WORKING PARTY REPORT

Guideline for the management of acute diarrhea in adults

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INTRODUCTION

Acute diarrhea in adults is one of the most common diagnoses in general practice,1,2 and is responsible for considerable morbidity around the world.3–5 While acute diarrhea is perceived as a major cause of childhood mortality in developing countries, adult mortality from diarrhea is also not uncommon particularly during epidemics of diarrhea. Contaminated food and water, together with unhygienic eating habits, account for the continuing high prevalence of acute diarrhea in adults. In industrialized countries, the incidence of acute diarrhea is estimated to average 0.5–2 episodes per person per year, and the corresponding figure could be much higher in developing and underdeveloped countries. In the USA, with a population of around 200 million, about 99 million episodes of acute diarrhea occur every year in adults. Twenty-five percent of hospitalizations in the USA were due to diarrhea and 85% of the mortality associated with diarrhea occurred in the elderly (>65 years old).6 It accounts for a large amount of economic loss and a waste of a country’s resources and labor forces in caring for this group of patients.7 It is hoped that the development of this guideline will be able to provide measures for general practitioners and health care workers around the world to effectively care for adult diarrhea patients so that the mortality and complications can be minimized.

Algorithm and definition

The final algorithm that was developed for the management of adult diarrhea was the result of intensive discussion among the experts. It particularly emphasized simplicity, feasibility and availability of options. It tries to be as general as possible without sacrificing the basic principles and theoretical background of sound management. The algorithm, in itself, should provide a complete document that would be applicable to the case management of diarrhea. However, some explanation and amplification is necessary to clarify the terms and phrases that have been used, as well as to explain the basis for certain decision pathways in the algorithm.

Adult: The definition of ‘adult’ varies from one country to another. As applied in this guideline, the term ‘adult’ refers to someone who is of age 12 years or above.

Acute diarrhea: This is defined as the passage of three or more than three loose or watery stool in 24 h, or passage of one or more bloody stool. Acute diarrhea refers to illness not lasting longer than 14 days.

Other conditions that may present as acute diarrhea: ‘Acute diarrhea’ is a clinical syndrome that is commonly understood to refer to infective gastroenteritis. However, as defined, acute diarrhea may be a symptom of other intra-abdominal or systemic illnesses. These other clinical conditions may require particular investigations and management, and will need to be recognized and excluded at the outset. Careful history and physical examination is necessary to exclude these conditions from the commonly understood ‘acute diarrhea’. Special attention should be paid to exclude signs of peritonism or peritonitis, which will indicate serious illnesses that might require surgical care. Examples of these diverse clinical conditions are presented in Table 1.

Specific conditions of acute diarrhea that require special consideration: Although the term ‘acute diarrhea’ commonly refers to infectious, toxin-induced and drug-induced diarrhea, there are specific acute diarrhea syndromes that may need a specifically tailored approach and management, and where the general algorithm may need to be modified. For example, during epidemic acute diarrhea such as cholera, it is important to quickly identify the organism in the first patients presenting with illness, and to initiate public health mea-
HISTORY AND PHYSICAL EXAMINATION

Acute diarrhea in adults is a complex symptom that may be caused by any of a number of diseases, both infectious and non-infectious. A proper history and physical examination is therefore necessary in these patients. Special attention should be paid to excluding conditions that may require a different approach and management.

History taking

In the history, it is essential to gather the following information: age, onset and duration of diarrhea, character of the stool (watery, loose or bloody), frequency and volume of stool, progression of severity of diarrhea, presence and severity of vomiting, presence of fever, its severity and duration, abdominal pain and its location and character, cramps, and tenesmus. The severity of diarrhea may be assessed in adults by the degree of disturbance of daily life and activities, debility, thirst, dizzi-

Table 1 Conditions presenting as acute diarrhea with or without signs of peritonitis that should be excluded in a patient presenting with acute diarrhea

- Appendicitis
- Adnexitis
- Diverticulitis
- Peritonitis secondary to bowel perforation
- Systemic infections: for example malaria, measles, typhoid, etc.
- Inflammatory bowel disease
- Ischemic enterocolitis
- Mesenteric artery/venous occlusion

Other conditions which may present as acute diarrhea (see Table 1)
ness, and syncope. The time of last urination should be noted in patients with dehydrating diarrhea.

Occurrence of diarrhea after eating a contaminated meal, the time interval between ingestion and development of diarrhea, and the occurrence of illness in others who also partook of the meal are pointers to a bacterial cause of the illness. The source of water supply may be helpful as evidence of a common-source outbreak.

