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Investigation and management of gastrointestinal motility disease

Robin Spiller MD, FRCP *Division of Gastroenterology, University Hospital, Queen's Medical Centre, Nottingham*

Gastrointestinal motility disorders vary from the rare and well defined, such as achalasia, to the common but nebulous, such as irritable bowel syndrome (IBS). Motility tests have made their biggest impact in the management of oesophageal and gastric disorders and have also found some use as tests of biliary and intestinal motility. Patients needing such investigations should be referred to a gastroenterologist once the preliminary investigations have been performed.

Oesophageal motility

Swallowing requires the coordinated, initially voluntary, action of the striated muscle of the tongue and pharyngeal constrictors, followed by the relaxation of the cricopharyngeus which forms the upper oesophageal sphincter. The bolus is then moved on by coordinated contraction of the smooth muscle of the oesophagus. Distension of the oesophagus induces a descending inhibition mediated by nitric oxide-releasing neurons and an ascending stimulation of the circular muscle by cholinergic neurons. The net effect is to produce a powerful aboral propulsion. Swallowing induces descending inhibition with an anticipatory relaxation of the lower oesophageal sphincter (LOS); this begins simultaneously with the contraction of the pharyngeal muscles. Once the bolus has passed the LOS, the sphincter returns to its resting state of tonic contraction just above intragastric pressure.

Disordered swallowing and peristalsis

Oropharyngeal disorders

Choking, nasal regurgitation and prolonged chewing with a fear of attempting to swallow are characteristic of diseases affecting the oropharyngeal muscle such as myopathies, motor neuron disease, and bulbar and 'pseudobulbar' palsies affecting the vagus and ninth cranial nerve. These disorders can usually be diagnosed by history and neurological examination.

Investigation

A cineradiographic contrast study shows oropharyngeal incoordination and frequently aspiration into the trachea. Rarely a fibrotic 'cricopharyngeal bar' may be detected which fails to distend as the bolus passes. This is often associated with high pharyngeal pressures and the development of a hypopharyngeal diverticulum.

Treatment

A cricopharyngeal bar can be cured by myotomy. If the underlying cause is not treatable, these patients often require alternative means of supplying fluids and nutrition, usually via a percutaneous endoscopic gastrostomy.

Oesophageal dysmotility

Achalasia, the commonest type of oesophageal dysmotility, is caused by a denervation of the circular smooth muscle of the LOS due to degeneration of ganglion cells in the myenteric plexus[1]. This initially leads to a failure of relaxation of the LOS and later to loss of peristalsis and dilation of the oesophageal body. It usually presents with a long history of gradually worsening dysphagia with intermittent bolus obstruction, often caused by meat. Regurgitation, especially on lying down, is a common feature and often brings on bouts of coughing at night.

Oesophageal spasm is caused by failure of the normal descending inhibition once swallowing has been initiated, leading to simultaneous contractions at different levels of the oesophagus with failure of peristalsis and chest pain, usually associated with swallowing. Total dysphagia with regurgitation may follow but, unlike mechanical obstruction with tumour or stricture, the dysphagia with dysmotility fluctuates widely even during the course of a single meal. Dysmotility is often aggravated by anxiety, and hence is worse when eating in public. The pain is often mistaken for angina since its relation to eating is inconsistent.

Investigation and management

Radiology and endoscopy. Mechanical obstruction by tumour or stricture must be carefully excluded by either endoscopy or barium swallow. The barium studies often give more information about motility than does endoscopy, with characteristic appearances in both achalasia (Fig 1) and oesophageal spasm (Fig 2), but normal in one-third of cases. Endoscopy is normal in one-third of cases with achalasia and is often normal in oesophageal spasm. Manometry is the 'gold standard' with which to confirm the diagnosis and quantify the problem more precisely[2].

