		
1 Cerebrovascular disease	4.2	10.5	1 Malaria	1.1	12.7
2 Ischemic heart disease	4.0	10.1	2 HIV/AIDS	1.0	12.0
3 COPD	2.4	6.1	3 Lower respiratory infections	0.8	9.3
4 Lower respiratory infections	2.3	5.9	4 Diarrheal diseases	0.5	6.6
5 Diarrheal diseases	1.4	3.6	5 Cerebrovascular disease	0.3	4.0
6 HIV/AIDS	1.4	3.4	6 Protein-energy malnutrition	0.3	4.0
7 Malaria	1.2	2.9	7 Tuberculosis	0.3	3.6
8 Road injury	1.2	2.9	8 Road injury	0.2	2.8
9 Tuberculosis	1.1	2.9	9 Preterm birth complications	0.2	2.8
10 Diabetes	1.0	2.6	10 Meningitis	0.2	2.6

[a]The term *developing countries* refers to low- and middle-income economies. See *data.worldbank.org/about/country-classifications*. [b]The World Bank classifies high-income countries as those whose gross national income per capita is $12,476 or more. See *data.worldbank.org/about/country-classifications*.

Abbreviation: COPD, chronic obstructive pulmonary disease.

Source: Institute for Health Metrics and Evaluation, University of Washington (2013). Data available through *www.healthmetricsandevaluation.org/gbd/visualizations/country*.

Severe vomiting in a patient with steady epigastric pain radiating to back

A 42-year-old Hispanic woman presents to the ED complaining of 24 hours of **severe, steady epigastric abdominal pain, radiating to her back**, with **several episodes of nausea and vomiting**. She has experienced **similar painful episodes in the past**, usually in the evening **following heavy meals**, but the episodes always resolved spontaneously within an hour or two. This time the pain did not improve, so she sought medical attention. She has no medical history and takes no medications. She is married, has three children, and **does not drink alcohol** or smoke cigarettes.

On examination, she is afebrile, tachycardic with a **heart rate of 104 bpm**, blood pressure 115/74 mm Hg, and **shallow respirations of 22 breaths per minute**. She is moving uncomfortably on the stretcher, her skin is warm and diaphoretic, and she has **scleral icterus**. Her abdomen is soft, mildly distended with **marked right upper quadrant and epigastric tenderness to palpation**, **hypoactive bowel sounds**, and no masses or organomegaly appreciated. Her stool is negative for occult blood. Laboratory studies are significant for a **total bilirubin (9.2 g/dL) with a direct fraction of 4.8 g/dL**, **alkaline phosphatase** 285 IU/L, **aspartate aminotransferase (**AST) 78 IU/L, **alanine aminotransferase** (ALT) 92 IU/L, and elevated **amylase level 1249 IU/L**. Her **leukocyte count is 16,500/mm^3** with 82% polymorphonuclear cells and 16% lymphocytes. A **plain film of the abdomen** shows a nonspecific gas pattern and no pneumoperitoneum.

What is the most likely diagnosis?
What is the most likely underlying etiology?
What is your next diagnostic step?

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What is the most likely diagnosis? Acute pancreatitis
What is the most likely underlying etiology? Choledocholithiasis (common bile duct stone)
What is your next diagnostic step? Right-upper quadrant abdominal ultrasonography

Acute pancreatitis

This unpredictable disease (mortality ~12%) is managed on surgical wards, but because surgery is often not involved, it's easy to think that there's no acute problem. There is: Self-perpetuating pancreatic inflammation by enzyme-mediated autodigestion; Oedema and fluid shifts causing hypovolaemia, as extracellular fluid is trapped in the gut, peritoneum, and retroperitoneum (worsened by vomiting). Progression may be rapid from mild oedema to necrotizing pancreatitis. ~50% of cases that advance to necrosis are further complicated by infection. Pancreatitis is mild in 80% of cases; 20% develop severe complicated and life-threatening disease.[214] For causes see MINIBOX.

Causes 'GET SMASHED'

- **G**allstones (38%)
- **E**thanol (35%)
- **T**rauma (1.5%)
- **S**teroids
- **M**umps
- **A**utoimmune (PAN)
- **S**corpion venom
- **H**yperlipidaemia, hypothermia, hypercalcaemia
- **E**RCP (5%) and emboli
- **D**rugs

Also pregnancy and neoplasia or no cause found (10-30%)

Symptoms Gradual or sudden severe epigastric or central abdominal pain (radiates to back, sitting forward may relieve); vomiting prominent.

Signs may be mild in serious disease! Tachycardia, fever, jaundice, shock, ileus, rigid abdomen ± local/general tenderness, periumbilical bruising (**Cullen's sign**) or flanks (**Grey Turner's sign**) from blood vessel autodigestion and retroperitoneal haemorrhage.

Tests Raised serum *amylase* (>1000U/mL or around 3-fold upper limit of normal). The degree of elevation is not related to severity of disease. ▶Amylase may be normal even in severe pancreatitis (levels starts to fall within the 1st 24–48h). Cholecystitis, mesenteric infarction, and GI perforation can cause lesser rises (usually). It is excreted renally so renal failure will ↑ levels. Serum *lipase* is more sensitive and specific for pancreatitis.[215] *ABG* to monitor oxygenation and acid-base status. *AXR:* No psoas shadow (retroperitoneal fluid↑), 'sentinel loop' of proximal jejunum from ileus (solitary air-filled dilatation). *Erect CXR* helps exclude other causes (eg perforation). *CT* is the standard choice of imaging to assess severity and for complications—*MRI* may be even better.[216] *US* (if gallstones+AST↑). *ERCP* if LFTs worsen. *CRP* >150mg/L at 36h after admission is a predictor of severe pancreatitis.

Modified Glasgow criteria for predicting severity of pancreatitis

►3 or more positive factors detected within 48h of onset suggest severe pancreatitis, and should prompt transfer to ITU/HDU. Mnemonic: **PANCREAS.**[221]

P_aO_2	<8kPa
Age	>55yrs
Neutrophilia	WBC >15 x 10^9/L
Calcium	<2mmol/L
Renal function	Urea >16mmol/L
Enzymes	LDH >600iu/L; AST >200iu/L
Albumin	<32g/L (serum)
Sugar	blood glucose >10mmol/L

Courtesy of Mr Etienne Moore FRCS.

Moore EM. A useful mnemonic for severity stratification in acute pancreatitis. *Ann R Coll Surg Engl* 2000; 82: 16-17. © The Royal College of Surgeons of England. Reproduced with permission.

These criteria have been validated for pancreatitis caused by gallstones and alcohol; Ranson's criteria are valid for alcohol-induced pancreatitis, and can only be fully applied after 48h, which does have its disadvantages. Other criteria for assessing severity include the Acute Physiology and Chronic Health Examination (APACHE)-II, and the Bedside Index for Severity in Acute Pancreatitis (BISAP).

Other methods of severity assessment: Severity can also be assessed with the help of CT (Computed Tomography Severity Index).[1] CRP can be a helpful marker.[222]

Table 16–8. Ranson criteria for assessing the severity of acute pancreatitis.

Three or more of the following predict a severe course complicated by pancreatic necrosis with a sensitivity of 60–80%
- Age over 55 years
- White blood cell count > 16 × 10^3/mcL (> 16 × 10^9/L)
- Blood glucose > 200 mg/dL (> 11 mmol/L)
- Serum lactic dehydrogenase > 350 units/L (> 7 mkat/L)
- Aspartate aminotransferase > 250 units/L (> 5 mkat/L)

Development of the following in the first 48 hours indicates a worsening prognosis
- Hematocrit drop of more than 10 percentage points
- Blood urea nitrogen rise > 5 mg/dL (> 1.8 mmol/L)
- Arterial Po_2 of < 60 mm Hg (< 7.8 kPa)
- Serum calcium of < 8 mg/dL (> 0.2 mmol/L)
- Base deficit over 4 mEq/L
- Estimated fluid sequestration of > 6 L

Mortality rates correlate with the number of criteria present[1]

Number of Criteria	Mortality Rate
0–2	1%
3–4	16%
5–6	40%
7–8	100%

[1]An APACHE II score ≥ 8 also correlates with mortality.