The location in which the patient develops diarrhea may be predictive of the causative organism, for example at home, in hospital or in an institution. History of recent travel and the area travelled, may also be helpful. If there is research to suggest that specific pathogens are more common during a specific season, this is an additional factor of which to remain aware.

It is always worthwhile to exclude the non-infectious causes of acute diarrhea and osmotic diarrhea, for example drugs and toxins. One should inquire if the patient has recently been taking medications or substances that can cause diarrhea, for example laxatives, antacids containing calcium or magnesium, colchicines, antibiotics, alcoholic beverages and sorbitol containing gums. If such a history is obtained, the suspected offending substance should be stopped before proceeding to any further evaluation.

In addition, it is important to take into account any underlying diseases that may be present, such as diabetes, hypertension, heart disease, chronic lung disease, chronic renal failure or cirrhosis, because these could complicate the management of diarrhea. Any condition that affects the patient’s immune status should be called to the physician’s attention, such as practices that may predispose the patient to HIV infection, history of administration of immunosuppressive drugs, steroids, and chemotherapy.

Physical examination

In the adult with diarrhea, it is important to look for signs of dehydration, including examination of the pulse, blood pressure (standing and sitting), jugular venous pressure, skin turgor, mucosal dryness, for example in the mouth and lips, evidence of sunken eye balls and capillary filling.

It should be stressed that, regardless of the severity of diarrhea, abdominal examination is strongly recommended for every patient. Both light and deep palpation should be carefully performed to exclude signs of peritonitis. Although minimal tenderness to deep palpation can be found in dysentery, it should be seriously observed and these patients must be closely monitored, because some surgical or serious medical conditions, for example appendicitis, diverticulitis, adenitis, pancreatitis and ischemic colitis, may present as acute diarrhea. In acute diarrhea, guarding, rigidity and rebound tenderness should not be present. If they are present at all, further investigations and appropriate measures should be taken.

Rectal examination should be part of the initial examination in every case, especially in patients over 50 years of age. This allows the physician to see with certainty the character of stool and accurately assess the type of diarrhea, whether it is watery or bloody. This is particularly helpful in situations in which patients, especially the elderly or those with poor eyesight, might not be able to give an accurate history.

MAJOR PRESENTATION: VOMITING

Diarrhoea is the predominating symptom in most patients presenting as ‘acute diarrhoea’. Having excluded the other conditions listed in Tables 1 and 2, we are left with a group of illnesses that comprise what is commonly understood as ‘acute diarrhoea’. These are further classified, on the basis of the stool character, as having either watery diarrhoea or bloody diarrhoea. This is one of the decision points in the algorithm, and is discussed further. On the other hand, there are some patients with ‘acute diarrhoea’ in whom vomiting overshadows diarrhoea as a symptom. In these patients, one should suspect that the illness is caused either by food poisoning (induced by preformed bacterial toxin) or viral gastroenteritis.

Bacterial toxin induced food poisoning

In patients with bacterial preformed heat-stable toxin induced food poisoning, the incubation period is usually 6–24 h, diarrhoea occurs 2–7 h after eating the contaminated food. These patients usually present with intense nausea and severe vomiting as the major symptoms. Diarrhoea may follow and usually is not so severe. Abdominal pain may also be present and is usually colicky in nature. Most patients are afebrile and not severely dehydrated unless vomiting or diarrhoea is intense. Clostridium perfringens is also a food-borne disease with a characteristic incubation period of 8–14 h. C. perfringens differs clinically from food poisoning due to Staphylococcus aureus and Bacillus cereus in the longer incubation period and in clinical symptoms. Vomiting is unusual in C. perfringens food-borne disease and it is the most important clinical finding in the other forms of food poisoning. Foods that are likely to be contaminated with toxin or infectious organisms