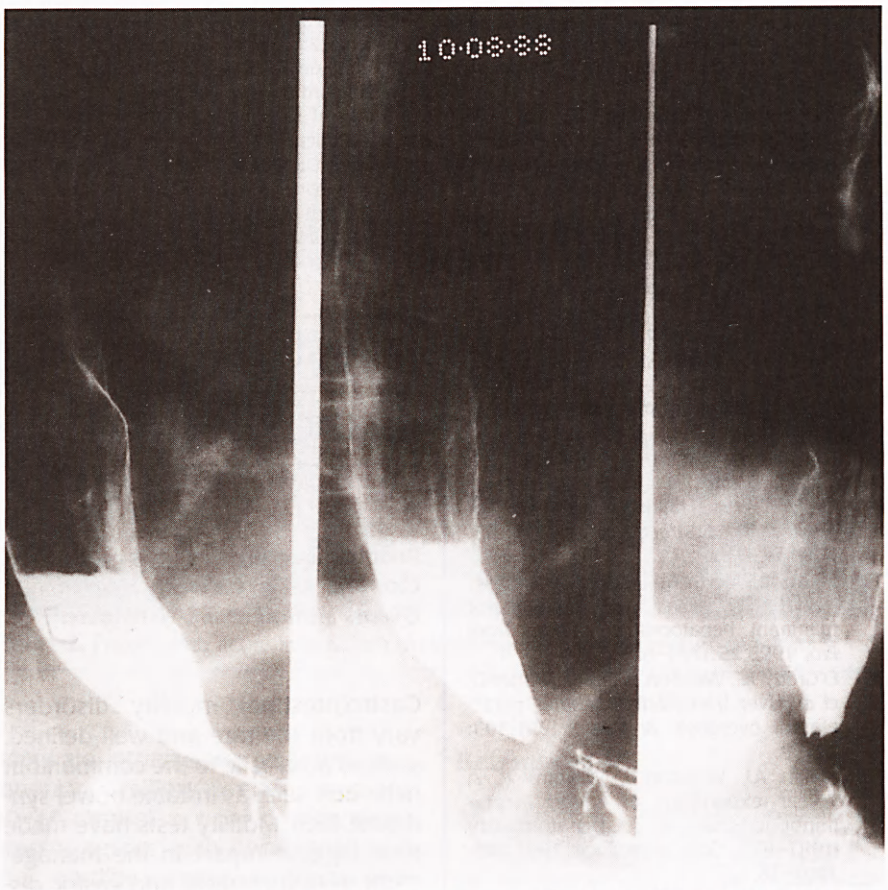


Figure 1. Barium swallow in achalasia, showing the smooth tapering 'beak' or 'rat's tail' of the unrelaxing lower oesophageal sphincter which holds up a substantial column of barium. The longer this process continues the more dilated the oesophagus becomes. Plain chest X-ray films may show an air fluid level in the mid-oesophagus in severe cases.

Oesophageal manometry. Manometry of the oesophagus is performed using a series of strain gauges mounted on a 3 mm tube which is passed via the nose into the stomach and then withdrawn in stepwise fashion. As the strain gauges pass the LOS, its pressure can be assessed and its response to swallowing noted (see Fig 3). The propagation of peristaltic pressure waves in response to swallowing a small amount of water can also be assessed.

Achalasia, the most common manometric diagnosis, is characterised by an elevated basal LOS pressure which fails to relax completely during swallowing (Fig 4). Other features are simultaneous pressure waves which become weaker as the oesophagus becomes a dilated aperistaltic tube.

