Symptoms and signs of upper gastrointestinal disease

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Abstract

Patients with upper gastrointestinal disease can present with a diverse array of symptoms, which are linked to significant morbidity and relatively few reliable signs. Upper gastrointestinal pathology can present as an acute abdomen, for which clinical diagnostic accuracy is approximately 50%. The aim of this article is to provide a systematic approach for formulating a differential diagnosis in patients with common symptoms and signs of upper gastrointestinal disease, highlighting 'red flags' for serious pathology.

Keywords Belching; chest pain; dyspepsia; dysphagia; gastro-oesophageal reflux; hiccoughs; MRCP; nausea; upper abdominal pain; vomiting

Introduction

Upper gastrointestinal (GI) disease presents with a variety of symptoms. It is essential that clinicians are able to formulate a differential diagnosis, investigate appropriately and urgently rule out serious pathology. This article highlights important differential diagnoses, and aims to give guidance on the assessment of patients presenting with diverse symptom complexes.

Swallowing difficulties (dysphagia, odynophagia)

Dysphagia can be divided into two distinct types: oropharyngeal and true oesophageal dysphagia. Identification of the type of dysphagia is important as the likely pathology, investigations and treatment pathways are different.

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Key points

- A focused history is key to establishing likely causes of upper gastrointestinal symptoms, and guides investigation pathways
- 'Red flag' symptoms should be actively sought, with urgent referral if found
- When assessing patients with upper gastrointestinal symptoms, remember to consider pathologies from other body systems when formulating a differential diagnosis

Oropharyngeal dysphagia

The voluntary, oropharyngeal swallow requires activation of a complex neurological pathway, damage to any part of which can lead to impairment. Clues in the history are difficulty initiating a swallow, choking, coughing and nasal regurgitation of food. On examination, there can be delayed swallowing, coughing or a wet voice, as a result of pooling in the pharynx. Dysarthria and cognitive impairment can point to an underlying neurological cause (see below). If a patient repeatedly chews food and spits it out before swallowing, consider dementia or an underlying psychiatric condition.

Oesophageal dysphagia

Impairment of the involuntary oesophageal swallow leads to compromised function and disorganization of coordination of the oesophageal musculature. Taking a focused history is important; dysphagia can be progressive, acute or intermittent, as well as complete or only for certain substances, for example solids only or both solids and liquid. The presence or absence of reflux symptoms also helps guide investigation.

Complete acute dysphagia, where a patient is unable to swallow their saliva, is a medical emergency requiring hospital admission. Food bolus impaction is the most common cause of the sudden onset of complete or partial dysphagia; oesophago-gastro-duodenoscopy (OGD), with bolus removal, should be performed within 24 hours.[1] Prolonged food bolus impaction can result in oesophageal ulceration and potential viscus perforation. A chest X-ray is indicated if the history suggests ingestion of a sharp object, or if there are concerns of pharyngeal perforation. Patients with tracheo-oesophageal fistulae, after chemo/radiotherapy, can also present with dysphagia associated with aspiration pneumonia or shortness of breath.

Dysphagia to solids, particularly if progressive, is likely to indicate an obstructive lesion. Progressive dysphagia, weight loss, anorexia and change of taste are 'red flag' symptoms, often indicating a worsening obstructive lesion; this is usually a peptic stricture or oesophageal carcinoma. In young patients with atopy or recurrent food bolus obstruction, consider eosinophilic oesophagitis. Long-standing eosinophilic oesophagitis can present with oesophageal stricturing. Biopsies from the mid and distal oesophagus support the diagnosis. Treatment includes dietary elimination of food allergy, acid suppression and topical corticosteroids (i.e. swallowing a metered dose of corticosteroid aerosol).

If dysphagia is equal for liquids and solids, or intermittent, consider dysmotility or inflammatory causes (see below). Differential diagnoses include achalasia, hypertonic lower oesophageal sphincter, oesophageal body dysmotility, systemic disorders including connective tissue disorders or functional dysphagia (defined by the Rome IV criteria).[2]

Globus sensation is a diagnosis of exclusion where patients describe a 'lump' in their throat, like a 'boiled sweet'. This is usually not related to food ingestion but can occur on swallowing saliva. This can be intermittent and can occur during times of stress. It is commonly associated with acid reflux.