Table 16–9. Severity index for acute pancreatitis.

CT Grade	Points	Pancreatic Necrosis	Additional Points	Severity Index[1]	Mortality Rate[2]
A Normal pancreas	0	0%	0	0	0%
B Pancreatic enlargement	1	0%	0	1	0%
C Pancreatic inflammation and/or peripancreatic fat	2	< 30%	2	4	< 3%
D Single acute peripancreatic fluid collection	3	30–50%	4	7	6%
E Two or more acute peripancreatic fluid collections or retroperitoneal air	4	> 50%	6	10	> 17%

[1]Severity index = CT Grade Points + Additional Points.
[2]Based on the severity index.
Adapted with permission from Balthazar EJ. Acute pancreatitis: assessment of severity with clinical and CT evaluation. Radiology. 2002 Jun; 223(3):603–13.

Management Severity assessment is essential (see BOX).

- Nil by mouth, likely to need NG tube (decrease pancreatic stimulation). Set up IVI and give lots of 0.9% saline, to counter third-space sequestration, until vital signs are satisfactory and urine flow stays at >30mL/h. Insert a urinary catheter and consider CVP monitoring. Think about nutrition early on (p586).
- Analgesia: *pethidine* 75–100mg/4h IM, or *morphine* (may cause Oddi's sphincter to contract more,[217] but it is a better analgesic and not contraindicated).[218]
- Hourly pulse, BP, and urine output; daily FBC, U&E, Ca^{2+}, glucose, amylase, ABG.
- If worsening: ITU, O_2 if P_aO_2↓. In suspected abscess formation or pancreatic necrosis (on CT), consider parenteral nutrition ± laparotomy & debridement ('necrosectomy'). Antibiotics may help in specific severe disease, eg *imipenem* if >30% necrosis.[219] There is no consensus on prophylactic use if necrosis is present.[220]
- ERCP + gallstone removal may be needed if there is progressive jaundice.
- Repeat imaging (usually CT) is performed in order to monitor progress.

ΔΔ Any acute abdomen (p608), myocardial infarct. **Prognosis** See BOX.

NUTRITION IN ACUTE PANCREATITIS

Mild disease

- The pancreas is “rested” by a regimen of withholding food and liquids by mouth, bed rest, and, in patients with moderately severe pain or ileus and abdominal distention or vomiting, nasogastric suction.
- Oral intake of fluid and foods can be resumed when the patient is largely free of pain and has bowel sounds (even if the serum amylase is still elevated).
- Clear liquids are given first (this step may be skipped in patients with mild acute pancreatitis), followed by gradual advancement to a low-fat diet, guided by the patient’s tolerance and by the absence of pain.
- Pain may recur on refeeding in 20% of patients.

Severe disease

- Enteral nutrition via a nasojejunal or possibly nasogastric feeding tube is preferable to parenteral nutrition in patients who will otherwise be without oral nutrition for at least 7–10 days.
- Enteral nutrition may not be tolerated in some patients with an ileus. Parenteral nutrition (including lipids) should be considered in patients who have severe pancreatitis and ileus.

CURRENT 2016

Enteral versus parenteral nutrition for acute pancreatitis. ***Cochrane Database Syst Rev. 2010*** *Jan 20;(1):CD002837.*
In patients with acute pancreatitis, enteral nutrition significantly reduced mortality, multiple organ failure, systemic infections, and the need for operative interventions compared to those who received TPN. In addition, there was a trend towards a reduction in length of hospital stay. These data suggest that EN should be considered the standard of care for patients with acute pancreatitis requiring nutritional support.

Early complications Shock, ARDS (p178), renal failure (►give lots of fluid!), DIC, sepsis, Ca^{2+}↓, glucose↑ (transient; 5% need insulin).

Late complications (>1wk) *Pancreatic necrosis* and *pseudocyst* (fluid in lesser sac, fig 1), with fever, a mass ± persistent ↑amylase/LFT; may resolve or need drainage. *Abscesses* need draining. *Bleeding* from elastase eroding a major vessel (eg splenic artery); embolization may be life-saving. *Thrombosis* may occur in the splenic/gastroduodenal arteries, or colic branches of the SMA, causing bowel necrosis. *Fistulae* normally close spontaneously. If purely pancreatic they do not irritate the skin. Some patients suffer *recurrent oedematous pancreatitis* so often that near-total pancreatectomy is contemplated. ►It can all be a miserable course.

Complications of Acute Pancreatitis

Local

- Necrosis
  - Sterile
  - Infected
  - Walled-off necrosis
- Pancreatic fluid collections
  - Pancreatic abscess
  - Pancreatic pseudocyst
    - Pain
    - Rupture
    - Hemorrhage
    - Infection
    - Obstruction of gastrointestinal tract (stomach, duodenum, colon)
- Pancreatic ascites
  - Disruption of main pancreatic duct
  - Leaking pseudocyst
- Involvement of contiguous organs by necrotizing pancreatitis
  - Massive intraperitoneal hemorrhage
  - Thrombosis of blood vessels (splenic vein, portal vein)
  - Bowel infarction
- Obstructive jaundice

Systemic

- Pulmonary
  - Pleural effusion
  - Atelectasis
  - Mediastinal abscess
  - Pneumonitis
  - Acute respiratory distress syndrome
- Cardiovascular
  - Hypotension
  - Hypovolemia
  - Sudden death
  - Nonspecific ST-T changes in electrocardiogram simulating myocardial infarction
- Pericardial effusion
- Hematologic
  - Disseminated intravascular coagulation
- Gastrointestinal hemorrhage
  - Peptic ulcer disease
  - Erosive gastritis
  - Hemorrhagic pancreatic necrosis with erosion into major blood vessels
  - Portal vein thrombosis, variceal hemorrhage
- Renal
  - Oliguria
  - Azotemia
  - Renal artery and/or renal vein thrombosis
  - Acute tubular necrosis
- Metabolic
  - Hyperglycemia
  - Hypertriglyceridemia
  - Hypocalcemia
  - Encephalopathy
  - Sudden blindness (Purtscher's retinopathy)
- Central nervous system
  - Psychosis
  - Fat emboli
- Fat necrosis
  - Subcutaneous tissues (erythematous nodules)
  - Bone
  - Miscellaneous (mediastinum, pleura, nervous system)