Diffuse oesophageal spasm is more difficult to diagnose. Manometry may show characteristic prolonged, often simultaneous, contractions throughout the gullet but the condition varies from day to day. A scintigraphic oesophageal transit study using a

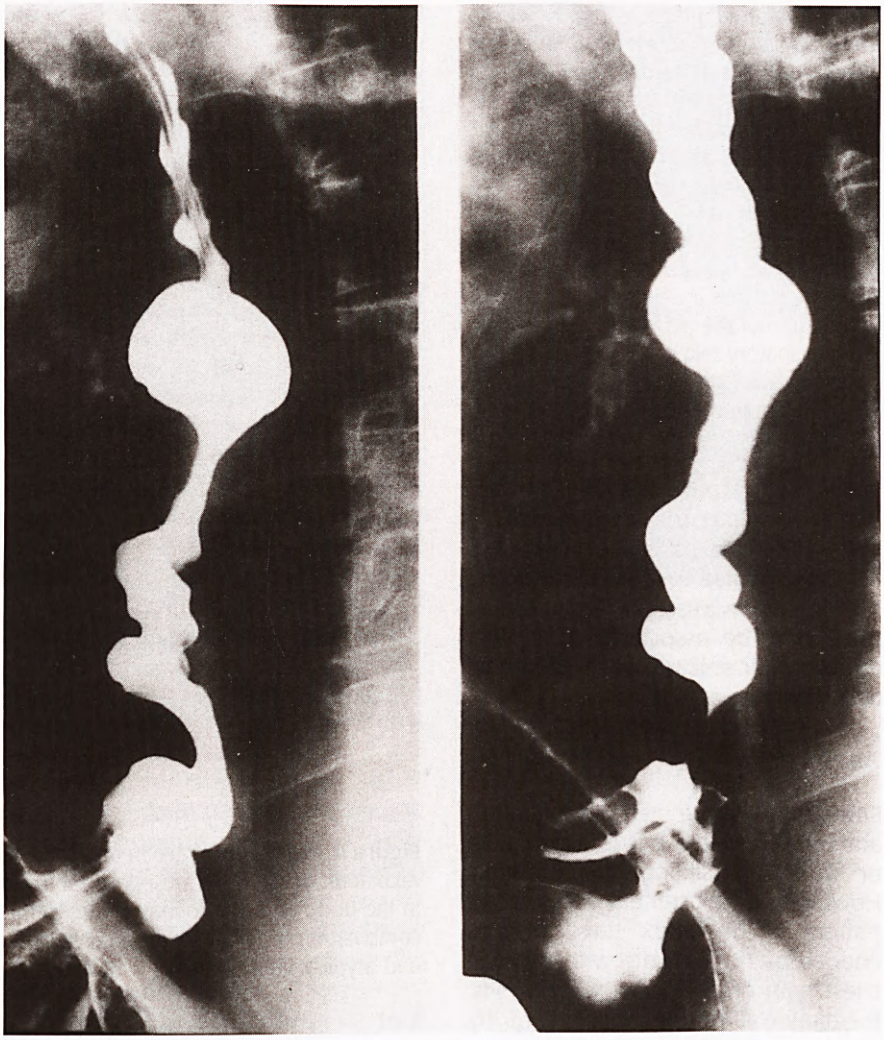


Figure 2. Barium swallow in diffuse oesophageal spasm, showing simultaneous contractions at several levels.

^{99m}Tc-labelled orange-juice bolus may be helpful in showing defects in the clearance of the gullet by the initial swallow (Fig 5).

Treatment

Graded balloon dilation under fluoroscopic control carries a low risk of perforation and often gives a good remission of symptoms for some years in *achalasia*. Recurrence is most common in those under 40 years or in whom LOS pressure remains above 20 mmHg after dilation[3]. Heller's cardiomyotomy gives good symptomatic relief, but at the cost of a large and sometimes painful thoracotomy scar. Laparoscopic cardiomyotomy is probably a more acceptable alternative to dilation[4], especially in younger patients. Endoscopic injections of botulinum toxin into the LOS gives transient relief, but the nerves regrow and further treatment is needed, often within a few months.