Odynophagia

Odynophagia (painful swallowing) is often mistaken for dysphagia. If odynophagia is sudden in onset, consider ingested (caustic) substances and foreign bodies. An emergency OGD can be required to assess mucosal damage to the upper GI tract; this aids prognostication, assessment of the development of strictures and possible therapy (removal of foreign bodies).

The leading cause of odynophagia is candidiasis. Odynophagia can be preceded by other symptoms pointing to the aetiology of the pain (e.g. heartburn can indicate reflux oesophagitis). A drug history is essential (e.g. inhaled or oral corticosteroids leading to oesophageal candidiasis, bisphosphonates causing oesophageal ulceration/stricturing) (Table 1).

Investigation pathway

Patients with oropharyngeal dysphagia should undergo a thorough neurological examination and assessment from the speech and language team. They should then be investigated with videofluoroscopy and may need referral to a neurologist for consideration of further investigations, as appropriate.

All patients with oesophageal dysphagia should be urgently investigated, usually with an OGD under the 2-week-wait rule, if malignancy is suspected. If the suspected diagnosis is dysmotility, patients should undergo a barium swallow examination and be considered for high-resolution oesophageal manometry. Patients with reflux often describe the sensation of difficulty with swallowing. Around 10% of patients referred with dysphagia/dyspepsia under the 2-week wait for upper GI cancer are found to have a malignant diagnosis.[3] The presence of candidiasis, without obvious cause, should raise the possibility of HIV or occult underlying malignancy.

Dyspepsia and reflux

Dyspepsia is common, with a prevalence of around 40%. It is defined as pain or discomfort in the upper abdomen and can be associated with other symptoms, such as early satiety, bloating, borborygmi or heartburn. A clear description is helpful in the history as patients often have very different ideas of 'indigestion pain' from those ascribed to dyspepsia by the medical profession. A pain history including timing (e.g. nocturnal), radiation (e.g. to the back) and relation to food (e.g. before or after eating), and a medication history (proton pump inhibitors, non-steroidal anti-inflammatory drugs) should be taken. Associated symptoms such as vomiting, nausea, weight loss, reflux and belching should be part of direct questioning.

Differential diagnosis of swallowing problems

Category	Differential diagnosis
Extrinsic compression	Thyroid mass, thoracic aortic aneurysm, osteophytes and skeletal abnormalities, enlarged left atrium, nodal mass, lung cancer
Obstructive	Pouch, diverticulum, web, Schatzki ring, benign stricture, radiation stricture, oesophageal cancer, food bolus
Inflammatory	Eosinophilic oesophagitis, chemical ingestion, gastro-oesophageal reflux disease, pill oesophagitis
Infective	CMV, HSV, *Candida*
Motility	Achalasia, oesophageal dysmotility, scleroderma, connective tissue disorders Sjögren's syndrome
Neuromuscular	Dementia, cerebral trauma, stroke, Guillain—Barré syndrome, movement disorders (e.g. Huntington's chorea), multiple sclerosis, encephalopathy, motor neurone disease, brainstem tumours
Psychological	Anxiety, depression, globus sensation
Other	Xerostomia
Odynophagia	*Candida*, viral oesophagitis (HSV, CMV), ingestion of corrosive substance, foreign body, dissecting intramural oesophageal haematoma (rare)

CMV, cytomegalovirus; HSV, herpes simplex virus.

Table 1

If a patient complains of worsening pain, early satiety, persistent vomiting and systemic features, such as unintentional weight loss, they should be urgently investigated. Abnormal laboratory findings, such as anaemia, or a raised platelet count or serum C-reactive protein concentration, increase the likelihood of organic pathology such as malignancy, inflammatory disease or bleeding peptic ulcer disease.

Investigation pathway

In certain circumstances, dyspepsia can be a red flag symptom and warrant urgent investigation. Patients presenting with associated upper GI bleeding should be referred urgently, on the same day, to a gastroenterologist.[4] Patients aged 55 years and above with associated weight loss should be offered urgent endoscopy investigation under the 2-week-wait pathway.[5] Patients with nausea or vomiting or an associated raised platelet should be offered OGD on non-urgent basis.

