Clinical Reviews

Acute management of the patient with Diarrhoea

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Abstract

Diarrhoea is a relatively common symptom in patients presenting to the acute medical take. The differential diagnosis is wide, although the commonest causes are infection, inflammatory bowel disease and motility disturbances. This article aims to summarise an approach which doctors working at the front door may use to enable rapid diagnosis of the cause of diarrhoea, along with management strategies for its treatment.

Keywords

Diarrhoea, Colitis, Inflammatory Bowel Disease

Key Points

1. A careful history and examination will usually enable identification of the cause of diarrhoea.
2. Immediate management should include assessment and treatment of volume depletion and early identification of those patients likely to require surgery.
3. Plain abdominal x-ray will enable exclusion of toxic mega-colon and help in establishing the extent and severity of inflammation in patients with suspected colitis.
4. Early specialist involvement is recommended for patient with suspected inflammatory bowel disease, or those with exacerbations of this condition.

Introduction

Even in the developed world, diarrhoea is a major health issue both in the community and in hospital. Every doctor involved in acute medicine needs to be competent in the initial assessment and management of acute and chronic diarrhoea. A strict definition of diarrhoea is based on a stool weight in excess of 200 grams in 24 hours. Clearly this definition is impractical to apply clinically as collecting and weighing stools is onerous, not to say unpleasant. It is more useful, therefore to describe diarrhoea as ***a significant increase in stool frequency or volume.*** Three or more loose or watery stools per day would usually be considered abnormal.

Epidemiology

The incidence of diarrhoea in the general population is difficult to estimate as most episodes are self-limiting and do not present to medical services. A UK study followed 8000 adults for a four month period and found that 8 percent suffered from at least one episode of diarrhoea in the preceding month.[1] This correlates to one episode per adult per year in the UK.

A further UK study calculated an incidence of 3.3 cases and 0.15 cases per 100 person years presenting to general practitioners and hospitals respectively.[2]

Pathophysiology

Up to 10 Litres of fluid enters the GI tract daily, representing oral intake and endogenous secretions. The majority of this, up to 75%, is absorbed in the small bowel. The remainder is reclaimed in the colon leaving between 100-200g to be passed. Water is passively absorbed depending on the osmotic gradient from lumen to intestinal mucosa.

Diarrhoea occurs when the water content of the stool is increased. The cause of this can be classified into 4 groups: osmotic, secretory, motility or inflammatory. In practise a combination may co-exist.

Osmotic diarrhoea arises when the concentration of a non-absorbable solute is increased within the lumen resulting in a higher quantity of luminal water. Certain forms of laxatives use this mechanism, which is also responsible for diarrhoea due to small bowel malapsorption.

Secretory diarrhoea results from abnormal ion transport into the lumen. Classic examples of diarrhoea caused through this mechanism include cholera and endocrine pathology, such as VIPoma, hyperthyroidism and carcinoid.

Motility diarrhoea results from rapid transit through the bowel , reducing the time available for fluid reabsorption. This is the usual mechanism of diarrhoea in irritable bowel syndrome (IBS).

Inflammatory diarrhoea results from injury to the colonic mucosa, resulting in impaired fluid absorption. Inflammatory bowel disease (IBD) and certain forms of infection cause diarrhoea through this mechanism.

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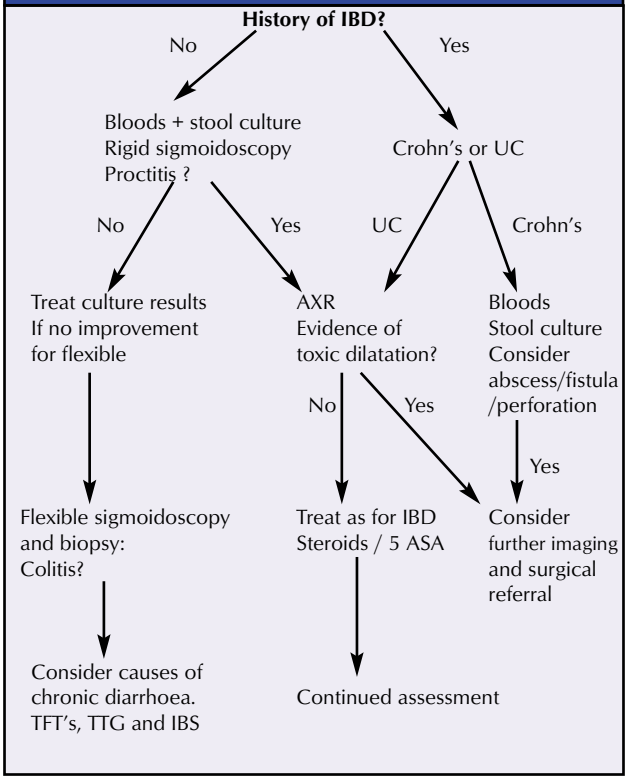
Figure 1. Algorithm for assessment of acute diarrhoea