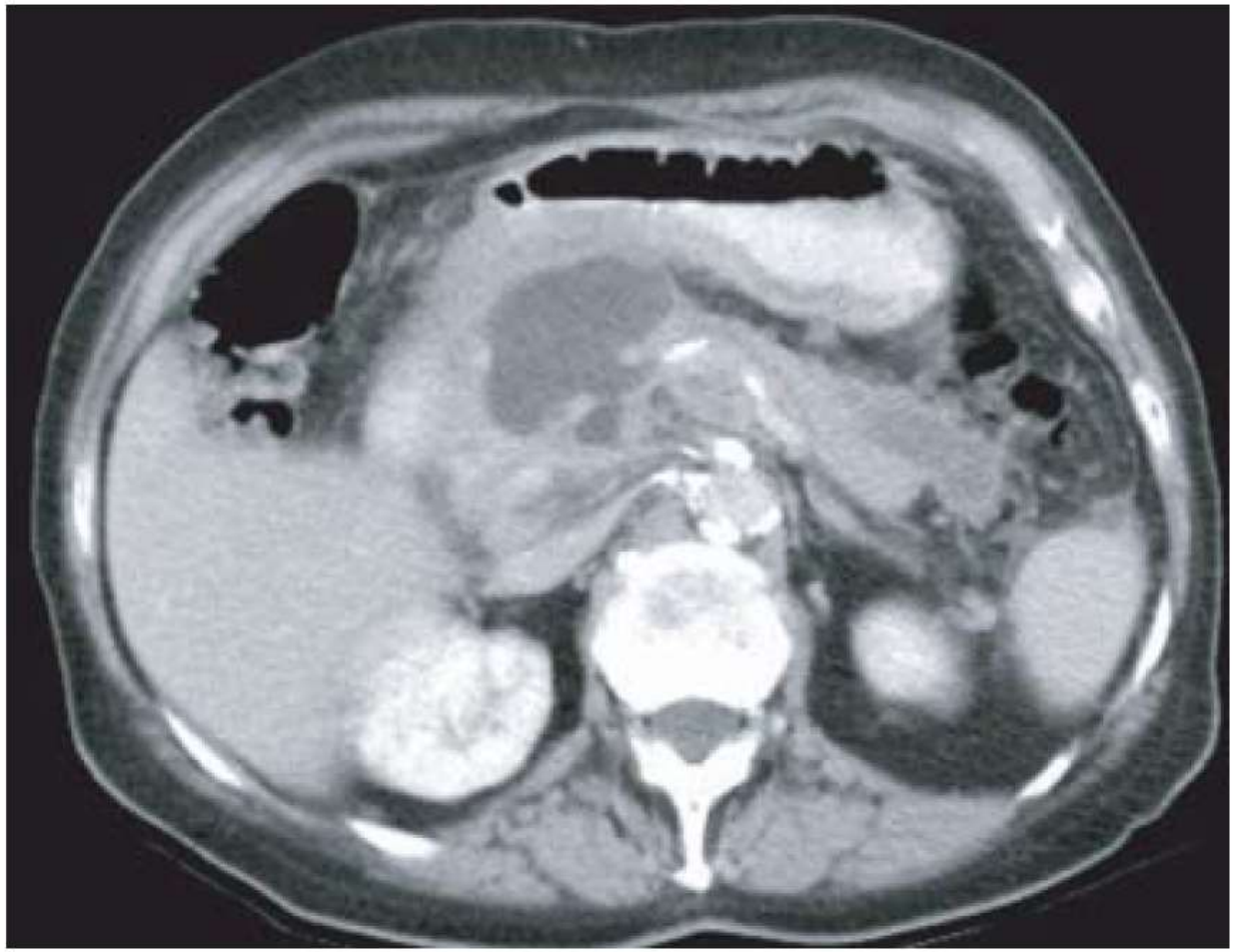


Fig 1. Axial CT of the abdomen (with IV and PO contrast media) showing a pancreatic pseudocyst occupying the lesser sac of the abdomen posterior to the stomach. It is called a 'pseudocyst' because it is not a true cyst, rather a collection of fluid in the lesser sac (ie not lined by epi/endothelium). It develops at ≥6wks. The cyst fluid is of low attenuation compared with the stomach contents because it has not been enhanced by the contrast media.

1 For a useful exposition on imaging in pancreatitis see www.emedicine.com/radio/topic521.htm.

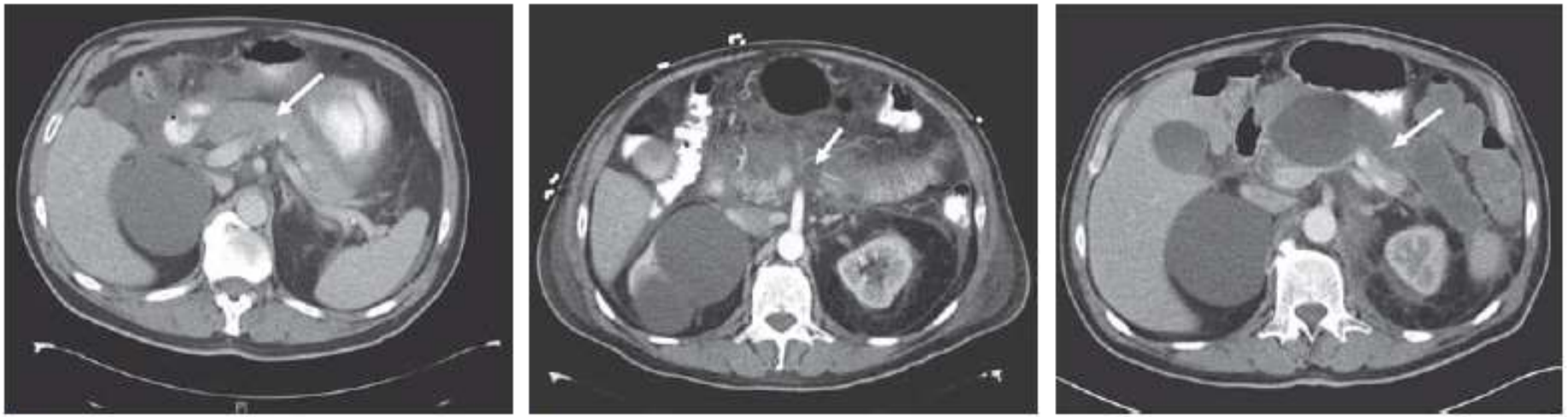


Figure 313-1 Acute pancreatitis: CT evolution. *A.* Contrast-enhanced CT scan of the abdomen performed on admission for a patient with clinical and biochemical parameters suggestive of acute pancreatitis. Note the abnormal enhancement of the pancreatic parenchyma (arrow) suggestive of interstitial pancreatitis. *B.* Contrast-enhanced CT scan of the abdomen performed on the same patient six days later for persistent fever and systemic inflammatory response syndrome. The pancreas now demonstrates significant areas of nonenhancement consistent with development of necrosis, particularly in the body and neck region (arrow). Note that an early CT scan obtained within the first 48 hours of hospitalization may underestimate or miss necrosis. *C.* Contrast-enhanced CT scan of the abdomen performed on the same patient two months after the initial episode of acute pancreatitis. CT now demonstrates evidence of a fluid collection consistent with walled-off pancreatic necrosis (arrow). *(Courtesy of Dr. KJ Mortele, Brigham and Women's Hospital; with permission.)*

