

Acute diarrhoea

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Abstract

Diarrhoea is a common disorder, affecting all ages, and is a common cause for admission to hospital. A careful history often indicates the likely cause. Rarely, diarrhoea is the first presentation of a more chronic process. Careful examination combined with investigations help determine the disease severity. Stool culture positivity decreases each day following symptom onset, and stool cultures should be taken only during the first few days of symptoms. Stool examination for ova, cysts and parasites is indicated in the context of an appropriate travel or sexual history. Treatment of acute diarrhoea is often based on fluid and electrolyte replacement only. Antibiotics are rarely required and can prolong carriage of infective organisms. *Clostridium difficile* diarrhoea causes significant morbidity and mortality in elderly patients; novel treatments are required to prevent persistent disease. Flexible sigmoidoscopy and rectosigmoid biopsies are used to assist diagnosis in patients suspected of having inflammatory bowel disease.

Keywords *Clostridium difficile*; diarrhoea; infectious diarrhoea; inflammatory bowel disease; probiotics

Introduction

Diarrhoea is one of the most frequent medical conditions worldwide, with prevalence in Western populations of 4–5%.^{1–3} Worldwide, there are 1.5 billion episodes of diarrhoea per year of which 1.5–2 million result in death, particularly among children aged under 5 years. Hospital admission is often required in immune compromised patients, young children or the elderly. In the UK, there are 9.4 million cases of acute diarrhoea annually,^{4,5} and infectious diarrhoea causes 300 deaths and 35,000 hospital admissions annually.

Definition

Acute diarrhoea is defined as passage of more than 250 g stool each day (>10 g/kg in children).⁶ Practically, it is better defined

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What's new?

- Racecadotril is a peripherally acting enkephalinase inhibitor. Unlike loperamide, it has antisecretory rather than antimotility properties and can be used in addition to oral rehydration treatment in acute diarrhoea
- Faecal transplantation is a potential novel treatment for *Clostridium difficile* infection. A donor faecal suspension is administered via an enteral tube or colonoscope. It may be of use in recurrent *C. difficile* but at present only case reports and case series exist
- The intestinal microbiome is likely to affect susceptibility to infectious diarrhoea. The role of probiotics in preventing and shortening the duration of diarrhoea is an expanding area, *Lactobacillus GG* treatment for norovirus being a current example
- Human genetic variations that confer susceptibility to infectious diarrhoea (polymorphisms within genes encoding CD14, interleukin-10 promoter and leptin) have been identified. To date, no role for host genetic biomarkers has been defined in clinical practice

as three or more liquid stools/day for up to 2 weeks. Stool consistency can be judged using the Bristol scale, which describes seven types of stool; type 7 refers to liquid faeces.⁷ Sometimes, patients describe a single loose motion or even discharge from the rectum as diarrhoea, so it is important to clarify stool frequency and consistency from the patient history, to avoid inappropriate care pathways being adopted.

Epidemiology

Infectious diarrhoea accounts for the majority of episodes and a potential pathogen (of which >70% are viral) can be identified in approximately 70% of cases in carefully performed clinical studies. In clinical practice the chance of identifying a pathogen is much lower as most clinical laboratories screen only for *norovirus*. Preformed toxins usually cause vomiting 1–6 hours after ingestion rather than diarrhoea (e.g. *Staphylococcus aureus* or *Bacillus cereus*) (Table 1).

Small bowel diarrhoea is often high volume and foul smelling. Some small bowel pathogens interfere with gut motility rather than fluid reabsorption, producing cramping, bloating and weight loss. Bacterial pathogens that infect the colon are often invasive, producing frequent, low volume, bloody diarrhoea and fever.

Pathology and pathogenesis

Diarrhoea is traditionally classified as being due to osmotic, secretory, motility or inflammatory processes.

Osmotic diarrhoea is due to an excess of malabsorbed, osmotically active substances that cause water to be retained in the bowel lumen, producing watery diarrhoea. It is characterized by a stool osmotic gap over 125 mOsm/kg {stool osmotic gap = stool osmolality – [2 × (stool Na⁺ + K⁺)]}. The diarrhoea stops when the patient fasts. Examples include laxative abuse and excessive intake of magnesium-containing medicines.