Clinical Features

The approach to the patient will depend on the clinical scenario, as outlined in figure 1. Patients generally fall into two categories: Firstly are patients with 'known' inflammatory bowel disease who present with an acute increase in their symptoms. Alternatively patients may present for the first time with an acute episode of diarrhoea of uncertain cause. Although the general principles are similar in both groups, the latter generally cause more diagnostic challenges. The general approach to the patient with diarrhoea is outlined below, while the specific management of exacerbations of IBD is discussed later in this article.

History

A comprehensive history will frequently enable the cause of diarrhoea to be identified. Certain features in the history may be particularly useful:

1. **Onset / Chronicity of Symptoms:** an abrupt onset of severe symptoms is suggestive of an infective cause, while more gradual onset, or recurrent bouts of diarrhoea spanning many months or years is more in keeping with a chronic inflammatory or neoplastic condition. Absence of weight loss in the context of a long history is suggestive of motility disturbance such as IBS.
2. **Nocturnal symptoms,** specifically diarrhoea which wakes the patient from sleep, are rarely found in IBS and are more likely to reflect an inflammatory or secretory cause.
3. **Food / Infective precipitants** may be identified from the history, and are particularly important as infective gastroenteritis is the commonest cause of acute diarrhoea. Patients should be asked about recent food intake and illness in family or friends. Consumption of unpasteurized dairy products, raw or undercooked meat may suggest certain pathogens. If food poisoning is suspected, the timing of symptoms can help implicate the pathogen. Early onset of symptoms within eight hours suggests a preformed toxin of Staphylococcus aureus. Clostridium perfringens causes illness between 8 to 14 hours after ingestion while symptoms related to salmonella and campylobacter infection usually start around 24 hours after consumption.
4. **Stool characteristics and associated abdominal symptoms** can give useful clues to the site of pathology and likely pathogen. Profuse watery diarrhoea with colicky abdominal pain, bloating and vomiting is often caused by small bowel disease. Blood stained stools suggest colonic pathology (eg colitis, neoplasia or ischaemia), and may be accompanied by other colonic symptoms (abdominal pain, tenesmus, etc). Green discolouration of stool results from the presence of bile salts, and often implies an infective cause. Ischaemic colitis may produce heavy blood staining, disproportionate to the frequency of diarrhoea.
5. **Drugs** are frequently implicated, and any recent changes in medication should be carefully documented. Antibiotics consumed within the previous two months may be responsible for the development of Pseudomembranous colitis resulting from *Clostridium difficile* (C.Diff) infection. Over the counter remedies, such as non-steridal anti-inflammatory drugs may cause colitis.
6. **Family history of bowel disease,** especially IBD or colonic neoplasia, should be established. 15% of patients presenting with IBD have a positive family history.[3]
7. **Recent foreign travel or prior immunocompromise (eg HIV)** alter the differential diagnosis and range of potential pathogens (see below).

Examination

Volume depletion or sepsis may result in serious illness, so that a careful assessment of a patient's circulatory status is essential. Hypotension, tachycardia and altered conscious level require urgent fluid resuscitation. Dehydration can be evaluated further using postural blood pressure, examination of mucous membranes, skin turgor and urine output.

Fever is often considered pathognomic of infection but may also occur in severe exacerbations of IBD. General examination should include a careful search for extra intestinal manifestations of IBD such as erythema nodosum, arthritis and iritis. (table 1). Signs of hyperthyroidism and Addison's disease should be specifically sought.