Diffuse spasm is more difficult to manage, being amenable to neither surgery nor dilation. Reassurance that it is not a life-threatening condition may help by relieving the associated anxiety. There are no proven treatments, and management is empiric. Antireflux treatment such as with proton pump inhibitors (PPI) may help in cases in which reflux is precipitating spasm. If it fails, calcium channel blockers or nitrates can be tried, but side effects often limit acceptability. Avoiding situations which induce symptoms, and swallowing ice-cold water which will usually inhibit spasm, may be more acceptable and give the patient some sense of control.

Gastro-oesophageal reflux

Gastro-oesophageal reflux is an increasingly common condition presenting with retrosternal burning,

Key Points

- Disordered swallowing requires initially endoscopy and/or barium swallow
- Oesophageal manometry is more sensitive for diagnosis of disorders of motility such as achalasia and oesophageal spasm
- Rarely, 24 h pH and symptom recording may be needed to confirm atypical chest pain due to gastro-oesophageal reflux
- Disordered gastric emptying is best assessed using γ-scintigraphy of a test meal
- Small bowel dysmotility is rare, and can be assessed from the manometric characteristics of the migrating motor complex
- Scintigraphic assessment of HIDA excretion is a less sensitive but safer alternative to biliary manometry for diagnosing papillary stenosis

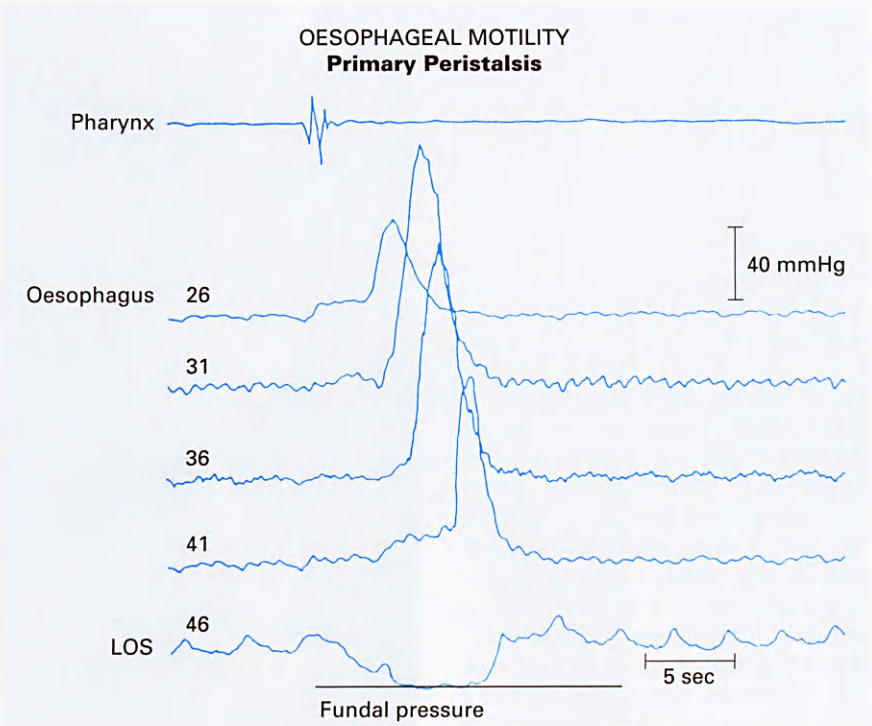


Figure 3. Normal pressure traces obtained during swallowing of a bolus of water by means of oesophageal manometry using five pressure ports, the lowest one straddling the lower oesophageal sphincter (LOS). Distances from the nares are marked on the vertical axis in cm. The pharyngeal signal is the surface EMG of the pharyngeal muscles, and indicates the initiation of swallowing. Note the uniform progression of the peristaltic wave and the anticipatory relaxation of the LOS, which regains its tonic contraction as the bolus passes into the stomach.

epigastric discomfort and reflux of bitter fluid into the mouth, usually 1–2 hours after a meal. Symptoms are often worse in the evening and on lying down to sleep. When severe, there may be associated dysphagia due to peptic stricture or oesophageal dysmotility.

