Part 1

A General Approach to Syndromes/Symptom Complexes

Chapter 1

Gastrointestinal presentations

The most important gastrointestinal presentation in the tropics is diarrhoea, and the majority of this chapter is devoted to this problem. However, other presentations of gastrointestinal disease are discussed first.

Dysphagia

Significant recent-onset dysphagia should always raise the possibility of oesophageal carcinoma. This malignancy is particularly common in certain parts of the tropics, for example, some areas of Central and East Africa. Oesophageal candidiasis (AIDS-related) is also a common cause of tropical dysphagia. In South America, the mega-oesophagus of Chagas' disease should be considered. Finally, peptic strictures, corrosive chemical ingestion and foreign bodies (fish bones especially in some areas) may also be important causes of impaired swallowing.

Haematemesis

In all areas of the world, an upper gastrointestinal haemorrhage can be caused by peptic ulceration, gastritis, oesophagitis and gastric or oesophageal carcinoma. Gastritis, gastric erosions and gastric ulcers may be drug related, for example, corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs). *Helicobacter pylori* is recognized globally as a major cause of gastric and duodenal inflammation and/or ulceration. Oesophageal varices may be a particularly common cause of haematemesis in many tropical areas—at least 25% of all cases in some series. The underlying liver disease can be the late result of chronic viral hepatitis or schistosomal hepatic fibrosis.

Abdominal pain

In 'western' populations, severe abdominal pain can result from appendicitis, mesenteric adenitis, perforated peptic ulcers, biliary colic, cholecystitis and intestinal obstruction (commonly because of adhesions or malignancy). This list is far from exhaustive, but serves to demonstrate that the spectrum of causes in the tropics is much wider. The following 'exotic' causes of acute severe abdominal pain may need to be considered.

- Abdominal tuberculosis (TB)
- Typhoid (including typhoid perforation)
- Hydatid cyst rupture
- Amoebic colitis (including perforation)
- Amoebic liver abscess (which may rupture)
- Intestinal obstruction caused by *Ascaris lumbricoides*
- Ectopic ascariasis (e.g. biliary and/or pancreatic obstruction)

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- Sickle cell crisis
- Splenic rupture
- Hyperinfection syndrome of strongyloidiasis.

Malabsorption

Malabsorption can be a feature of infection with *Giardia lamblia*, *Strongyloides stercoralis*, intestinal TB, as well as AIDS. Perhaps the most common cause, however, is the temporary lactase-deficient situation that may occur after any significant acute infective diarrhoeal illness. Milk and milk products may need to be avoided, although yoghurt is usually tolerated, because of its high bacterial lactase content.

Tropical sprue

A particularly well-described form of tropical malabsorption is 'tropical sprue'. This occurs predominantly in India and South East Asia, as well as in the Caribbean and Central America. Patients develop non-bloody diarrhoea (sometimes steatorrhoea) often with abdominal bloating and significant weight loss. There may be a history of initial acute diarrhoeal illness, which is thought to be the precipitant (although the exact mechanism is unknown). Duodenal biopsy, as well as biochemical features of malabsorption, typically shows partial villous atrophy. The illness can be prolonged and debilitating. Traditional treatment with tetracycline (for associated bacterial small bowel overgrowth) and folic acid is often highly effective.

Diarrhoea

Diarrhoeal illness is one of the most important causes of morbidity and mortality in the tropics, causing over six million deaths per year, and is clearly linked with poor hygiene and contamination of water and food. A wide variety of viral, bacterial and parasitic pathogens have been implicated in the pathogenesis of diarrhoea, but it is impossible and unnecessary to test for all these in individual cases. Systematic review of epidemiological, clinical and host factors usually enables a sensible working aetiological diagnosis to be established. The working diagnosis can be used to decide whether specific investigation should be performed, or to direct empirical antimicrobial therapy in the minority of cases in which it is required. The mainstay of management of diarrhoeal illness is the assessment and maintenance of adequate hydration and electrolyte balance, irrespective of the aetiology, as well as the introduction of control measures in an epidemic setting to prevent further cases.