Infectious causes of diarrhoea

Organism	Bowel site	Blood in stool	Incubation time
Enteroadhesive <i>E. coli</i>	S	No	8–18 h
Enterotoxigenic <i>E. coli</i>	S	No	16–72 h
Enterohaemorrhagic <i>E. coli</i>	L	Yes	72–120 h
<i>Salmonella</i>	S + L	Yes	16–72 h
<i>Shigella</i>	L	Yes	16–72 h
<i>Campylobacter</i>	L + S	Yes	16–72 h
Norovirus	S	No	16–72 h
Adenovirus	S	No	10 d
<i>Giardia lamblia</i>	Proximal S	No	1–2 w
<i>Strongyloides stercoralis</i>	S	No	1 w–y
<i>Entamoeba histolytica</i>	L	Yes	1–3 w
<i>Cryptosporidium</i>	S	No	1–2 w

d, days; h, hours; S, small bowel; L, large bowel; w, weeks; y, years.
Adapted from Emergencies in Gastroenterology and Hepatology.⁶

Table 1

Secretory diarrhoea is produced by toxins or peptides that cause abnormal ion transport across intestinal epithelial cells. It is characterized by a fasting stool osmotic gap less than 50 mOsm/kg; diarrhoea persists despite fasting for 3 days. Examples are enterotoxins and tumours secreting vasoactive intestinal polypeptide (VIPomas).

Deranged gut motility can cause diarrhoea and in these cases measurement of osmotic gap and response to fasting is unhelpful. Common examples include irritable bowel syndrome and bacterial overgrowth.

Inflammatory diseases may cause altered mucosal permeability, with diarrhoea resulting from aberrant osmotic, secretory and motility gut function. Examples include the inflammatory bowel diseases and gut ischaemia.^{2–4,8}

Diagnosis

History

Important aspects include establishing several key facts including:

- speed of onset, duration, stool frequency, volume and consistency:
 - nocturnal diarrhoea suggests an inflammatory cause
 - weight loss suggests a small bowel aetiology
 - urgency suggests rectal inflammation
 - presence of blood in the stool may suggest colonic inflammation
 - steatorrhoea is indicative of a malabsorptive disorder (usually a cause of chronic rather than acute diarrhoea)
- co-existent abdominal pain, nausea, vomiting or fever, suggesting toxins or small intestine pathogens
- contact with possible infected food or water
- family members or friends similarly affected, suggesting infection
- recent travel history may suggest potential sources of infectious diarrhoea. It is important to note that malaria

can present as diarrhoea and should always be excluded in a patient returning from an endemic area

- recent hospital admissions or achlorhydria (pernicious anaemia, *Helicobacter pylori*, proton pump inhibitor (PPI) use), especially if recently treated with antibiotics, can predispose to *Clostridium difficile* infection
- current or recent medication (e.g. antibiotics, PPI, β -blockers, NSAIDs, magnesium-containing drugs)
- co-morbidities (chemotherapy, thyrotoxicosis, diabetes mellitus, systemic sclerosis, parathyroid disease) that can cause diarrhoea
- bulimia, suggested by a history of persisting vomiting and weight loss.

Physical examination: it is important to assess fluid status and exclude volume depletion, suggested by postural hypotension or, less reliably, by tachycardia, hypotension and decreased skin turgor. Abdominal tenderness is important; involuntary guarding suggests peritoneal involvement and merits urgent surgical review. A temperature may be present in invasive bacterial or viral disease but can be present in inflammatory bowel disease. Weight should be measured and overall nutritional status assessed.

Investigations: stool samples should be sent for microscopy, culture, viral PCR (norovirus) and *C. difficile* assay. Stool for ova, cysts and parasites should be sent on three consecutive days if the patient has returned from the developing world in the past 4 weeks, or in men who sleep with men (MSM) with multiple sexual partners. Blood tests include full blood count, serum urea and electrolytes, calcium, phosphate, magnesium and C-reactive protein, and liver function tests, as well as blood cultures in pyrexial patients.