<table>
<thead>
<tr>
<th>Table 2 Specific acute diarrhea syndromes that require special consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute diarrhea in the elderly (age ≥ 65-years-old)</td>
</tr>
<tr>
<td>Traveler’s diarrhoea</td>
</tr>
<tr>
<td>Antibiotic associated enterocolitis</td>
</tr>
<tr>
<td>Hemorrhagic colitis (due to enterohaemorrhagic E. coli, EHEC or Shiga-toxin producing E. coli, STEC)</td>
</tr>
<tr>
<td>Outbreak diarrhoea</td>
</tr>
<tr>
<td>Acute diarrhoea in immunocompromised hosts</td>
</tr>
<tr>
<td>Institutional diarrhoea</td>
</tr>
<tr>
<td>Nosocomial diarrhoea (hospital acquired)</td>
</tr>
<tr>
<td>Gay bowel syndrome</td>
</tr>
<tr>
<td>Acute diarrhoea in septicemia prone conditions</td>
</tr>
</tbody>
</table>
are cake, bread and cooked rice that have been left for a period of time. Bacteria that could produce such toxins include S. aureus, B. cereus, C. perfringens, etc. Most symptoms subside within 48–72 h. Symptomatic and supportive treatment is usually sufficient. If the patient can drink, oral rehydration therapy is highly encouraged. If vomiting is severe and dehydration is significant, intravenous therapy may be necessary. Antispasmodics, such as metoclopramide, are not effective if given orally, but intramuscular injection may be efficient. Abdominal cramping pain may respond to antispasmodics, for example hyoscine, hyoscyamine and dicyclomine.

**Viral gastroenteritis**

The Norwalk virus is the most common cause of viral gastroenteritis in adults. However, rotavirus and other viruses, for example astrovirus, calicivirus, coronavirus, enterovirus, and small round virus-like particles, may also be the cause. The illness has an incubation period of between 18 and 72 h, and is characterized by the abrupt onset of nausea and abdominal cramps followed by vomiting and/or diarrhea. Low-grade fever (above 37.5°C or 99.5°F) develops in about half of affected individuals. Headache, myalgias, upper respiratory tract symptoms and abdominal pain are common. Red and white cells are not normally found in the stool. The illness is usually mild and self-limiting, lasting 24–48 h. In some cases, diarrhea and vomiting may persist for a week or longer. In general, oral rehydration treatment is adequate and only in rare cases intravenous rehydration may be needed. Bismuth subsalicylate has been shown to improve the clinical symptoms of viral gastroenteritis.

**Major Presentation: Diarrhea**

**Watery diarrhea**

Watery diarrhea, that is, stool of decreased form from normal-looking, semiformed to loose or watery, without the presence of blood, is often the clinical presentation of enterotoxin induced diarrhea. Examples of such diarrhea include cholera caused by *Vibrio cholerae* and *Vibrio O139*, and diarrhea due to non-O1 vibrios, enterotoxigenic *Escherichia coli*, and enteropathogenic *E. coli*. Some cases of infection with *Vibrio parahemolyticus*, *Salmonella*, *Aeromonas* spp., *Campylobacter jejuni*, *Yersinia enterocolitica* and *Clostridium difficile* may also present as watery diarrhea, especially in the initial stages of their course (see Table 3).

**Bloody diarrhea**

Diarrhoea where the stool on macroscopic observation contains blood mixed up with feces or inseparable from the stool is classified as bloody diarrhea. Microscopically, the feces generally contain numerous red blood cells and white blood cells.

**Table 3** Enteropathogens responsible for infectious diarrhea (modified from Farthing M.)

<table>
<thead>
<tr>
<th>Enteropathogen</th>
<th>Watery diarrhea</th>
<th>Bloody diarrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Viruses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotavirus</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Enteric adenovirus (types 40,41)</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Caliciviruses</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Astrovirus</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Bacteria</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>V. cholerae</em> O1</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td><em>Vibrio O139</em></td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Non-O1 Vibrios</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td><em>Vibrio parahemolyticus</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>Aeromonas</em></td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>ETEC</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>EPEC</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>EAggEC</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>EIEC</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>EHEC (STEC)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Shigella spp.</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Salmonella spp.</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Campylobacter spp.</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>Yersinia enterocolitica</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>Clostridium difficile</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>Plesiomonas shigelloides</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Protozoa</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Giardia intestinalis</em></td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td><em>Cryptosporidium parvum</em></td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Microsporidia</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td><em>Isospora belli</em></td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td><em>Cyclospora cayetanensis</em></td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td><em>Entamoeba histolytica</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>Balantidium coli</em></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Helminths</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Strongyloides stercolis</em></td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><em>Schistosoma spp.</em></td>
<td>–</td>
<td>+</td>
</tr>
</tbody>
</table>

ETEC, enterotoxigenic *Escherichia coli*; EPEC, enteropathogenic *E. coli*; EAggEC, enteroaggregative *E. coli*; EIEC, enteroinvasive *E. coli*; EHEC, enterohaemorrhagic *E. coli*.