History

It is essential to establish that both the doctor and the patient are talking about the same thing, especially if interpreters are being used to take the clinical history. A useful working definition of diarrhoea is the passage of three or more loose or watery bowel motions in 24 h. The distinction between soft and loose diarrhoea is more difficult, but bowel motions can be described as diarrhoeal, when they assume the shape of the collecting container. This definition works with acute diarrhoeal illness but is less satisfactory with chronic diarrhoeal illness related to malabsorption in which bulky, sticky soft bowel motions are abnormal but may not be fluid enough to move around in the container. Key features in the history are the presence or absence of visible blood in the stool (dysentery), the presence and degree of abdominal pain, the presence of tenesmus and the presence of fever. The duration of illness is important—chronic diarrhoea can usefully be defined as diarrhoea lasting more than 14 days, although a more precise definition (especially in the context of an immunocompromised host) is the passage of three or more loose or watery stools a day for 28 days or more.

In the historical assessment of fluid balance, the volume and frequency of faecal loss should be estimated together with the frequency and approximate volume of any vomiting. The amount of fluid intake should be checked, as should the frequency of urinary output during the last 24 h.

The epidemiological setting is important. Illness in close family contacts should be ascertained, and enquiry should be made about whether the patient has attended any functions or eaten unusual foods in the preceding 48–72 h. If so, have any other

guests had similar illness? Point source outbreaks can be caused by toxin-mediated food poisoning in which case vomiting is often a predominant feature and incubation periods are usually shorter than 24 h. This may be difficult to distinguish from outbreaks of norovirus infection in which vomiting is a predominant feature and contacts are readily infected. Unusual systemic pathogens (e.g. anthrax of the gut) or non-infectious poisoning caused by adulterated or contaminated food products must always be considered. Bacterial pathogens causing small or large bowel diarrhoea usually have intermediate incubation periods of 12–72 h. More detailed food histories are not otherwise very helpful, except in the case of expatriates who have unwisely overindulged in very spicy foods ('tasting the chilli twice') or who have recently arrived in the tropics (traveller's diarrhoea). Diarrhoea developing in patients who are already hospitalized suggests a nosocomial or antibiotic-associated cause, while outbreaks of diarrhoeal illness in a refugee or camp setting imply specific infections such as shigellosis or cholera (see later) (Fig. 1.1).

Other illness

Diarrhoea can be a prominent feature of many systemic illnesses, including malaria, pneumonia and enteric fever, especially in children, and evaluation of the patient should exclude these as potential causes. Surgical and other intra-abdominal conditions may mimic gastroenteritis, as can inflammatory bowel disease. In older or immobile patients, constipation with overflow diarrhoea must be excluded. Alcohol and drugs frequently cause diarrhoea with or without nausea and vomiting.

Figure 1.1 Though it looks like urine, this is the `ricewater' stool from a patient with cholera.

Host factors

Conditions that cause hypochlorhydria (e.g. gastric surgery, H_2 antagonists and proton pump inhibitors) reduce the gastric acid barrier to many bacterial pathogens, so a smaller infective dose is required. Patients with established cardiovascular or renal disease are less likely to tolerate dehydration, as are those on diuretics and patients with poorly controlled diabetes. Pre-existing large bowel problems such as inflammatory bowel disease predispose to complications of dysenteric infections such as toxic megacolon, signs of which may be partly masked by concurrent steroid therapy. Bowel tumours can produce diarrhoea with or without blood or weight loss. Small bowel problems, including lymphoma, can cause prolonged diarrhoea. Immunosuppression of the patient, particularly by HIV, predisposes to increased invasiveness (local and systemic) of bacterial pathogens such as non-typhoidal *Salmonella*, increased recurrence of such pathogens and chronic diarrhoea caused by a variety of protozoa.