If indicated, an abdominal X-ray should be taken to assess intestinal dilatation or faecal impaction (equivalent to 4 months' background radiation, so this should be requested selectively in those aged under 50 years). Sigmoidoscopy with biopsies should be performed if there is associated rectal bleeding and in patients with known inflammatory bowel disease.^{6,8}

Criteria for admission

Any of the following indicate a need for hospitalization:

- haemodynamically unstable (systolic BP <100 mmHg and pulse >100 beats/minute)
- Severe abdominal pain or excessive bloody diarrhoea (more than five bloody motions/day)
- Severe weight loss (>10% body weight in previous 2 weeks)
- Fever >38.5°C

A lower threshold for hospital admission is needed for patients who are elderly or immune compromised, have significant co-morbidities or suffer from inflammatory bowel disease.

Management

Treatment should be directed at correcting electrolyte and fluid losses. Only in certain cases does the underlying cause require treatment.

- Fluid
 - Oral rehydration is best provided using oral rehydration solutions (ORS). Over-the-counter formulations (e.g.

Dioralyte™) are more palatable but less effective as they contain less salt. A suitable home preparation can be made (1/2 teaspoon of salt, 1/2 teaspoon of baking soda (sodium bicarbonate), 4 tablespoons of sugar, all dissolved in 1 litre of boiled water)

- Intravenous fluids, if the enteral route is not available or insufficient, usually sodium chloride 0.9% with potassium (as guided by serum electrolytes) – 4 litres daily may be necessary initially
- Monitor and replace electrolytes (Na⁺, K⁺, Mg⁺⁺, Ca⁺⁺, PO₄³⁻) guided by blood results
- Consider loperamide to reduce stool frequency (2 mg orally 6-hourly as required), but avoid in acute gastroenteritis as there is a risk of developing toxic megacolon. Codeine phosphate acts both as an effective painkiller and to reduce stool frequency, but does not redistribute intraluminal fluid to the intravascular space. Racecadotril, available in some European countries (but not in the UK at present), is a peripherally acting enkephalinase inhibitor that reduces intestinal secretion rather than preventing symptoms through inhibiting gut motility, and may be useful^{9,10}
- Antibiotics (e.g. azithromycin 500 mg orally daily for 1–3 days; or metronidazole for amoeba or *C. difficile*) are usually indicated only for:
 - Persistent (>3 days) diarrhoea with mild systemic symptoms (temperature >37.5°C, pulse >100 beats/minute)
 - Severe systemic symptoms (temperature >38.5°C, haemodynamic instability)
 - Proven shigella or *C. difficile* infection
 - Traveller's diarrhoea
 - Proven parasitic infection; *Entamoeba histolytica*

Avoid using antibiotics, unless the patient is overtly septic, or if entero-haemorrhagic *Escherichia coli* (EHEC) or non-typhoidal salmonella are suspected as the cause of the diarrhoea. Their use can promote haemolytic–uraemic syndrome (HUS) or prolong carriage of infection.¹¹

Eating food during an episode of diarrhoea is encouraged, as this helps assist fluid absorption and enterocyte repair. A soft bland diet is recommended. Dairy products, alcohol, caffeine and fizzy drinks should be avoided as these can aggravate symptoms.^{12,13}

Patients often ask about the value of probiotics. Daily administration of preparations that contain about 10 billion colony-forming units of *Lactobacillus* reduce diarrhoea duration by about 1 day, if commenced within 48 hours.¹⁴ Avoid preparations containing *Saccharomyces* (yeast) in immune-compromised patients as fatal cases of septicaemia have been reported.

Special circumstances

Traveller's diarrhoea: often caused by viruses or enterotoxigenic *E. coli* (ETEC). It is self-limiting but can be treated empirically with antibiotics as this reduces the duration of diarrhoea from 3 days to 2 days. The best preventive advice for travellers is to ensure proper hand washing and sanitation. Drinks should be from sealed bottles or recently boiled water and foods washed in safe water or peeled or cooked. When travelling, beware slow-cooked food that has been kept continually warm, for example buffet food.