Investigation

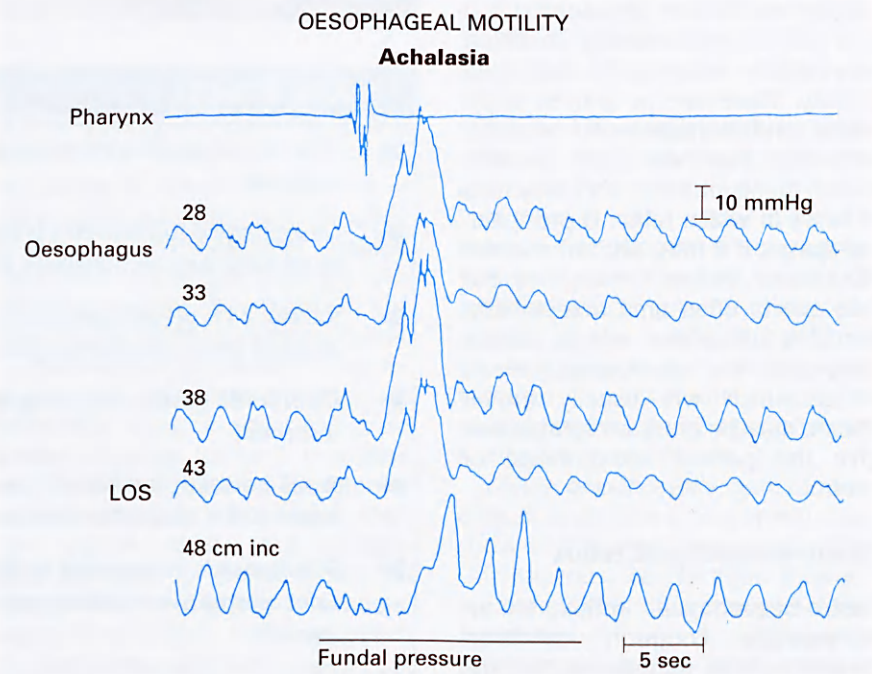
Endoscopy is the key investigation and often reveals oesophagitis with or without a sliding hiatus hernia. However, a substantial number of patients with reflux have normal endoscopy. In patients with atypical chest pain or poor response to PPIs, the diagnosis can be made clearer by performing a 24-hour pH recording 5 cm above the LOS, using an antimony electrode and a portable recorder. Patients indicate when they have symptoms using an event marker. The per cent of time when the pH is below 4 (normal <7%) indicates the severity of reflux, and the relation of pH dips to pain show whether reflux accounts for the pain.

Manometry has surprisingly little to add. Low LOS pressure and poor distal peristalsis are common, but they neither correlate with symptoms nor predict response to treatment.

Treatment

The initial treatment is weight reduction, avoidance of aggravating foods such as fats and of large meals late at night. Most patients with erosive

Figure 4. Manometry trace in achalasia (set out as for Fig 3). This trace shows failure of relaxation of the lower oesophageal sphincter (LOS) and simultaneous pressure waves in the body of the oesophagus due to the 'common cavity phenomenon'. This combination of failed LOS relaxation and ineffective peristalsis causes the dysphagia and atypical chest pain.



oesophagitis need treatment with PPIs. Those with normal oesophageal mucosa can be treated symptomatically with antacids, alginates, prokinetics such as cisapride, H_2-receptor antagonists or PPIs, using the least potent medication compatible with adequate symptom control.

If severe symptoms fail to respond to medical therapy, surgery is indicated. Poor distal peristalsis is not an exclusion; if it is secondary to reflux and inflammation, it may improve after fundoplication. However, care should be taken to exclude systemic sclerosis or CREST (calcinosis Raynaud's phenomenon, (o)esophageal dysfunction, sclerodactyly and telangiectasia) syndrome[5].