Examination

General examination must include assessment of the state of hydration. This is more difficult to quantify clinically in adults than in children, but key features are summarized in Table 1.1. Measurement of any postural drop in blood pressure (BP) is particularly useful. Rectal examination should be performed, except in obvious cases of cholera, and is particularly important in older patients who are more likely to have non-infectious bowel problems. Systemic causes of diarrhoea and signs of immunosuppression (e.g. zoster scars and oral candidiasis) should be sought out.

Clinical syndromes of diarrhoea

Apart from acute toxin-mediated food poisoning, diarrhoeal illness can be broadly classified into small bowel secretory diarrhoea, small

Table 1.1 Clinical classification of severity of dehydration in adults

	Mild	Moderate	Severe
Subjective			
General state	Alert, active, up and about	Weak, lethargic, able to sit and walk	Dull, inactive, unable to sit or walk
Ability to perform daily activities	Able to perform daily activities without difficulty	Able to perform daily activities with some difficulty, for example, stays away from work and needs support	Unable to perform daily activities, stays in bed or needs hospitalization
Thirst	Not increased	Increased thirst	Feels very thirsty
Objective			
Pulse	Normal	Tachycardia	Tachycardia
Blood pressure	Normal	Normal or decrease, 10–20 mmHg systolic	Decrease >20 mm Hg systolic
Postural hypotension	No	Yes or no	Yes
Jugular venous pressure	Normal	Normal or slightly flat	Flat
Dry mucosa (mouth, tongue)	No	Slight	Severe
Skin turgor	Good	Fair	Poor
Sunken eye balls	No	Minimal	Sunken
Body weight loss	<5%	5–10%	>10%

Table 1.2 Clinical features of inflammatory and non-inflammatory diarrhoea

Non-inflammatory	Inflammatory
Symptoms	
Nausea, vomiting; abdominal pain and fever not major features	Abdominal pain, tenesmus, fever
Stool	
Voluminous, watery	Frequent, small volume; blood-stained, pus cells present, mucus
Site	
Proximal small intestine	Distal ileum, colon
Mechanism	
Osmotic or secretory	Invasion of enterocytes leading to mucosal cell death and inflammatory response

bowel malabsorption and large bowel inflammatory diarrhoea. Each of these groups may be acute or chronic, and there is considerable overlap (Table 1.2).

Small bowel secretory diarrhoea is exemplified by cholera and non-invasive *Escherichia coli* infections in which toxins specifically promote secretion of water and electrolytes into the bowel lumen and inhibit their reabsorption. Such secretion can be competitively overcome by a steady intake of balanced electrolyte solutions containing adequate amounts of glucose but not too much to produce an osmotic diarrhoea. This is the scientific basis for the success of oral rehydration therapy in which the correct quantities of salts and glucose are added to sterile water for rehydration.

Table 1.3 Pathogens in inflammatory and non-inflammatory diarrhoea

Inflammatory	Non-inflammatory
Viruses	
Nil	Rotavirus
	Adenovirus 40/41
	Astrovirus
	Norovirus (Norwalk agent)
	Calicivirus
	Small round structureless virus
	Coronavirus
	Torovirus
	Bredavirus
	Picobirnavirus
Bacteria	
Enteroinvasive *Escherichia coli* (EIEC)	Enterotoxigenic *E. coli* (ETEC)
Enterohaemorrhagic *E. coli* (EHEC), for example, 0157	Enteropathogenic *E. coli* (EPEC)
Enteroaggregative *E. coli* (EAggEC)	*Vibrio cholerae*
Aeromonas hydrophila	*Vibrio parahaemolyticus*
Campylobacter spp.	*Campylobacter* spp.
Salmonella spp.	*Salmonella* spp.
Shigella spp.	*Plesiomonas shigelloides*
Yersinia enterocolitica	*Bacillus cereus*
Clostridium difficile	*Clostridium perfringens*
Protozoa	
Entamoeba histolytica	*Cryptosporidium* spp.
Balantidium coli	*Giardia intestinalis*
	Cyclospora cayetanensis
	Isospora belli
	Microsporidia (e.g. *Enterocytozoon bieneusi*)
Helminths	
Schistosoma spp.	*Strongyloides stercoralis*