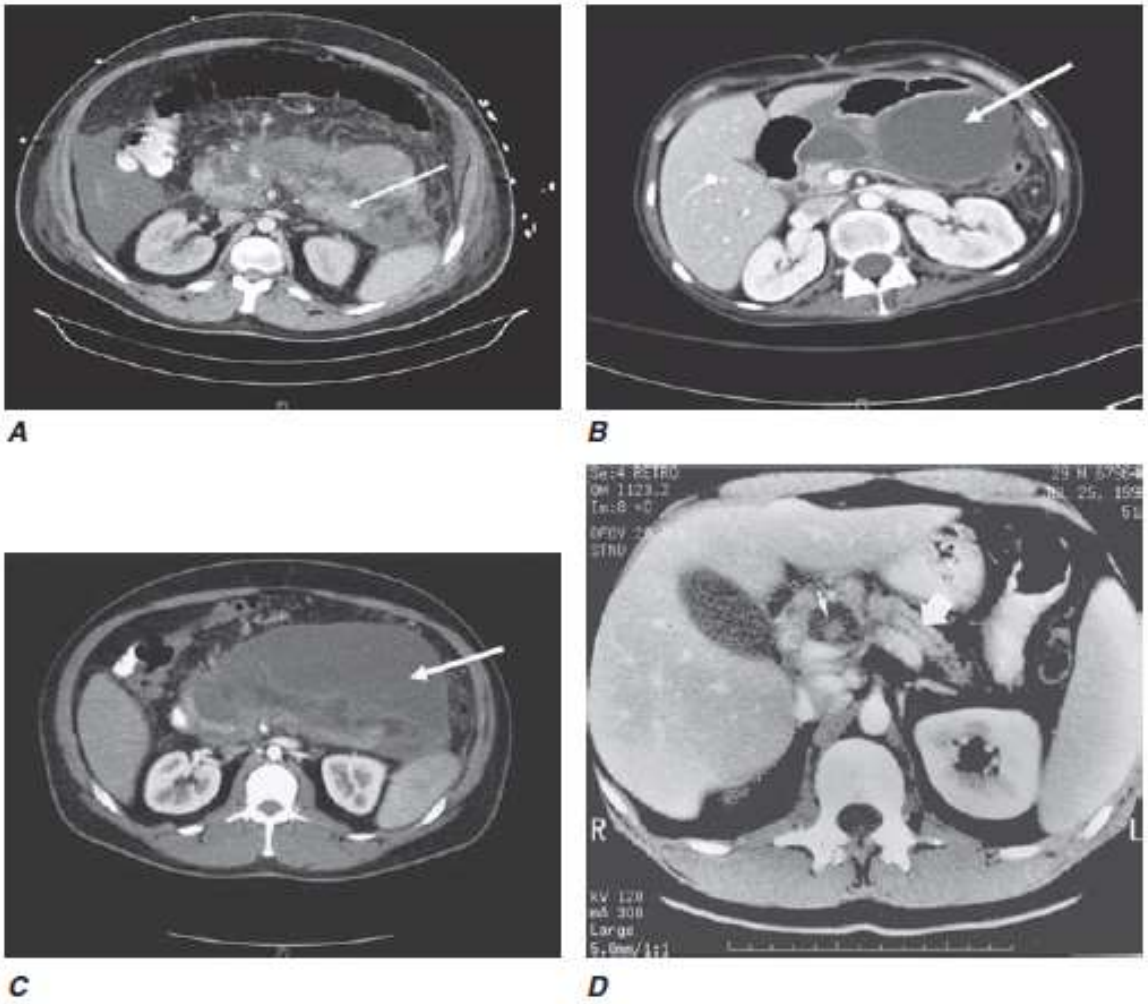


Figure 313-2 *A.* Acute necrotizing pancreatitis: CT scan. Contrast-enhanced CT scan showing acute pancreatitis with necrosis. Arrow shows partially enhancing body/tail of pancreas surrounded by fluid with decreased enhancement in the neck/body of the pancreas. *B.* Acute fluid collection: CT scan. Contrast-enhanced CT scan showing fluid collection in the retroperitoneum (arrow) compressing the air-filled stomach arising from the pancreas in a patient with asparaginase-induced acute necrotizing pancreatitis. *C.* Walled-off pancreatic necrosis: CT scan. CT scan showing marked walled-off necrosis of the pancreas and peripancreatic area (arrow) in a patient with necrotizing pancreatitis. Addendum: In past years, both of these CT findings (Figs. 313-2B and 313-2C) would have been misinterpreted as pseudocysts. *D.* Spiral CT showing a pseudocyst (small arrow) with a pseudoaneurysm (light area in pseudocyst). Note the demonstration of the main pancreatic duct (big arrow), even though this duct is minimally dilated by ERCP. *(A, B, C, courtesy of Dr. KJ Mortele, Brigham and Women's Hospital; D, courtesy of Dr. PR Ros, Brigham and Women's Hospital; with permission.)*

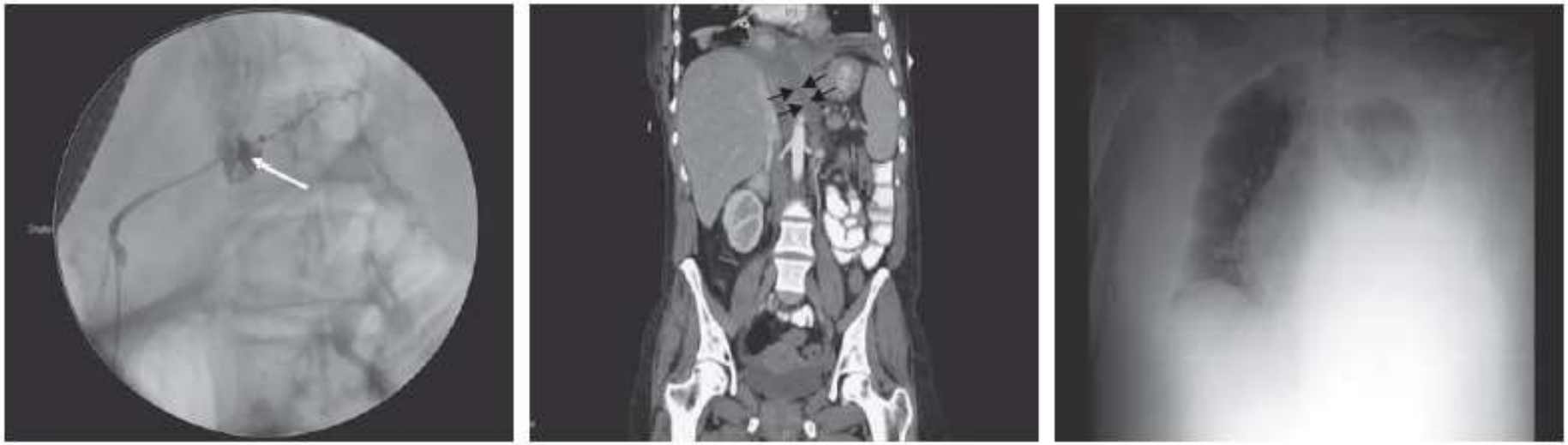


Figure 313-3 *A.* **Pancreaticopleural fistula: pancreatic duct leak on ERCP.** Pancreatic duct leak demonstrated (arrow) at the time of retrograde pancreatogram in a patient with acute exacerbation of alcohol-induced acute or chronic pancreatitis. *B.* Pancreaticopleural fistula: CT Scan. Contrast-enhanced CT scan (coronal view) with arrows showing fistula tract from pancreatic duct disruption in the pancreatic pleural fistula. *C.* Pancreaticopleural fistula: Chest x-ray. Large pleural effusion in the left hemithorax from a disrupted pancreatic duct. Analysis of pleural fluid revealed elevated amylase concentration. *(Courtesy of Dr. KJ Mortele, Brigham and Women's Hospital; with permission.)*

14.1 A 43-year-old man who is an alcoholic is admitted to the hospital with acute pancreatitis. He is given intravenous hydration and is placed NPO. Which of the following findings is a poor prognostic sign?

A. His age
B. Initial serum glucose level of 60 mg/dL
C. Blood urea nitrogen (BUN) level rises 7 mg/dL over 48 hours
D. Hematocrit drops 3%
E. Amylase level of 1000 IU/L

14.2 A 37-year-old woman is noted to have gallstones on ultrasonography. She is placed on a low-fat diet. After 3 months she is noted to have severe right-upper quadrant pain, fever to 102°F, and nausea. Which of the following is the most likely diagnosis?

A. Acute cholangitis
B. Acute cholecystitis
C. Acute pancreatitis
D. Acute perforation of the gallbladder

14.3 A 45-year-old man was admitted for acute pancreatitis, thought to be a result of blunt abdominal trauma. After 3 months he still has epigastric pain but is able to eat solid food. His amylase level is elevated at 260 IU/L. Which of the following is the most likely diagnosis?

A. Recurrent pancreatitis
B. Diverticulitis
C. Peptic ulcer disease
D. Pancreatic pseudocyst

14.1 **C.** When the BUN rises by 5 mg/dL after 48 hours despite IV hydration, it is a poor prognostic sign. Notably, the amylase level does not correlate to the severity of the disease. An elevated serum glucose would be a poor prognostic factor. A drop in hematocrit of at least 10% is a significant poor prognostic criterion.

14.2 **B.** Acute cholecystitis is one of the most common complications of gallstones. This patient with fever, right-upper quadrant pain, and a history of gallstones likely has acute cholecystitis.

14.3 **D.** A pancreatic pseudocyst has a clinical presentation of abdominal pain and mass and persistent hyperamylasemia in a patient with prior pancreatitis.