In patients who do not meet the criteria for urgent referral, an appropriate management strategy is testing for *Helicobacter pylori*, with eradication if results are positive, followed by a trial of a proton pump inhibitor. The use of the carbon-13 urea breath test requires a 2-week washout of proton pump inhibitor, and no antibiotic use (for any infection) for the 4 weeks before the investigation.[4] Guidelines state that patients of any age with gastro-oesophageal symptoms that are unexplained or do not

respond to treatment should be referred to a gastroenterologist and considered for OGD.[4] Endoscopy can reveal a hiatus hernia, reflux oesophagitis, Barrett's oesophagus, peptic ulcer disease or underlying malignancy.

In patients with a normal endoscopic examination, especially those whose dyspepsia is associated with other systemic features, such as weight loss or diarrhoea, rarer causes should be considered. These include coeliac disease, pancreatic pathology, 'intestinal angina' (mesenteric ischaemia) and metabolic causes (e.g. hypercalcaemia). Infiltrative conditions (e.g. sarcoid, Crohn's disease) can be detected on biopsy of the gastric mucosa, or occasionally have a recognizable macroscopic appearance at endoscopy (e.g. 'bamboo stomach' in gastric Crohn's disease).

Functional dyspepsia is a diagnosis of exclusion and should be diagnosed according to the Rome IV criteria for functional GI conditions. It can be subdivided into postprandial distress and epigastric pain syndrome.[2]

Acute abdominal pain

Upper GI symptoms presenting acutely form part of the differential diagnosis of the acute abdomen (Table 2). It is important to enquire about site, character, onset, duration, severity, radiation and exacerbating and relieving factors in relation to the pain. Direct questions should cover previous abdominal surgery, nausea, vomiting and abdominal distension. It is relevant to ask about bowel habit in this context (including passing flatus) as subacute obstruction can present with upper abdominal pain.

When patients complain of epigastric pain, it is important to rule out pain emanating from abdominal wall pain, so-called anterior cutaneous nerve entrapment syndrome. This is confirmed by replication of pain on palpation of the abdominal wall while the patient tenses the abdominal muscles, such as when sitting up (Carnett's sign).

Differential diagnosis of upper abdominal pain

Category	Differential diagnosis
Gastrointestinal	Perforated viscus, pancreatitis, biliary colic, cholecystitis, sphincter of Oddi dysfunction
Infective	Pneumonia (especially right lower lobe), mesenteric adenitis, dermatological herpes zoster (pre-rash, thoracic distribution), Lyme disease radiculopathy (very rare)
Musculoskeletal	Prolapsed intervertebral disc, abdominal wall pain
Cardiovascular	Myocardial infarction (high index of suspicion in patients with diabetes mellitus), mesenteric ischaemia, splenic infarction, aortic aneurysm
Metabolic	Diabetic ketoacidosis, addisonian crisis, porphyria
Other	Sickle cell crisis, splenic rupture (consider in context with Epstein–Barr virus)

Table 2

Retrosternal chest pain

Oesophageal pain can mimic cardiac chest pain, as it can radiate to the neck and be described as 'heavy'. As a result, patients should be investigated for cardiac pathology before an oesophageal cause is considered. Oesophageal spasm, often triggered by oesophageal reflux, is an excellent mimic of angina or myocardial infarction, and can be severe. Oesophageal pain can be associated with food but should not be triggered by exertion. A dissecting intramural oesophageal haematoma (rare) can also mimic angina; the diagnosis is made by endoscopy and a consistent history.

If a patient presents unwell, haemodynamically compromised or with severe chest pain, particularly after vomiting, investigations should exclude oesophageal rupture (Boorhaave's syndrome). A chest X-ray can reveal a pneumomediastinum, or a pleural effusion with or without an associated pneumothorax. Gastric volvulus is often overlooked as a diagnosis. It usually presents with large-volume coffee ground vomiting and severe epigastric or lower chest pain. Complete volvulus is a surgical emergency and patients can have concurrent dysphagia. A chest X-ray often demonstrates the hernia, but no other features.

Investigation pathway

Investigation of patients with acute retrosternal chest pain depends on the presentation but should usually begin with a chest X-ray and electrocardiogram to rule out non-GI causes of this symptom. After discussion with a gastroenterologist, an OGD and/or thoracic/abdominal computed tomography (CT) scan may be indicated.