Malabsorption is a common complication of infectious diarrhoea in the tropics, as many races have relatively low disaccharidase activity in the small bowel enterocytes. Disruption of 'normal' bowel activity readily leads to failure to break down sugars and a moderately prolonged lactose intolerance. This is particularly common after infections that cause flattening of the small bowel mucosa (such as giardiasis and cryptosporidiosis). Large bowel diarrhoea is usually caused by direct invasion of the bowel by pathogens such as *Entamoeba histolytica*, bacteria such as *Campylobacter* species or *Clostridium difficile* after antibiotic therapy. Other parasites such as *Schistosoma mansoni* can also cause prolonged large bowel diarrhoea. In heavy *Trichuris trichiura* infections, oedema of the rectal mucosa together with continued efforts to defaecate resulting from tenesmus can lead to rectal prolapse. A summary of the major pathogens in inflammatory and non-inflammatory diarrhoea is shown in Table 1.3.

Investigations

A useful algorithmic approach to individual patient diagnosis and management is shown in Figure 1.2. In most tropical settings, microbiological investigation proves impossible or very

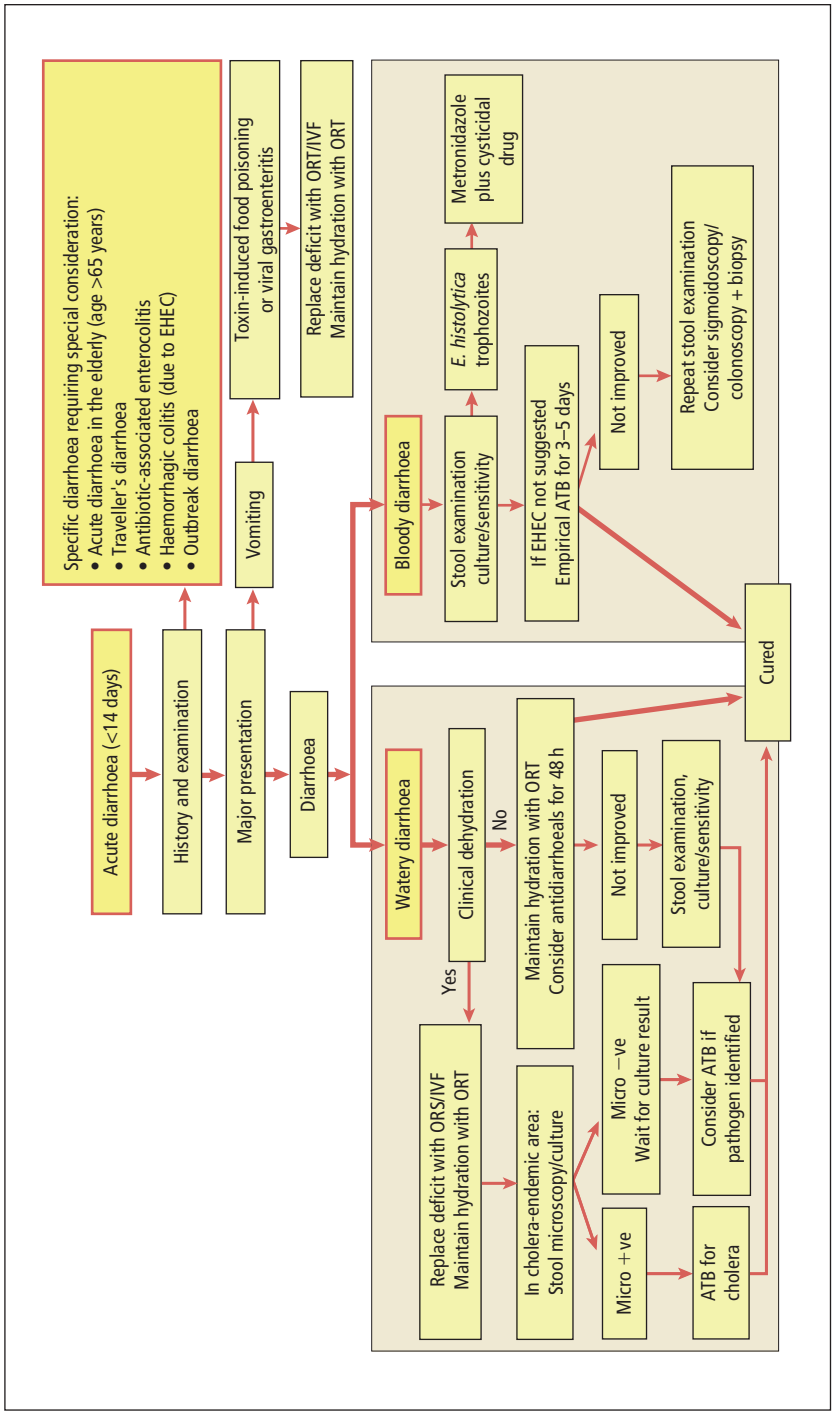

Figure 1.2 Algorithm for the management of diarrhoea in adults. (Adapted from Manatsathit *et al.* [2002] with permission.) Stool examination and culture depend on local availability, affordability and practice. In suspected cholera, dark field microscopy is ideal (or, if not available, a search for 'shooting star' bacteria on light microscopy will do). In epidemic situations, a clinical diagnosis is sufficient. When antibiotics are used, the choice depends either on culture and sensitivity results or on local experience. If available, ciprofloxacin is a good choice except in Asia where resistant campylobacter responds better to azithromycin. ATB, antibiotic; EHEC, enterohaemorrhagic *Escherichia coli*; IVF, intravenous fluids; ORT, oral rehydration therapy.