Acute management of the patient with Diarrhoea

Table 1. Frequency of extaintestinal signs in inflammatory bowel disease

Extraintestinal manifestation	Crohn's Disease	Ulcerative Colitis
Apthous Ulceration	+++ A	++ A
Erythema Nodosum	+++ A	+ A
Pyoderma Gangrenosum	+ A	++ A
Arthropathy	+++ A	+++ A
Episcleritis/Iritis	+++ A	++ A
Sacroilitis	+++	++
Primary Sclerosing Cholangitis		++
Chronic Active Hepatitis		+
A = activity related signs		

A careful examination of the abdomen should identify signs of obstruction and peritonism. Appendicitis can present with pain, vomiting and diarrhoea. Rectal examination should exclude malaena as a cause for diarrhoea, and may be particularly useful in the elderly where faecal impaction with 'overflow' diarrhoea is relatively common. Where possible the stool should always be inspected by the doctor, however distasteful this may seem.

Investigations

1. Stool Culture

Stool cultures should be sent from the majority of patients with diarrhoea, although the diagnostic yield is low. Estimates vary between 2 – 15% of unselected stool specimens.[4] The sensitivity can be increased to around 75% if stool culture is reserved for septic patients, or in the presence of blood or leucocytes. Culture media routinely identify Salmonella, Shigela and Campylobacter. E Coli 0157 is detected with an agglutination test. When other pathogens, such as Yersinia, are suspected they need to be specifically requested.

Ova and parasites are shed in the stool intermittently and thus three consecutive samples should be sent. Parasitic infection should be suspected in chronic small bowel diarrhoea or in travellers to endemic areas.

Bloody diarrhoea without leucocytes suggests ameobiasis, which requires a, 'hot stool', to be analysed. This is also true for strongyloides larvae. Special stains and cultures for mycobacterium need to be requested specifically.

Antibiotic associated diarrhoea is common, of which, only 20% of cases are positive for toxigenic C. Diff .[5] Two toxins are produced: enterotoxic toxin A and cytotoxic toxin B. Specimens from patients suspected of having C Diff diarrhoea should be cultured and tested for toxins. Stool culture is the most sensitive test (89-100%) where as toxin B is the most specific.[6]

2. Blood tests

Full blood count, U&E, liver function, ESR and CRP should be requested for all patients. Electrolyte disturbance, particularly hypokalaemia, is common, as a result of water and salt loss. Renal failure may result from volume depletion, sepsis or, occasionally, from the haemolytic uraemic syndrome, associated with E.Coli 0157 infection. Serum albumin level is particularly useful. Significant hypoalbuminaemia is suggestive of a severe or chronic inflammatory process, or a protein-losing enteropathy. Thyroid function should be assessed when clinical features suggest over activity. In patients with cardiovascular compromise out of proportion to symptoms, Addison's disease should be considered, especially if hypoglycaemia, hyponatraemia or hyperkalaemia coexist. Measurement of random cortisol, followed by short synacthen test may prove diagnostic.

3. Abdominal X-ray

This will give clues to the site, severity and extent of colonic inflammation, as well as ruling out constipation with overflow as a cause for symptoms. Since stool does not accumulate in inflamed colon, the presence of stool usually indicates relatively normal mucosa. Colonic loading in the context of bloody diarrhoea may imply distal colitis or localised proctitis, while an empty colon suggests a more extensive (total or subtotal) colitis (figure 2). Abdominal x-ray will also enable the diagnosis or exclusion of toxic megacolon, which may occur in the context of colitis from any source (see below).

Figure 2. Plain abdominal X-ray of a patient with left sided colitis. Note proximal faecal loading. Sigmoid and descending colon is empty with marked thickening of the colonic wall and loss of normal haustral pattern



4. Sigmoidoscopy

When undertaken by an experienced operator, rigid sigmoidoscopy may enable the diagnosis of proctitis and distal colitis to be confirmed; biopsies should always be taken, although the results are frequently non-specific in the context of acute inflammation. The phrase 'features consistent with inflammatory bowel disease although infection cannot be excluded' will be familiar to many readers. In ulcerative colitis, inflammation extends proximally from the rectum, so that normal rectal mucosa makes this condition unlikely. By contrast, in crohns disease rectal sparing is common, and colonic inflammation may be patchy. Flexible sigmoidoscopy may therefore give more useful information about the condition of the mucosa and extent / distribution of inflammation. Full colonoscopy is generally contraindicated in the acute setting, because of the need for bowel preparation and the dangers of perforation of acutely inflamed mucosa.