The acute abdomen

Someone who becomes acutely ill and in whom symptoms and signs are chiefly related to the abdomen has an acute abdomen. Prompt laparotomy is sometimes essential: **repeated examination is the key to making the decision.**

★ Clinical syndromes that usually require laparotomy

1 *Rupture of an organ* (Spleen, aorta, ectopic pregnancy) Shock is a leading sign—see TABLE for assessment of blood loss. Abdominal swelling may be seen. Any history of trauma: blunt trauma → spleen; penetrating trauma → liver. **Delayed** rupture of the spleen may occur weeks after trauma. Peritonism may be mild.

2 *Peritonitis* (Perforation of peptic ulcer/duodenal ulcer, diverticulum, appendix, bowel, or gallbladder) Signs: prostration, shock, lying still, +ve cough test (p62), tenderness (± rebound/percussion pain, p62), board-like abdominal rigidity, guarding, and no bowel sounds. Erect CXR may show gas under the diaphragm (fig 2). NB: acute pancreatitis (p638) causes these signs, but does **not** require a laparotomy so don't be caught out and ►*always check serum amylase.*

★ Obstruction of the bowel

★ Syndromes that may not require a laparotomy

Local peritonitis: Eg diverticulitis, cholecystitis, salpingitis, and appendicitis (the latter **will** need surgery). If abscess formation is suspected (swelling, swinging fever, and WCC↑) do ultrasound or CT. Drainage can be percutaneous (ultrasound or CT-guided), or by laparotomy. Local peritoneal inflammation can cause localized ileus with a 'sentinel loop' of intraluminal gas visible on plain AXR (p743).

Colic is a regularly waxing and waning pain, caused by muscular spasm in a hollow viscus, eg gut, ureter, salpinx, uterus, bile duct, or gallbladder (in the latter, pain is often dull and constant). Colic, unlike peritonitis, causes restlessness and the patient may well be pacing around when you go to see him!

★ **The medical acute abdomen** Irritable bowel syndrome (p276) is the chief cause, so always ask about episodes of pain associated with loose stools, relieved by defecation, bloating, and urgency (but **not** blood—this may be UC). Other causes:

- ►►Myocardial infarction
- Gastroenteritis or UTI
- Diabetes mellitus/DKA (p19
- Bornholm disease (p376)
- Pneumococcal peritonitis
- Henoch-Schönlein (p716)
- Tabes dorsalis (p431)

- Pneumonia (p160)
- Thyroid storm (p84
- Zoster (p400)
- Tuberculosis (p398)
- Porphyria (p706)
- Narcotic addiction
- PAN (p558)

- Sickle-cell crisis (p335)
- Phaeochromocytoma (
- Malaria (p394)
- Typhoid fever (p426)
- Cholera (p426)
- *Yersinia enterocolitica*
- Lead colic

★ **Hidden diagnoses** ►►Mesenteric ischaemia (p622), ►►acute pancreatitis (p638) and ►►a leaking AAA (p656) are the *Unterseebooten* of the acute abdomen—unsuspected, undetectable unless carefully looked for, and underestimatedly deadly. They may have non-specific symptoms and signs that are surprisingly mild, so always think of them when assessing the acute abdomen and hopefully you will 'spot' them!

►Finally: *always exclude pregnancy (± ectopic?) in females.*

Tests U&E; FBC; amylase; LFT; CRP; ABG (is there mesenteric ischaemia?); urinalysis. Erect CXR (fig 2), AXR may show Rigler's sign (p742). Laparoscopy may avert open surgery. CT can be helpful provided it is readily available and causes no delay (p746-747); USS may identify perforation or free fluid immediately, but appropriate performer training is important.

Pre-op ►Don't rush to theatre. **Anaesthesia compounds shock**, so resuscitate properly first (p805) unless blood being lost faster than can be replaced, eg ruptured ectopic pregnancy, (*OHCS* p262), aneurysm leak (p656), trauma.

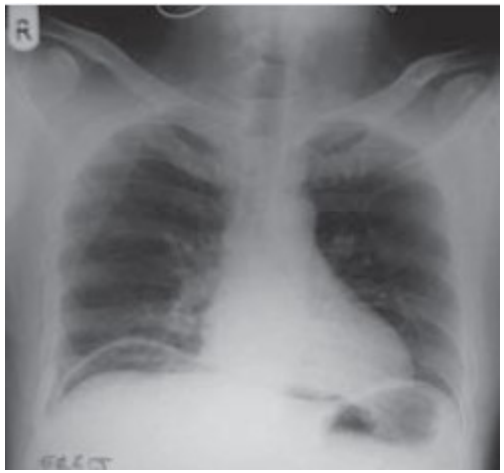


Fig 2. Erect CXR showing air beneath the right hemidiaphragm, indicating presence of a pneumoperitoneum. *Causes:*
- Perforation of the bowel (visible only in 75%)

***Plan:* Bed rest—then:**

- Treat shock (p804)
- Crossmatch/group and save
- Blood culture
- Antibiotics[1]
- Relieve pain (p576)
- IVI (0.9% saline)
- Plain abdominal film
- CXR if peritonitic or >50yrs
- ECG if >50yrs
- Consent
- NBM

Abdominal pain

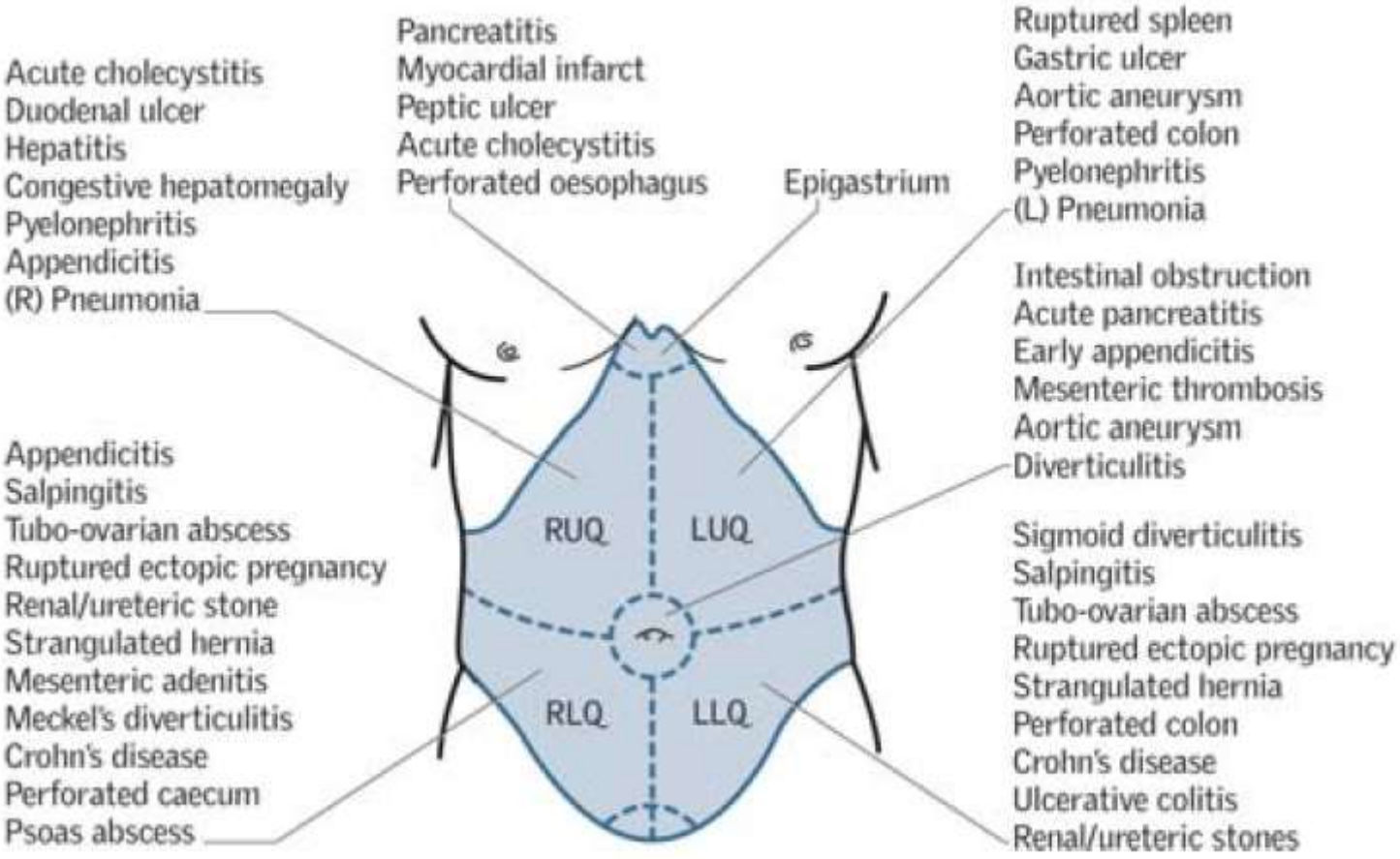
Varies depending on the underlying cause. Examples: irritation of the mucosa (acute gastritis), smooth muscle spasm (acute enterocolitis), capsular stretching (liver congestion in CCF), peritoneal inflammation (acute appendicitis) and direct splanchnic nerve stimulation (retroperitoneal extension of tumour). The *character* (constant or colicky, sharp or dull), *duration,* and *frequency* depend on the mechanism of production. The *location* and *distribution* of referred pain depend on the anatomical site. *Time of occurrence* and *aggravating* or *relieving factors* such as meals, defecation, and sleep also have special significance related to the underlying disease process. The site of the pain may provide a clue:

- **Epigastric** Pancreatitis, gastritis/duodenitis, peptic ulcer, gallbladder disease, aortic aneurysm.
- **Left upper quadrant** Peptic ulcer, gastric or colonic (splenic flexure) cancer, splenic rupture, subphrenic or perinephric abscess, renal (colic, pyelonephritis).
- **Right upper quadrant** Cholecystitis, biliary colic, hepatitis, peptic ulcer, colonic cancer (hepatic flexure), renal (colic, pyelonephritis), subphrenic/perinephric abscess.
- **Loin** (lateral ⅓ of back between thorax and pelvis—merges with the flank, p567) Renal colic, pyelonephritis, renal tumour, perinephric abscess, pain referred from vertebral column. Causes of *flank pain* are similar (see index for fuller list).
- **Left iliac fossa** Diverticulitis, volvulus, colon cancer, pelvic abscess, inflammatory bowel disease, hip pathology, renal colic, urinary tract infection (UTI), cancer in undescended testis; zoster—wait for the rash! (p458). *Gynae:* Torsion of ovarian cyst, salpingitis, ectopic pregnancy.
- **Right iliac fossa pain** All causes of left iliac fossa pain plus appendicitis and Crohn's ileitis, but usually excluding diverticulitis.
- **Pelvic** *Urological:* UTI, retention, stones. *Gynae:* Menstruation, pregnancy, endometriosis (*OHCS* p288), salpingitis, endometritis (*OHCS* p274), ovarian cyst torsion.
- **Generalized** Gastroenteritis, irritable bowel syndrome, peritonitis, constipation.
- **Central** Mesenteric ischaemia, abdominal aneurysm, pancreatitis.

Remember referred pain: Myocardial infarct → epigastrium; pleural pathology.

Mechanism

Causes of abdominal pain



Assessing hypovolaemia from blood loss

The most likely cause of shock in a surgical patient is hypovolaemia (but don't forget the other causes—p804). The chief physiological parameters for assessing shock assess target organ perfusion rather than the direct measurement of BP and pulse, which may be 'normal' in one individual and yet totally abnormal for another. The most perfused organs in a normal state are the kidney, brain, and skin, so check **urine output**, GCS and **capillary refill** (CR). ▶▶ *The best quick test is:* "do you feel dizzy if you sit up?"

Of course, BP, pulse, and respirations are still **vital** signs, but the message here is: ▶▶ treat suspected shock rather than wait for BP to fall. When there is any blood loss (eg a trauma situation), assess the status of the following:

Parameter	Class I	Class II	Class III	Class IV
Blood loss	<750mL	750–1500mL	1500–2000mL	>2000mL
	<15%	15–30%	30–40%	>40%
Pulse	<100bpm	>100bpm	>120bpm	>140bpm
BP	↔	↔	↓	↓
Pulse pressure	↔ or ↑	↓	↓	↓
Respirations	14–20/min	20–30/min	30–40/min	>35/min
Urine output	>30mL/h	20–30mL/h	5–15mL/h	Negligible
Mental state	Slightly anxious	Anxious	Confused →	→Lethargic
Fluid to give	Crystalloid	Crystalloid	Crystalloid + blood	

Assumes a body mass of 70kg and a circulating blood volume of 5L

Obstruction of the bowel

Features of obstruction Vomiting, nausea and anorexia. Fermentation of the intestinal contents in established obstruction causes 'faeculent' vomiting ('faecal' vomiting is found when there is a colonic fistula with the proximal gut). Colic occurs early (may be absent in long-standing complete obstruction). Constipation need not be absolute (ie no faeces or flatus passed) if obstruction is high, though in distal obstruction nothing will be passed. Abdominal distension is more marked as the obstruction progresses. There are active, 'tinkling' bowel sounds.

Cardinal features of intestinal obstruction

- Vomiting
- Colicky pain
- Constipation
- Distension

Causes: small bowel

- Adhesions (p567)
- Hernias (p614)

Causes: large bowel

- Colon ca (p618)
- Constipation (p248)
- Diverticular stricture
- Volvulus
  - Sigmoid (see BOX)
  - Caecal

Rarer causes

- Crohn's stricture
- Gallstone ileus (p636)
- Intussusception (p628)
- TB (developing world)
- Foreign body

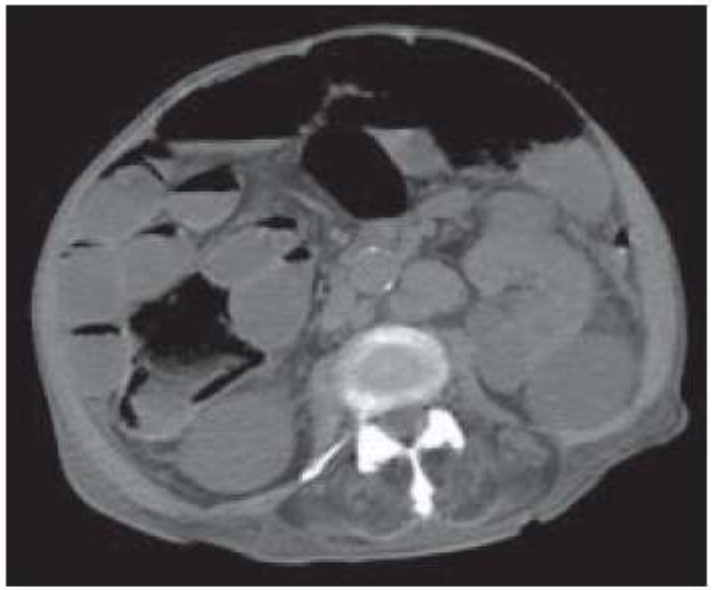


Fig 1. Unenhanced axial CT of the abdomen showing multiple loops of dilated, fluid-filled small bowel in a patient with small bowel obstruction.

Both images courtesy of Norwich Radiology Dept.