limited. Microscopic inspection of faeces for leucocytes, suggestive of invasive pathogens in the large bowel, is commonly advocated but is of questionable time-effectiveness compared with macroscopic inspection of faeces for blood (and smell) when resources are limited. However, cholera vibrios may be observed with their characteristic 'shooting star' motility even without dark ground facilities, and this is very useful when culture is not available. Investigations for faecal parasites should be limited to specific settings (e.g. chronic diarrhoea complicating HIV) and are almost never indicated in nosocomial diarrhoea. Fresh stool microscopy for active trophozoites should only be requested when amoebic dysentery is truly suspected. Blanket requests for faecal microscopy for 'ova, cysts and parasites' on all patients are a waste of time in most settings. Such requesting patterns overload laboratories, demoralize their staff and lead to reports of questionable quality with little effect on clinical management decisions.

In an outbreak setting, full microbiological identification of the pathogen and assessment of the antimicrobial resistance patterns are very helpful, and it should be pursued even if outside assistance is required. In sporadic cases, detailed microbiological tests may be inappropriate, but clinicians need to be aware of the local antibiotic sensitivities of organisms such as *Shigella*, *Salmonella* and *Campylobacter* if they are to use empirical antimicrobial therapy in a responsible and effective manner. Other investigations, such as serum electrolytes, peripheral white cell count and blood cultures, are performed in a hospital setting but again may not be available routinely.