Gastric motility

Fasting motor pattern

There is a cyclical fluctuation in activity:

- a prolonged (30–60 min) quiescent phase (phase I)
- a 20–30 min period of increasing phasic contractions (phase II)
- a period of intense regular contractions of high amplitude at 3 per min lasting 4–6 min (phase III).

This 'migrating motor complex' (MMC) may start at the LOS, progress through the stomach, squeezing its contents into the small intestine, and continue down the small intestine, often as far as the terminal ileum. About half such MMCs start in the upper jejunum and miss out the more proximal gut.

Postprandial motility

Soon after ingestion of a mixed solid/liquid meal, most of it resides in the body and fundus of the stomach which relaxes to accommodate up to 1 litre of contents with minimal rise in pressure. Chyme then passes into the antrum where regular contractions at a rate of three per minute migrate from the incisura towards the pylorus. The pyloric outlet narrows as contractions approach, forcing most antral contents back into the body of the stomach. This repetitive 'to and fro' movement breaks up the particulate matter which is usually smaller than 2 mm before leaving the stomach. Larger particles can leave the stomach, but usually do so during fasting phase III.

Gastric emptying of fatty meals is faster in those with higher habitual fat intake. This adaptation to calorie intake tends to slow emptying in those with prolonged low fat intake and may explain part of the delay observed in anorexia nervosa. Premenopausal women have slower gastric emptying than men, but this difference disappears after the menopause.

Disordered gastric motility

The most common dysmotility affecting the stomach is antral hypomotility which leads to reduced grinding and delayed gastric emptying. The loss of the fasting pattern leads to retention in the stomach of fibrous nonnutrients, which can form enormous masses of vegetable matter (phytobezoars). Symptoms of disordered emptying include postprandial bloating, early satiety, nausea and vomiting, characteristically of food eaten 6–12 hours previously.

Investigation and management

It is vital to exclude antropyloric ulceration, scarring or tumour by initial endoscopy or barium meal. The latter is not a physiological test of emptying, which must be done scintigraphically using a dual radiolabelled solid/liquid mixed meal. Emptying of solids is slower and requires more antral activity than liquids, so it is more sensitive to antral hypomotility than liquid emptying (Fig 6). Manometry rarely adds significant information.

Now that peptic ulceration and its complications, including surgery, are less common, metabolic and neurological factors have become more important causes of delayed gastric emptying (Table 1). However, many cases have no obvious cause and must be managed empirically.

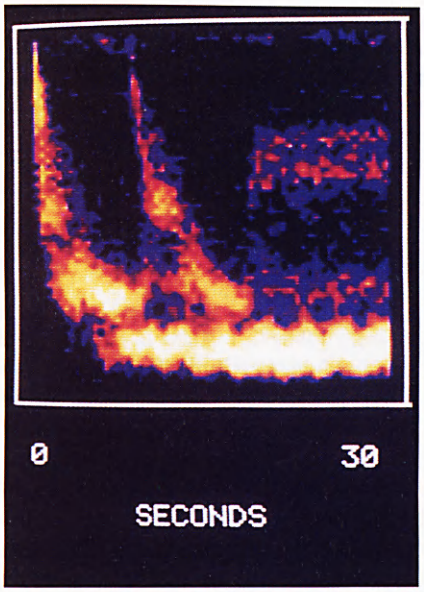
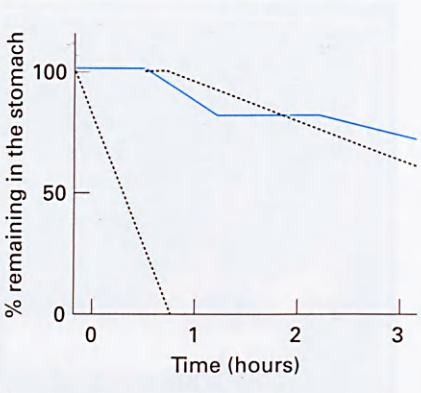


Figure 5. Oesophageal transit study. Subjects are given 40 mBq ^{99m}Tc-EDTA in a glass containing 20 ml water; they are asked to swallow on command, then not to swallow again for 30–40 sec while serial 1-sec scans are obtained. These scans are compressed to a single line, each of which is then aligned to give an activity vs time curve. This scan shows disruption of the normally rapid clearance of isotope into the stomach, with proximal movement of isotope after about 10 sec (top of scan: at the level of the sternal notch; bottom dense line: indicates isotope in the stomach).