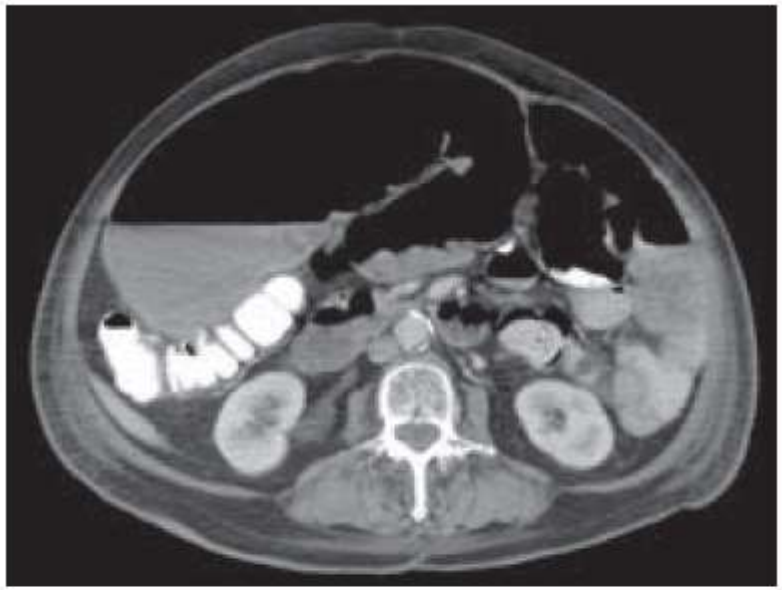


Fig 2. Axial CT of the abdomen post-oral contrast showing dilated loops of fluid and air-filled large bowel (contrast medium is in the small bowel). The cause or level of obstruction is not clear.

The key decisions:

1 *Is it obstruction of the small or large bowel?* In small bowel obstruction, vomiting occurs earlier, distension is less, and pain is higher in the abdomen. The AXR plays a key role in diagnosis—see p742. In small bowel obstruction, AXR shows central gas shadows with *valvulae conniventes* that completely cross the lumen and no gas in the large bowel. In large bowel obstruction, pain is more constant; AXR shows peripheral gas shadows proximal to the blockage (eg in caecum) but not in the rectum, unless you have done a PR examination ►which is always essential! Large bowel *haustra* do not cross all the lumen's width. If the ileocaecal valve is competent (ie doesn't allow reflux) pain may be felt over a distended caecum (see below).

2 *Is there an ileus or mechanical obstruction?* Ileus is functional obstruction from reduced bowel motility
There is no pain and bowel sounds are absent.

3 *Is the obstructed bowel simple/closed loop/strangulated?* **Simple:** One obstructing point and no vascular compromise. **Closed loop:** Obstruction at two points (eg sigmoid volvulus, distension with competent ileocaecal valve) forming a loop of grossly distended bowel at risk of perforation (tenderness and perforation usually at caecum where the bowel is thinnest and widest; >12cm requires urgent decompression). **Strangulated:** Blood supply is compromised and the patient is more ill than you would expect. There is sharper, more constant and *localized* pain. Peritonism is the cardinal sign. There may be fever + WCC↑ with other signs of mesenteric ischaemia (p622).

Management

- *General principles:* Cause, site, speed of onset, and completeness of obstruction determine definitive therapy: strangulation and large bowel obstruction require surgery; ileus and incomplete small bowel obstruction can be managed conservatively, at least initially.
- *Immediate action:* ►'Drip and suck'—NGT and IV fluids to rehydrate and correct electrolyte imbalance (p680). Being NBM does not give adequate rest for the bowel because it can produce up to 9L of fluid/d. Also: analgesia, blood tests (inc. amylase, FBC, U&E), AXR, erect CXR, catheterize to monitor fluid status.
- *Further imaging:* Consider early CT if clinical and radiographic findings are inconclusive: it finds the cause and level of obstruction. It may show dilated, fluid-filled bowel and a transition zone at the site of obstruction (figs 1 & 2). There is a case for investigating the cause of large bowel obstruction by colonoscopy in some instances of suspected mechanical obstruction, though there is a danger of inducing perforation. Oral Gastrografin® can help identify partial small bowel obstruction (if contrast solution present in the colon within 24h it predicts conservative resolution).[104] It may also have mild therapeutic action against mechanical obstruction.
- *Surgery:* ►Strangulation needs emergency surgery, as does 'closed loop obstruction'. Stents may be used for obstructing large bowel malignancies either in palliation or as a bridge to surgery in acute obstruction (p618). Small bowel obstruction secondary to adhesions should rarely lead to surgery—see BOX, p583.

Paralytic ileus or pseudo-obstruction?

Paralytic ileus is adynamic bowel due to the absence of normal peristaltic contractions. Contributing factors include abdominal surgery, pancreatitis (or any localized peritonitis), spinal injury, hypokalaemia, hyponatraemia, uraemia, peritoneal sepsis and drugs (eg tricyclic antidepressants).

Pseudo-obstruction is like mechanical GI obstruction but with no cause for obstruction found. Acute colonic pseudo-obstruction is called Ogilvie's syndrome (p720), and clinical features are similar to that of mechanical obstruction.[105] Predisposing factors: puerperium; pelvic surgery; trauma; cardiorespiratory disorders. *Treatment: Neostigmine* or colonoscopic decompression are sometimes useful. In chronic pseudo-obstruction weight loss from malabsorption is a problem.[106]

Abdominal masses

As with any mass (see p596), determine size, site, shape, and surface. Find out if it is pulsatile and if it is mobile. Examine supraclavicular and inguinal nodes. Is the lump ballotable (like bobbing an apple up and down in water)?

Right iliac fossa masses:

- Appendix mass/abscess
- Caecal carcinoma
- Crohn's disease
- Pelvic mass (see below)
- Intussusception
- TB mass
- Amoebic abscess
- Actinomycosis (p421)
- Transplanted kidney
- Kidney malformation
- Tumour in an undescended testis

Pelvic masses

- Fibroids
- Fetus
- Bladder
- Ovarian cysts or malignancies

Pelvic masses *Is it truly pelvic?*—Yes, if by palpation you cannot get 'below it'.

Smooth hepatomegaly Hepatitis, CCF, sarcoidosis, early alcoholic cirrhosis (a small liver is typical later); tricuspid incompetence (→ pulsatile liver).

Craggy hepatomegaly Secondaries or 1° hepatoma. (Nodular cirrhosis typically causes a small, shrunken liver, not an enlarged craggy one.)

Left upper quadrant mass Is it spleen, stomach, kidney, colon, pancreas, or a rare cause (eg neurofibroma)? Pancreatic cysts may be true (congenital; cystadenomas; retention cysts of chronic pancreatitis; cystic fibrosis) or pseudocysts (fluid in lesser sac from acute pancreatitis).

Splenomegaly Causes are often said to be infective, haematological, neoplastic, etc, but grouping by associated feature is more useful clinically:

Splenomegaly with fever	With lymphadenopathy	With purpura
• Infection[HS] (malaria, SBE/IE hepatitis,[HS] EBV,[HS] TB, CMV, HIV) • Sarcoid; malignancy[HS]	• Glandular fever[HS] • Leukaemias; lymphoma • Sjögren's syndrome	• Septicaemia; typhus • DIC; amyloid[HS] • Meningococcaemia
With arthritis	**With ascites**	**With a murmur**
• Sjögren's syndrome • Rheumatoid arthritis; SLE • Infection, eg Lyme (p430) • Vasculitis/Behçet's (p558)	• Carcinoma • Portal hypertension[HS]	• SBE/IE • Rheumatic fever • Hypereosinophilia • Amyloid[HS] (p364)
With anaemia	**With weight↓ + *CNS* signs**	**Massive splenomegaly**
• Sickle-cell;[HS] thalassaemia[HS] • Leishmaniasis;[HS] leukaemia[HS] • Pernicious anaemia (p328) • POEMS syn. (p212)	• Cancer; lymphoma • TB; arsenic poisoning • Paraproteinaemia[HS]	• Malaria (hyper-reactivity after chronic exposure) • Myelofibrosis; CML[HS] • Gaucher's syndrome[HS] • Leishmaniasis

HS=causes of hepatosplenomegaly.

Abdominal distension Flatus, fat, fluid, faeces, or fetus (p57)? Fluid may be outside the gut (ascites) or sequestered in bowel (obstruction; ileus). To demonstrate ascites elicit signs of a fluid thrill and/or shifting dullness (p60).