Management

Detailed management of individual pathogens is beyond the scope of this chapter. The key is the correction of fluid and electrolyte imbalance. Severely dehydrated patients need rapid intravenous replacement of fluid loss, preferably using a physiologically balanced electrolyte solution such as Ringer's solution (see Chapter 21, p. 197). Large volumes of dextrose solution can be dangerous. Intravenous fluid can be supplemented and rapidly replaced by oral rehydration, which is more successful if small volumes of fluid are taken steadily rather than large volumes at a time. Specific World Health Organization (WHO) oral rehydration solution (ORS) is ideal, but the water in which it is dissolved must be clean and safe to drink—preferably by prior boiling and cooling. Alternative oral rehydration therapy mixtures can also be used for adults, and food, including milk products, is usually reintroduced as early as possible after initial resuscitation of children. Fluid balance should be carefully monitored, and a cholera bed is useful for less mobile patients with profuse diarrhoea. The fluid faeces can then be collected through a hole in the middle of the bed directly into a measuring bucket. If a large-bore disposable Foley's urinary catheter is available, this can be inserted into the rectum when diarrhoea is profuse and watery (e.g. in cholera), removing the need for frequent evacuation, and allowing accurate measurement of faecal losses by volume.

Antidiarrhoeal agents such as codeine or loperamide should be avoided in patients with acute invasive or large bowel disease and should not be used in young children. Antiemetics should be used sparingly and again avoided in young children. Zinc supplementation is beneficial for children, but the roles of probiotics and use of lactose-free feeds are less clear. Empirical or specific antimicrobial treatment should be reserved for specific situations such as proven amoebiasis, prolonged severe infection in a vulnerable host or in outbreak settings—for example cholera or shigellosis. Chronic diarrhoea presents a different challenge and patients with HIV-related diarrhoea often progress through successive therapeutic trials of co-trimoxazole, metronidazole, fluoroquinolones, albendazole or nitazoxanide. Such patients may need 'hospital at home' support including provision of adequate antidiarrhoeal medications.

In a refugee camp outbreak setting, logistical support must be requested at an early stage for detailed epidemiological investigation, triage and treatment facilities, as well as provision of an adequate water supply, rehydration solutions and latrines (Chapter 60).

Further reading

Al-Abri SA, Beeching NJ, Nye FJ. Traveller's diarrhoea. *Lancet Infect Dis* 2005; 5: 349–360. [Overview of aetiology, epidemiology, management and prevention of this common problem for travellers.]

Elliott EJ. Acute gastroenteritis in children. *BMJ* 2007; 334: 35–40. [Concise evidence based review, very practical and useful.]

Hart CA. Introduction to acute infective diarrhoea. In: Cook GC, Zumla A, eds. *Manson's Tropical Diseases*, 21st edn. London: Elsevier Science, 2003: 907–913. [Good overview with references of both adult and paediatric diarrhoea causes and effects.]

Manatsathit S, DuPont H, Farthing M *et al*. Guideline for the management of acute diarrhoea in adults. *J Gastroenterol Hepatol* 2002; 17 (Suppl): S54–S71. [Superb working party report produced by acknowledged experts from Thailand, India and Africa as well as 'western' authorities. Detailed definitions, practical approaches and many references.]

Thomas PD *et al*. Guidelines for the investigation of chronic diarrhoea, 2nd edition. *Gut* 2003; 52: 1–15. [British guidelines for assessment of both infectious and non-infectious causes of chronic diarrhoea.]

WHO. *Handbook IMCI Integrated Management of Childhood Illness*. WHO 2005. Chapter 8 Diarrhoea—assessment and management of diarrhoea in children in tropical settings pages 25–31. [Summary of WHO guidelines for use at clinic level. Full manual and other IMCI and nutrition-related resources freely downloadable from WHO child and adolescent health development website http://www.who.int/child_adolescent_health/topics/en/]

WHO. *Implementing the New Recommendations on the Clinical Management of Diarrhoea. Guidelines for Policy Makers and Programme Managers*. WHO 2006. [Summary of new recommendations for use of the 2003 low osmolarity ORS mixture and zinc supplementation, plus programme guidance.]

WHO. *The Treatment of Diarrhoea. A Manual for Physicians and Other Senior Health Workers*, 4th edn. WHO 2005. [Comprehensive review with algorithms for assessment and management of children and adolescents in particular, appropriate for resource poor settings.]