Nausea and vomiting

Nausea and vomiting are complex symptoms with a variety of causes, including local obstruction of the GI tract, a peripheral stimulus to vomiting or centrally mediated mechanisms, relayed through the chemoreceptor trigger zone in the medulla. The latter can be as diverse as drug-induced (e.g. chemotherapy-induced nausea and vomiting) or neurologically induced (e.g. raised intracranial pressure). When assessing patients with nausea, it is essential to differentiate this from anorexia or food revulsion. It is also important to ascertain whether a patient has true vomiting, which is preceded by hypersalivation and then contraction of the abdominal muscles, or regurgitation, which is effortless.

Vomiting

Vomiting is a common symptom and, as such, occurs in a variety of circumstances (Table 3). Remember to consider simple causes such as gastroenteritis, especially in patients who give an association with ingestion of a suspect foodstuff, or where other people are unwell. In elderly patients, vomiting and nausea can be a non-localizing sign suggesting infection elsewhere.

Drugs, including non-prescription or recreational drugs, are a common trigger for vomiting; this is particularly true of chemotherapy agents. Excess alcohol intake can lead to nausea and vomiting, from either bingeing or long-term alcohol misuse.

The timing of vomiting in relation to food can be a useful clue. In immediate or early vomiting, consider psychological causes, whereas if it is delayed by hours, consider mechanical causes,

Differential diagnosis of nausea and vomiting

Category	Differential diagnosis
Central	Migraine, traumatic brain injury, meningitis, encephalitis, space-occupying lesion, cerebrovascular events, intracerebral bleeds
Vestibular	Labyrynthitis, benign paroxysmal positional vertigo, Ménière's disease, acoustic neuroma
Obstructive	Gastric outlet obstruction, small bowel obstruction
Gastrointestinal	Gastroenteritis, peptic ulcer disease, cholecystitis, pancreatitis, severe constipation, gastroparesis, pseudo-obstruction, gastric dysrhythmia
Psychological	Anxiety, stress, eating disorders, rumination syndrome
Metabolic	Hypercalcaemia, hypothyroidism, uraemia, adrenal insufficiency, hyperthyroidism, hypopituitarism
Malignancy	Gastric cancer, pancreatic cancer, renal cancer, small cell lung cancer, ovarian cancer, carcinomatous peritonitis, VIPoma, carcinoid
Drugs	Opioids, antibiotics, anaesthetics, alcohol, cannabinoids, chemotherapy, NSAIDs, antidepressants, antiarrhythmics, oestrogen/progesterone, digoxin, metformin, theophylline, exenatide
Pregnancy	Normal physiological response, hyperemesis gravidarum (molar pregnancy, multiple birth), acute fatty liver disease of pregnancy, pre-eclampsia
Other	Pain, myocardial infarction, gastroparesis, motion sickness, post-surgical, cyclical vomiting syndrome, nephrolithiasis, chronic mesenteric ischaemia

NSAID, non-steroidal anti-inflammatory drug; VIP, vasoactive intestinal polypeptide.

Table 3

such as small bowel obstruction or ileus. Anxiety and stress can lead to nausea and vomiting, as can pain from any cause. It is also important to ask all patients specifically about eating disorders, as they are unlikely to mention this without direct questioning.

In individuals with recurrent attacks, consider cyclical vomiting syndrome, which presents with repeated attacks of severe nausea, vomiting and physical exhaustion, lasting from hours to days. These attacks are similar in their nature, but can vary between patients. Between attacks, the patient feels well. The condition presents more commonly in childhood, but can present in adulthood and can last from months to decades. Cyclical vomiting syndrome is a clinical diagnosis, and organic causes should be excluded before a diagnosis is confirmed. One mimic for cyclical vomiting syndrome is cannabinoid-induced hyperemesis. This condition is always linked to regular cannabis usage, has a male preponderance and patients often describe temporary relief from a hot bath. Cannabinoid-induced hyperemesis responds completely to withdrawal of cannabis.

Coffee ground vomiting can be a sign of upper GI bleeding, but can also reflect gastric stasis, caused by gastric outlet obstruction or gastroparesis. To justify use of the term 'coffee ground', the vomit must be black as opposed to merely dark. If the patient presents acutely with large-volume, coffee ground vomiting or fresh haematemesis, associated with severe pain, consider gastric volvulus (see above).