Further Management

After initial resuscitative measures have been instituted and investigations sent, further management will be determined according to the provisional diagnosis. Specific management of some of the more common clinical scenarios is described below.

1. Gastrointestinal Infections

Infections are the commonest cause of acute diarrhoea. A microbiological diagnosis usually takes 24-48 hours to obtain, so consideration should be given to the most likely source, based on the history, to determine initial therapy.

It may be useful to use the symptoms to classify diarrhoea as being of small or large bowel origin, in order to narrow the list of potential pathogens (table 2). Colonic infection causes frequent, small volume diarrhoea, with painful bowel movements, often with fever and bloody stools. Stool microscopy may reveal red and white cells.

The small bowel secretes a large volume of fluids and absorbs nutrients. Infection disrupts these processes, preventing absorption, leading to large volume watery diarrhoea, abdominal cramping, bloating and weight loss.[7] Fever is rare and the stool does not contain blood or inflammatory cells.

In the community, viruses cause the majority of cases of gastroenteritis. The most common pathogens are Rotavirus, Norovirus, Adenovirus and Astrovirus.[8] Treatment is supportative with oral or intravenous fluids.

The presence of blood and leukocytes suggests a bacterial cause of diarrhoea. Examples of common bacteria affecting the small bowel include E. coli, Clostridium perfinges, Staphyllococcus aeurus, Bacillus cereus and salmonella. Salmonella is one of the most common pathogens and can affect both small and large bowel.[9] Campylobacter, shigella and E. coli are invasive agents which affect the colon, resulting in dysentery. Yersinia is often invasive in the terminal ileum causing pain and fever. This can mimic acute appendicitis and Crohn's disease. Reiter's syndrome (arthritis , urethritis and conjunctivitis) can occur with yersinia or other enteric pathogens.

Protozoal infection usually causes small bowel symptoms with large volume diarrhoea and can cause malabsorption. Immunocompromised patients are susceptible to large bowel protozoal infections. Examples include giardia, cryptosporidium and microspridium.

Treatment with a combination of oral ciprofloxacin 500mg twice daily and metronidazole 400mg tds will cover the majority of bacterial and protozoal infections.

2. Antibiotic-associated diarrhoea

Any patient developing diarrhoea within 2-3 months of antibiotic treatment should be suspected of having C. diff infection. Clindamycin, cephalosporins and amoxicillin carry the greatest risk.

A 10-day course of oral metronidazole (400mg tds) is considered the best first line treatment for C.diff. Symptoms will resolve, without treatment, in 15-25% of patients simply by stopping the offending antibiotic. If symptoms recur then a further course of metronidazole will treat 90% of patients and vancomycin should be reserved for further treatment failure.[6] Resistant disease has been treated in many ways, such as six week reducing course of vancomycin, rifampicin, lactobacillus, cholestyramine and faecal enemas. Antimotility agents should not be used in C. Diff diarrhoea, as toxic megacolon is more common in these conditions. If diarrhoea has resolved by the end of the treatment, repeat cultures are not necessary as stool may remain toxin positive for several weeks.

3. Diarrhoea in the traveller

50% of travellers to the developing world will complain of diarrhoea. Infectious diarrhoea is the second leading cause of mortality worldwide. Transmission is usually via the oral route. Bacteria are the cause in over 75% of episodes, of which Escherichia Coli is the most prevalent. The highest risk areas are Asia, South/Central America and North Africa. The risk of diarrhoea is related to the oral load of organisms and the host's defences. For example immunocompromise, achlorhydria (whether medication-induced or pathological) and previous gastrointestinal surgery increase the risk. The traveller is prone to similar organisms to those described above, but bacterial infection is more common. Salmonella, Shigella, Campylobacter and E.Coli are the commonest.

Table 2. Typical Pathogens in Infective Diarrhoea

Pathogen	Small Bowel	Colon
Viral	Rotavirus	Cytomegalovirus
	Norovirus	Herpes simplex virus
Bacterial	Salmonella	Campylobacter
	E.Coli	Shigella
	Clostridium	Clostridium Difficile
	perfringens	
	Staph Aureus	E.Coli
	Vibrio Cholerae	Yersinia
		Salmonella
Protazoal	Giardia	Amoeba
	Cryptosporidium	
	Microsporidium	
	Cyclospora	

Acute management of the patient with Diarrhoea

Parasitic infection is less common and is related to contaminated water supplies. Giardia lamblia and Cyclospora are endemic in parts of Russia, Nepal and mountainous regions of the west USA.