These patients have often lost weight and are usually anxious. Reassurance and encouragement is important, together with diet modification, avoidance of fibrous foods and increase of calorie intake by means of liquid diet supplements. Centrally-acting antiemetics such as domperidone 10–20 mg three times daily may help with nausea, while peripherally acting prokinetics like cisapride (10–20 mg three times daily) may improve gastric emptying and associated symptoms. Intravenous erythromycin is a powerful stimulant of antral activity and has occasionally



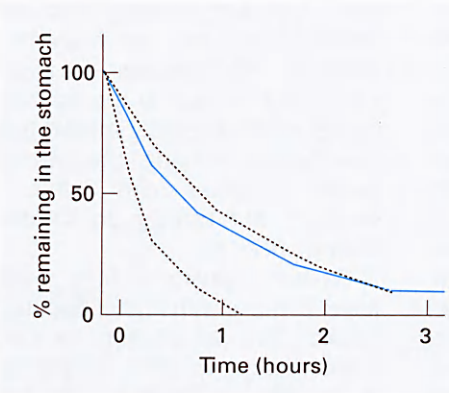


Figure 6. Gastric emptying curves showing per cent remaining in the stomach vs time in hours: **(a)** solids; **(b)** liquids (dotted lines: normal ranges). Note that this patient with idiopathic gastroparesis has borderline slow liquid emptying and abnormal solid emptying.

been used to treat prolonged post-operative gastroparesis. It can be successful orally in diabetic gastroparesis[6], though its long-term value is unproven.

Small bowel motility

The small intestine has a characteristic fasting cycle which recurs with variable regularity every 1–2 hours. During phase III (which lasts 4–6 minutes) intense, high amplitude, regular contractions empty the small intestinal segments 'sweeping all before'. This 'interdigestive housekeeper' keeps the small bowel bacterial population sparse; its interruption by visceral myopathy or neuropathy leads to small bowel contamination, with malabsorption and abdominal pain. Feeding disrupts the fasting cycle, replacing it with irregular phase II-like activity.

Small bowel dysmotility

Disorders of small bowel motility are poorly defined. Visceral myopathies/neuropathies, either acquired or inherited, are extremely rare. They produce a 'chronic intestinal pseudo-obstruction syndrome' characterised by apparent obstruction, with abdominal distension, nausea, vomiting and pain associated with dilated loops of bowel and fluid levels on plain X-ray. Such patients often undergo laparotomy, which can complicate the picture by causing adhesions.

Investigation

A barium follow-through may show dilated loops of otherwise normal bowel; a radiolabelled nutrient test meal shows delayed transit. Manometry is helpful in the diagnosis of myopathy (low amplitude trace) and neuropathy (disruption of the normal MMC propagation)[7]. The diagnosis can be confirmed by a full thickness biopsy of abnormal dilated bowel at the time of laparotomy.