Patients with gastroparesis present with abdominal distension, nausea, large-volume vomiting, early satiety and sometimes associated weight loss and anorexia. Symptoms are difficult to control, and the focus of treatment is on hydration and nutrition. In patients with diabetic gastroparesis, there is limited evidence on any available antiemetic therapy. The mainstays of treatment are dietary interventions (lower fat, lower volume, more frequent meals), and tight diabetic control including consideration of a continuous insulin infusion in type 1 diabetes mellitus. In some cases, post-pyloric jejunal feeding and a venting gastrostomy are necessary.

Symptoms that point towards a neurological cause for vomiting are headache, double vision and gait abnormalities. Red flag symptoms are the absence of any warning, and vomiting that occurs early in the morning or is forceful in nature. Such patients should be referred for urgent cross-sectional imaging of the brain. Associated vertigo or tinnitus indicates possible vestibular pathology. In women of childbearing age, pregnancy is a common cause for nausea and vomiting.

Regurgitation

Regurgitation is a voluntary or involuntary return of partly digested food into the oropharynx. It is important to differentiate this from vomiting, as patients struggle to do this unless specifically asked. If regurgitation is associated with reflux symptoms and is worse on lying flat, think about gastro-oesophageal reflux disease or hiatus hernia. If involuntary, with undigested food, consider an oesophageal pouch; the investigation of choice might then be a barium swallow, rather than an OGD, as there is an increased risk of perforation when performing endoscopy on these patients. Although regurgitation can be pathological, it can also have psychological causes and these should be considered and addressed if no cause is found.

Rumination syndrome is an often under-recognized disorder of learned behaviour, where a focused history is key to making the correct diagnosis. Patients present with repetitive regurgitation of undigested food, without effort, usually occurring less than half an hour after eating and often with every meal.

Investigation pathway

The cause of vomiting is often evident once a careful history has been obtained, and pregnancy testing is mandatory for all female patients of childbearing age. However, if vomiting persists, further investigation is warranted, usually beginning with an OGD and a laboratory work-up to exclude metabolic abnormalities. If these reveal no abnormality, the next step is abdominal imaging and, in selected patients, gastric emptying studies. If symptoms suggest a neurological cause, an urgent CT scan of head is the initial investigation of choice.

Belching

Gastric belching occurs when there is a transient relaxation of the lower oesophageal sphincter, allowing gas to escape from the stomach. This is triggered by distension of the proximal stomach; it is an involuntary reflex and normally occurs 20–30 times a day.

Supragastric belching is caused by air that is ingested immediately before it is expelled; diaphragmatic contractions lead to a negative pressure in the oesophagus, causing air ingestion. Patients audibly swallow, then immediately expel air, often with great force, and generate a loud noise. This is behavioural, not a reflex, and is the cause of excessive belching. It is often not possible to identify an underlying cause, although stress and anxiety can worsen the symptoms. Many patients are genuinely unaware of the behavioural pattern they have adopted, so gentle behavioural therapy is appropriate. If belching is associated with other symptoms, consider further investigation as this can indicate an underlying pathology.

Hiccoughs

A multitude of conditions can lead to hiccoughs, which should be investigated if the symptom persists (Table 4).

Post-gastric surgery symptoms

After gastric surgery, patients can experience a variety of symptoms, including early satiety, dyspepsia, reflux and vomiting. This is particularly true after a gastric bypass, as patients' gastric remnant is smaller than the stomach they are used to; they should therefore reduce their oral intake to accommodate this.

After gastric resection or pyloroplasty, patients can experience dumping syndrome. This results from rapid gastric emptying leading to hypovolaemia because of the hyperosmolar load entering the proximal small bowel. The characteristic symptoms occur 15–30 minutes after a meal, and comprise tiredness, syncope and peripheral vasodilatation, sweating, palpitations, nausea, vomiting, borborygmi and diarrhoea. Initial management includes small frequent meals, avoiding simple sugars and carbohydrate-rich meals and separating solids from liquid intake.