Combinations of oral ciprofloxacin and metronidazole are usually effective.

4. Diarrhea in patients with HIV / AIDS

Diarrhoea is very common in HIV infected patients. Approximately 75% patients with HIV complain of at least one episode each year. In an outpatients department between 1-15% complain of diarrhoea.[10]

The majority of cases are infection related. A pathogen is identified in 50% of patients with significant diarrhoea.[11] Many infections are caused by the 'normal' organisms listed in table 2, although the course of the illness may be more prolonged than in immunocompetent patients. Alternatively patients may be infected by opportunistic infections specific to immunocompromised patients e.g. atypical mycobacterium. Opportunistic infections are rare if the CD4 count is > 200. The treatment is guided per organism detected but certain organisms have no definitive treatment, such as cryptosporidium.

a) Mycobacterial infection

Tuberculosis occurs early in AIDS and extra pulmonary, including gastrointesinal infection is found in 50% of patients with pulmonary disease.[12] Infection can mimic inflammatory bowel disease with similar endoscopic appearances. Stool stain for acid fast bacilli (AFB), culture for mycobacterium or histology may be diagnostic. Differentiation from atypical mycobacterium infection can be difficult. Mycobacterium avium intracellulare (M.A.I.) is a common environmental organism which may infect the bowel causing diarrhoea in patients with a CD4 count <100. Diagnosis is made by identifying AFB in the stool.

b) Protozoal infection

Protozoal infection of the small bowel , causing weight loss and malabsorption, commonly occurs with cryptosporidia. The organism infects the columnar lining causing villous atrophy. Infection becomes chronic with CD4 counts less than 180 and can be identified by careful stool examination with acid/alcohol fast stain. Unfortunately treatment options for this organism are limited, but symptoms may improve with treatment of the underlying disease process. Isospora Beli may produce a similar clinical picture and is treated with co-trimoxazole.

c) Viral infection

Viral infections with herpes simlex (HSV) and cytomegalovirus (CMV) are common. HSV causes ulceration and can affect any membrane but does not commonly result in diarrhoea. When CD4 counts are less than 100, CMV infection can cause a colitis mimicking idiopathic IBD. Diagnosis is made histologically from endoscopic specimens and may be limited to the right side of the colon.

d) Other causes

Although infection is by far the commonest cause of diarrhoea in AIDS, other diagnoses must be considered. Medication, especially protease inhibitors, commonly cause diarrhoea and can often be the culprit for chronic diarrhoea with a normal CD4 count. Lymphoma is common and occurs in approximately 10% of Post-mortem examinations. The majority of disease is B cell and 50% of patients with NHL have GI disease.[13] IBD can be unmasked as immune dysregulation occurs in disease progression.

5. Inflammatory Bowel Disease

The relapsing / remitting nature of IBD means that patients admitted with an acute exacerbation of this condition will frequently have experienced previous episodes. Even if the diagnosis is well established it is important to consider an infective cause for the exacerbation; stool samples for microscopy, culture and C. diff toxin should be sent. The most relevant clinical distinction between crohns disease and ulcerative colitis relates to the distribution of the disease. Crohns disease affects both small and large bowel and may be patchy, while ulcerative colitis is confined to the colon, extending proximally from the rectum. Exacerbations of small bowel crohns disease may occur without diarrhoea, while diarrhoea is invariable in exacerbations of ulcerative and crohns colitis.

In addition to the investigation and supportive measure described above, assessment of patients with suspected exacerbation of IBD should involve attention to the following questions:

- How severe is the exacerbation?
- What is the extent / distribution of the disease?
- Are there any features to suggest imminent perforation?

These questions may be addressed by careful clinical, radiological laboratory and sigmoidoscopic assessment. Factors which predict failure of medical treatment and therefore a more severe exacerbation are highlighted in table 3. It should be remembered, however, that disease confined to the rectum may produce significant symptoms with very frequent bloodstained stool, while rarely becoming life-threatening. Faecal loading on x-ray or the ability to get beyond the level of inflammation on sigmoidoscopy in a patient with known ulcerative colitis imply localised proctitis, and should be considered reassuring features.