Irritable bowel syndrome

IBS is a common disorder which affects about one in ten of the population and contributes a third of gastroenterological outpatients. Symptoms are often long-standing and consist of abdominal pain related to defaecation and/or eating, with disordered stool frequency and consistency, bloating, and passage of mucus per rectum (Table 2). The more symptoms and the longer the history, the more certain the diagnosis becomes. Disordered motor patterns are inconsistent and of no help in establishing the diagnosis[8]. The most consistent finding is lowered threshold for discomfort and pain on distending the rectum[9], but the wide normal range makes this unreliable in distinguishing IBS from other conditions. Small bowel transit is accelerated in patients with diarrhoea as their main symptom, but is of no help in diagnosis since many diarrhoeal diseases, with which IBS may be confused, have similar acceleration. The only situation in which a motility test is currently helpful is in IBS patients who complain of constipation. Their colonic transit can be assessed from the progression of a radioisotope bolus delivered to the terminal ileum by means of an enteric-coated gelatin capsule. The test usually demonstrates normal transit (>90% excreted within 5 days), clearly distinguishing these patients from those with colonic inertia who

Table 1. Causes of delayed gastric emptying

Disorder	Examples
Pyloric stenosis	Peptic ulceration, tumour
Autonomic neuropathies	Diabetes, Shy-Drager syndrome
Infiltrative disorders	Amyloid
Connective tissue diseases	Scleroderma
Drugs	Anticholinergics, opiates, tricyclic antidepressants

Table 2. The Rome criteria for irritable bowel syndrome

Continuous or recurrent symptoms for at least three months:

1. Abdominal pain or discomfort, relieved by defaecation or associated with a change in frequency or consistency of stool, together with:
2. Irregular (varying) pattern of defaecation at least 25% of the time (three or more of the following symptoms)
   - altered stool frequency
   - altered stool form (hard or loose/watery stool)
   - altered stool passage (straining, feeling of incomplete evacuation or urgency)
   - passage of mucus per rectum
   - bloating or sense of distension

have greatly prolonged transit times and need colonic stimulants, which will not help IBS patients.

Investigation and management

Patients under the age of 40 years who meet all the Rome criteria (Table 2) need no further investigation, provided that they have no sinister symptoms such as weight loss, anaemia, rectal bleeding or recent change in bowel habit. Those with less than a 'full house' of symptoms need more cautious evaluation, and may warrant some simple screening blood tests such as haemoglobin, albumin, calcium and erythrocyte sedimentation rate/C reactive protein.

Management includes firm reassurance, and modification of fibre, lactose or fruit intake in those IBS patients who are intolerant of high fibre diets, especially bran. Treatment of associated anxiety or depression is often indicated. A minority benefit from antispasmodics, especially those with anticholinergic properties[10], while those with diarrhoea as the main symptom may respond to loperamide[11]. Hypnotherapy and other forms of counselling are as successful as drug treatment[12].

Biliary dysmotility

A normal gall bladder fills during fasting and contracts soon after a fatty meal. The sphincter of Oddi (SOD) relaxes simultaneously to allow pancreatic and biliary secretions to mix with duodenal chyme. Pregnancy or prolonged starvation inhibits gall bladder emptying and allows biliary sludge, and later gall stones, to develop. Cholecystectomy may disrupt the normal relaxation of the SOD; it is often followed by recurrent postprandial colic, which in some cases is due to SOD dysfunction.

Investigation

Recurrent pain may be associated with abnormal liver function tests and/or a dilated common bile duct. Biliary flow can be assessed scintigraphically with ^{99m}Tc-labelled hepatic imino-diacetic acid (HIDA), which is rapidly excreted in bile after intravenous injection. SOD dysfunction causes delayed excretion, and may show a paradoxical response to cholecystokinin infusion with an increase in pressure and delayed HIDA excretion instead of the expected relaxation and acceleration of bile flow. This technique is probably not as sensitive as SOD manometry, which may show a range of abnormalities in such patients but is not widely available and carries a substantial risk of pancreatitis. High basal pressure (>40 mmHg) is the best predictor of a good response to sphincterotomy[13].

Treatment

Patients with pain, abnormal liver function tests and delayed HIDA excretion respond well to endoscopic sphincterotomy, while those with pain alone often do not. In view of the relatively high complication rate after sphincterotomy in such patients (up to 30%), a conservative approach is usually best.

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