Causes of ascites:		Ascites with portal hypertension:	
• Malignancy★	• CCF; pericarditis	• Cirrhosis	• Portal nodes
• Infections★—esp TB	• Pancreatitis★	• Budd-Chiari syndrome★ (p710)	
• ↓Albumin (eg nephrosis)	• Myxoedema	• IVC or portal vein thrombosis	

Tests: Aspirate ascitic fluid (paracentesis, p778–779) for cytology, culture, and protein level (≥30g/L in diseases marked★); ultrasound.

Investigating lumps There is much to be said for performing an early CT to save time and money compared with leaving the test to be the last in a long chain. If unavailable, *ultrasound* is the first test (transvaginal approach may be useful). *Others:* IVU; liver and spleen radioisotope scans; Mantoux test (p398). Routine tests: FBC (with film); ESR; U&E; LFT; proteins; Ca^{2+}; CXR; AXR; biopsy—a tissue diagnosis may be made using a fine needle guided by ultrasound or CT control. MRI also has a role.

Flushing in a 50-year-old woman with recurrent episodes of abdominal pain

A **50-year-old woman** presents with a long history of atypical **flushing**, initially attributed to menopause. The flushing is associated with purplish discolouration of the face with each episode lasting 30 minutes. She also reports **palpitations on exertion** and **recurrent episodes of abdominal pain.**

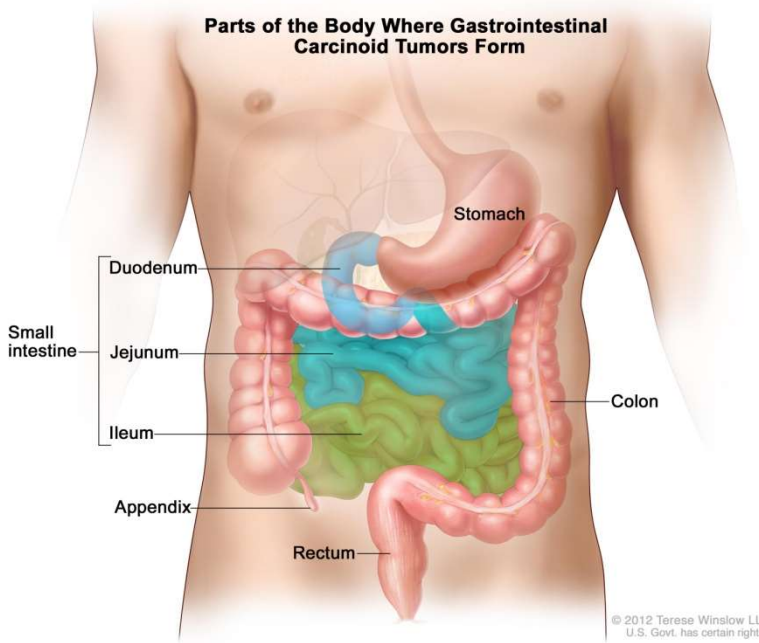
A 60-year-old man presents with a **3-year history of diarrhoea**, with no clear precipitating factors. Over the past few months he has noticed **flushing** affecting his face. These episodes occur at any time but are worse during times of stress and exercise. His wife has also noticed intermittent reddening of his face, which lasts for a few minutes. More recently he **has not tolerated alcohol, chocolate, or bananas.**

Coincidental finding of liver metastases while other unrelated symptoms are being investigated is an alternative presentation. Other presentations include occasional abdominal pain, especially following large meals, and associated weight loss. Recurrent abdominal pain leading to development of sub-acute bowel obstruction can also occur. Patients can also present with cardiac signs, such as **right heart failure** and **cardiac murmurs.**

Carcinoid tumours

SEROTONIN

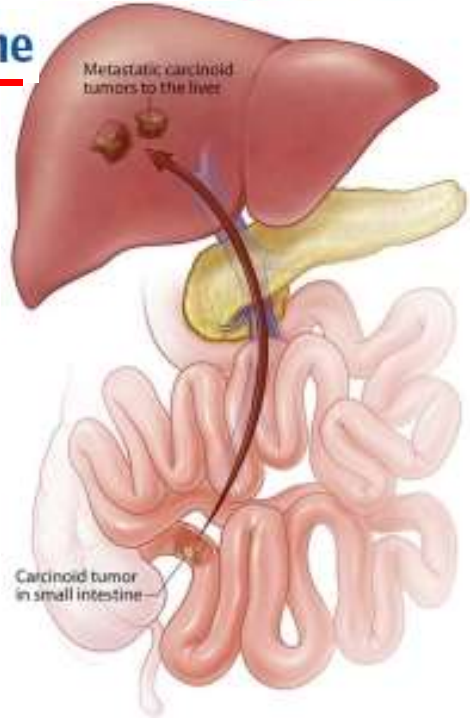
This is a specialized area! A diverse group of tumours of enterochromaffin cell (neural crest) origin, by definition capable of producing 5HT. Common sites: appendix (45%), ileum (30%) or rectum (20%).[2] They also occur elsewhere in the GI tract, ovary, testis, and bronchi. 80% of tumours >2cm across will metastasize (ie consider all as malignant). *Symptoms & signs:* Initially few. GI tumours can cause appendicitis, intussusception, or obstruction. Hepatic metastases may cause RUQ pain. Tumours may secrete bradykinin, tachykinin, substance P, VIP, gastrin, insulin, glucagon, ACTH (∴ Cushing's syndrome), parathyroid, and thyroid hormones. 10% are part of MEN-1 syndrome (p215); 10% occur with other neuroendocrine tumours.[249]



Carcinoid syndrome

occurs in ~5%

implies hepatic involvement.



2 Some are never clinically detected: 1 in 300 autopsies have a small bowel carcinoid tumour.

Carcinoid syndrome occurs in ~5% and implies hepatic involvement.

Symptoms and signs: Bronchoconstriction; paroxysmal flushing especially in upper body (± migrating weals); diarrhoea; CCF (tricuspid incompetence and pulmonary stenosis from 5HT-induced fibrosis). *CNS effects:* Many, eg enhanced ability to learn new stimulus-response associations.[250] ►*Carcinoid crisis:* See BOX.

►►Carcinoid crisis

When a tumour outgrows its blood supply or is handled too much during surgery, mediators flood out. There is life-threatening vasodilatation, hypotension, tachycardia, bronchoconstriction and hyperglycaemia. It is treated with high-dose *octreotide*, supportive measures and careful management of fluid balance (ie a central line is needed—see p789 for insertion technique).

Δ 24h urine 5-hydroxyindoleacetic acid↑ (5HIAA, a 5HT metabolite; levels change with drugs and diet, eg bananas, avocado, walnuts, pineapple, coffee, chocolate: discuss with lab). CXR + chest/pelvis MRI/CT help locate primary tumours. Plasma chromogranin A (reflects tumour mass); ^{111}Indium octreotide scintigraphy (octreoscan);[251] and positron emission tomography (p753) also have a role. Echocardiography and BNP (p131) can be used to investigate carcinoid heart disease.[252] ΔΔ: GIST.[3]

3 Gastrointestinal stromal tumours (GISTs) are mesenchymal tumours arising from interstitial Cajal cells of the wall of the gut. They may co-exist with carcinoid tumours.[257]

℞ *Carcinoid syndrome:* ***Octreotide*** (somatostatin analogue) blocks release of tumour mediators and counters peripheral effects. Alternative: ***lanreotide***. Effects lessen over time. Other options: ***loperamide*** or ***cyproheptadine*** for diarrhoea;[253] ***interferon-α*** as add-in therapy with ***octreotide***.[254] *Tumour therapy:* Resection is the only cure for carcinoid tumours (fig 1), so it is vital to find the primary site (see above). At surgery, tumours are an intense yellow. Procedures depend on site, eg rectal carcinoid tumours <1cm can be resected endoscopically.[255] Debulking (eg enucleating), embolization, or radiofrequency ablation of hepatic metastases can ↓symptoms. Give ***octreotide*** cover to avoid precipitating a massive carcinoid crisis.

Median survival 5-8yrs (~3yrs if metastases are present, but may be up to 20yrs; so beware of giving up too easily, even in metastatic disease).[249]