***E. coli* O157:H7 and O104:H4:** EHEC causes severe bloody diarrhoea, abdominal pain, leucocytosis, and low-grade fever. It often occurs after eating undercooked meat or unpasteurized milk. Its toxins can cause HUS in 5% of cases (acute renal failure, thrombocytopenia and haemolytic anaemia). Treatment is supportive. Antibiotics can worsen HUS, particularly associated with a new strain of *E. coli*, O104:H4.¹¹

Norovirus: this contagious virus is transmitted by faecally contaminated food or water, or by person-to-person contact. Norovirus is a common cause of acute viral gastroenteritis, and affects all age groups. The virus continues to shed after symptoms have subsided for many weeks after infection. Acute symptoms are self-limiting (lasting 2 days). The virus is rapidly inactivated by heating or chlorine-based disinfectants.⁵

C. difficile: this organism is a major problem due to the associated colitis that causes significant morbidity and mortality, especially in vulnerable, elderly adults. Risk factors include old age, chronic hospitalization, recurrent antibiotic or PPI use, achlorhydria, immune compromise and enteral tube feeding. Treatment involves infection control measures and metronidazole 400 mg orally 8-hourly for 14 days as a first-line treatment. This fails in about one-third of patients, who require vancomycin 125 mg orally 6-hourly for 14 days.¹⁵ Potential alternative therapies include other poorly absorbed antibiotics, such as fidaxomicin 200 mg orally 12-hourly for 10 days, or rifaximin 200 mg orally 8-hourly for 3 days. Monoclonal antibodies (CDA1, CDB1)¹⁶ or faecal transplant¹⁷ have been used experimentally but are not as yet routine clinical practice.^{16,17}

Giardiasis: this is common in travellers returning from the Rocky Mountains, India or Mexico and is more common in MSM. Symptoms include nausea, foregut bloating, early satiety, excess flatus and the frequent passage of pale, bulky stools. Malabsorption causes weight loss. Diagnosis requires three stool samples taken on three consecutive days (90% sensitive), although empirical treatment may be appropriate with tinidazole 2 g orally, repeated after 1 week. Several weeks' post-infective irritable bowel is common.

Inflammatory bowel disease (IBD) or infective diarrhoea? Infective diarrhoea is suggested by rapid symptom onset (days rather than weeks), cramping abdominal pain and fever, and improvement within 1 week. If stool cultures are non-diagnostic and symptoms persist or worsen, flexible sigmoidoscopy is required. Histology can differentiate between a flare of IBD and infective colitis but is more useful to exclude IBD, in which crypt architecture is preserved (excluding, perhaps, the first few weeks of colitis). A gastroenterologist should be involved when treating a patient with possible IBD. If corticosteroids are required and infective colitis has not been excluded, or if amoebic colitis is suspected until histology and microscopy is available, treat with ciprofloxacin 500 mg orally 12-hourly and metronidazole 400 mg orally 8-hourly for 5 days.⁶

Outcome

Most acute diarrhoea symptoms last less than 1 week, merely requiring supportive management. Viral gastroenteritis typically heals rapidly with little residual injury, whilst infections caused by bacteria often have a more prolonged illness and may be

Chronic conditions that may present with acute diarrhoea

Adenocarcinoma	Neuroendocrine tumour (carcinoid, VIPoma, gastrinoma)
Coeliac disease	IBD
Diverticular disease	Exocrine pancreatic insufficiency
Hyperthyroidism	Bile salt malabsorption
Lactose intolerance	Bacterial overgrowth
Medication-related conditions	Ischaemic colitis

IBD, inflammatory bowel disease; VIP, vasoactive intestinal polypeptide.

Table 2

associated with post-infectious irritable bowel syndrome (IBS). In this case symptoms persist for a median of 6 months.¹⁸ Patients with *Salmonella* or *Campylobacter* infection should be advised to avoid preparing uncooked food for at least 4 weeks, as about 20–50% of individuals still secrete the infectious organism after 2 weeks.¹² Usually, no routine follow-up is required.

Post-infective sequelae may occur:

- *Campylobacter* diarrhoea: Guillain–Barré syndrome supervenes in 1:3000, occurring 1–2 weeks after the infection onset
- bacterial diarrhoea: self-limiting reactive arthritis in 1–2%, occurs after 1–6 weeks; secondary lactose intolerance may persist for months (reduce dairy intake); IBD increases in incidence from 3/10,000 to 7/10,000 during the year following infection; post-infective IBS occurs in about 3%

Rarely, diarrhoea is the first presentation of a more chronic process, which should be suspected if diarrhoea persists for more than 2 weeks.^{1,4,6}

Table 2 gives examples of some common conditions that present in this way.^{2,3} ◆

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