Imminent perforation my be heralded by the development of a tachycardia, significant abdominal pain

Table 3.[16] Factors predicting outcome in Fulminant colitis

Sign	Failure rate for medical treatment
8 stools or more per day	33%
Tachycardia	36%
Temperature > 38 °C	56%
Albumin < 30 g/L	42%
Mucosal islands on AxR	75%
Small bowel Dilatation	73%

with peritonism and pyrexia, abdominal distension and the absence of bowel sounds. Abdominal X-ray may show the appearance of toxic megacolon, which complicates around 10% of severe attacks .[14] A diameter of 6cm in the transverse colon or 9cm in the caecum signifies toxic megacolon and needs specialist care and usually surgical intervention. Mucosal islands present on x-ray represent relatively normal mucosa surrounded by full thickness damage to the bowel and are highly likely to progress to megacolon or perforation. Dilated loops of small bowel in the context of colitis predict a poor outcome. (table 3).

a) Initial Treatment

Early surgical review is essential for patients with features suggesting imminent perforation or toxic megacolon. Such patients should be kept nil-by-mouth until improvement is documented.

Intravenous hydrocortisone (100mg qds) is the mainstay of medical treatment for acute exacerbations of IBD. Addition of oral 5-aminosalicylate (5-ASA) derivatives such as sulphasalazine (1-2g qds) or mesalazine (800mg tds) may be beneficial. When the disease involves the rectum, rectal hydrocortisone may be a useful adjunct to intravenous treatment. Pre-packed liquid and foam hydrocortisone enemas are available; however in the context of an acute episode rectal steroid may be easier to retain if administered via 'rectal drip'. 100mg hydrocortisone is mixed with 100ml saline and can be dripped into the rectum over 30-60 minutes via a standard intravenous fluid giving set, two or three times each day.

b) Monitoring

Meticulous temperature, pulse and blood pressure monitoring are essential in order to identify patients in whom medical treatment is failing. Haemoglobin, electrolytes, albumin and inflammatory markers should be measured frequently. The stool frequency and presence of blood need to be recorded daily and predict poor outcome. The presence of 8 or more bloody stools per day on day 3 has been shown to be predictive of colectomy in 85% of fulminent disease. This is also true of patients with 4-8 stools and a CRP > 45 on day 3 .[15]

In patient with crohn's disease development of obstruction, fistula or abscess need to considered Abdominal tenderness, mass, elevated CRP and WCC should prompt ultrasound or CT scanning.

Table 4. Features suggesting hospital admission is required

Clinical	Fever (>38c)
	Tachycardia (>100/min), Hypotension (systolic <100)
	Abdminal pain) / tenderness /distension / peritonism
	Immunocompromise / HIV +ve
Stool	>10 bloody stools per day
Investigations	Significant anaemia
	Hypokalaemia / abnormal renal function
	Hypoalbuminaemia
	Total colitis or colonic dilatation on AXR

As symptoms improve patients can be converted to oral prednisolone (30-40mg daily) The dose should be weaned much more slowly than would normally considered for patients with conditions such as asthma; gradual reduction by 5mg per week, while maintaining the patient on a oral 5-ASA agent will reduce the likelihood of early relapse of colitis.

Early involvement of a specialist gastroenterology team is essential in the management of any patient with a suspected diagnosis of acute IBD. Ideally this should involve a multidisciplinary approach with regular surgical review and nursing care by individuals experienced in the assessment of such patients. Transferring the patient to a specialist gastrointestinal ward should be undertaken as soon as possible after initial stabilisation. If patients are discharged directly from an Acute Medicine Unit, early follow-up in a gastrointestinal outpatient clinic is essential.

Which patients with diarrhoea require hospital admission?

Although patients with life-threatening fulminant colitis clearly require admission to hospital and close observation, patients with diarrhoea can often be managed in the community. Many patients with exacerbations of IBD can be treated with oral steroids, or self-administered rectal preparations. Such patients are frequently managed via gastroenterology outpatient clinics, and many will have direct emergency access systems in place for patients with known IBD in the event of an exacerbation. When such patients present for the first time, or self present to A&E out of hours, they may be admitted to hospital un-necessarily. Provided early specialist follow-up can be arranged, and none of the features listed in table 4 are present, hospital admission may be avoided in many cases.

Acute management of the patient with Diarrhoea

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