Differential diagnosis of hiccoughs

Category	Differential diagnosis
Neurological	Space-occupying lesion, infective, multiple sclerosis, arteriovenous malformations
Vagal/phrenic nerve irritation	Neck mass, abnormality of the diaphragm
Gastrointestinal	Gastric cancer, pancreatic cancer, gastro-oesophageal reflux disease
Thoracic	Lymphadenopathy, aortic aneurysm, pneumonia
Cardiac	Myocardial infarction, pericarditis
Metabolic	Uraemia, hyponatraemia
Postoperative	General anaesthetic-induced, visceral irritation
Drugs	Benzodiazepines, dexamethasone, methyldopa
Psychogenic	Anxiety, stress

Table 4

Differential diagnosis using signs of GI disease

Sign	Differential diagnosis
Neck mass	Thyroid goitre, lymphadenopathy
Virchow's node	Intra-abdominal malignancy
Epigastric mass	Hepatomegaly, gastric mass, pancreatic mass, lymphadenopathy, peritoneal mass
Facial flushing	VIPoma, carcinoid
Murphy's sign	Cholecystitis
Carnett's sign	Abdominal wall pain
Neurofibromatosis	Rare cause of small bowel obstruction
Necrolytic migratory erythema	Glucagonoma
Migratory thrombophlebitis	Pancreatic cancer
Sister Mary Joseph nodule	Intra-abdominal malignancy
Acanthosis nigrans	Diabetes mellitus, gastric cancer
Succession splash	Gastric outlet obstruction, gastric stasis
Cullen's sign (oedema and bruising around the umbilicus) and Grey Turner's sign (bruising in the flanks)	Pancreatitis, retroperitoneal haematoma

GI, gastrointestinal; VIP, vasoactive intestinal polypeptide.

Table 5

Signs of upper gastrointestinal disease

Examination of patients with symptoms of upper GI pathology usually shows no abnormal findings. However, there are some useful pointers to underlying conditions (Table 5). ◆

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

A 76-year-old man presented with acute onset of severe epigastric and chest pain, followed by small-volume, 'coffee ground' vomiting. He was known to have a hiatus hernia that had been diagnosed many years previously. He was not taking any regular medication.

On clinical examination, there was localized epigastric tenderness.

Investigations

- Haemoglobin 139 g/litre (130–180)
- Urea 4.5 mmol/litre (2.5–7.0)
- Arterial blood gases on breathing air:
  - pH 7. 40 (7.35–7.45)
  - PO_2 13 kPa (10–14)
  - PCO_2 4.6 kPa (4.5–6.0)
  - HCO_3^- 22 mmol/litre (20–28)
- Plasma lactate 3.8 mmol/litre (0.6–1.8)
- ECG was normal
- Erect chest X-ray showed a large hiatus hernia

What is the most likely diagnosis?

A Pulmonary embolism
B Gastric volvulus
C Peptic ulcer disease
D Acute coronary syndrome
E Oesophageal rupture

Question 2

A 29-year-old man presented with dysphagia after eating steak. He was found to have a food bolus requiring endoscopic removal. He had had two previous episodes of food bolus obstruction that had resolved spontaneously. He had mild asthma and was using inhalers for this; he also had annual hay fever He was otherwise fit and well, and was a non-smoker. There was no significant family history.

What is the most likely diagnosis?

A Eosinophilic oesophagitis
B Oesophageal pouch
C Achalasia
D Functional dysphagia
E Oesophageal cancer

Question 3

A 45-year-old woman presented with a 4-month history of recurrent nausea and large-volume vomiting that had gradually worsened. She became bloated every time she ate, and described early satiety. She had seen undigested food in her vomit, often from hours previously. At the age of 7 years, she had been found to have type I diabetes mellitus. She had been struggling with her glycaemic control as she had two small children. Six months previously, she had been found to have peripheral neuropathy.

Investigations

- White cell count 7.7 $\times$ 10^9/litre (4.0–11.0)
- pH 7.49 (7.35–7.45)
- Ketones 0.3 mmol/litre (<0.6)
- C-reactive protein 6 mg/litre (<10)
- Capillary blood glucose 10 mmol/litre (5–7)
- Urine β-human chorionic gonadotropin was negative

What is the most likely diagnosis?

A Gastroenteritis
B Coeliac disease
C Gastroparesis
D Rumination syndrome
E Gastro-oesophgeal reflux disease