Bloody diarrhea is the clinical presentation of severe bacterial colitis, which is caused by invasive enteric pathogens, for example Shigella spp., Salmonella spp., Campylobacter jejuni, Yersinia enterocolitica, enteroinvasive *E. coli*, enterohemorrhagic *E. coli*, Entamoeba histolytica and Balantidium coli. Some cases of *Vibrio parahemolyticus*, *Aeromonas* spp., and *Plesiomonas* spp. may also present as bloody diarrhea, especially later in the course of acute diarrhea (see Table 3).

**Clinical dehydration**

For the purpose of this guideline, the term ‘clinical dehydration’ refers to moderate and/or severe dehydra-
tion, and does not include mild diarrhea or mild dehydration.

All cases of acute diarrhea would have dehydration due to loss of fluid and electrolytes. Even mild diarrhea would have some degree of dehydration, but this may be difficult to assess quantitatively. Adults normally have better compensatory mechanisms than children through the larger body fluid reserve, the better kidney compensatory mechanisms, and better response to correct thirst. Together with poorer tissue elasticity and slower shift of extra cellular fluid, the clinical signs of dehydration in adults would be less obvious than in children. Severity of dehydration does not always correlate with severity of diarrhea. Some may rely on the subjective symptoms alone to classify severity of diarrhea while it is more reliable to evaluate the severity of dehydration from objective signs. The proper assessment of severity of dehydration should utilize both subjective and objective evidence (see Table 4).

**Watery diarrhea with clinical dehydration**

In general, severe watery diarrhea with severe dehydration is mostly caused by *V. cholerae* serogroup O1. There are also other organisms that cause a similar clinical picture as cholera. They are *Vibrio O139*, other-Non-O1 vibios and sometimes *Vibrio parahemolyticus, Aeromonas* spp., and diarrheagenic *E. Coli.* Although diarrhea caused by these organisms is often milder than cholera, more severe cases may occur, which should be treated in the same fashion as severe watery diarrhea. On the other hand, it should be noted that during epidemics, or even in an endemic area for cholera, patients with cholera may be found to have only mild diarrhea, and they should be managed differently from the suggested algorithm (see Appendix).

Although severe profuse watery diarrhea alone is highly suggestive of cholera, it should be stressed that other features are also important, for example the very abrupt onset of acute diarrhea that occurs in a matter of hours, the rapid progression to profound dehydration, the absence of fever and abdominal pain, and the presence of muscle cramps. In the obvious cases, stools are often greenish-yellow clear watery with very little food residue. Signs of dehydration should be present and sometimes are very prominent. Dark field microscopy (DFM) and stool culture should be done in all cases. Stool examination with fine microscopic adjustment could also reveal shooting bacteria, but there are no red blood cells or white blood cells. In nonendemic areas, once DFM or stool culture is positive for cholera, notification of the area health authority should be done as soon as possible.

It should be noted that in endemic areas, during outbreaks or seasonal epidemics of cholera, watery diarrhea of all severity should be treated as cholera and stool culture should be done to confirm in all cases (see Appendix).

**Treatment:** The treatment of watery diarrhea should focus mainly on fluid and electrolyte replacement. In patients with mild dehydration, and with little or no vomiting, oral rehydration therapy using oral rehydration salts solution (ORS) should be administered at approximately 1.5 times the volume of stool loss in 24 h without discontinuing dietary intake. In moderate to severe dehydration, prompt aggressive intravenous fluid repletion and supportive care can obviate the high mortality that is associated with the disease. Also if vomiting is severe and the deficit cannot be replaced solely by ORS, intravenous fluids in the form of Ringer lactate will be required. In moderate to severe diarrhea, at least half of the calculated deficit should be replaced within 4 h and the rest is to be replaced within 24 h. Evaluation of fluid and electrolyte deficit is crucial in calculating the amount of fluids to replace. Hence, stool volume loss should be closely monitored.

**Table 4** Classification of severity of dehydration

<table>
<thead>
<tr>
<th>Subjective</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General state</strong></td>
<td>Alert, active, up and about</td>
<td>Weak, lethargic.</td>
<td>Dull, inactive.</td>
</tr>
<tr>
<td>Ability to perform daily activities</td>
<td>Able to perform daily activities without difficulty</td>
<td>Able to perform daily activities with some difficulty, e.g. stays away from work, needs support</td>
<td>Unable to sit or walk</td>
</tr>
<tr>
<td>Thirst</td>
<td>Not increased</td>
<td>Increased thirst</td>
<td>Feels very thirsty</td>
</tr>
<tr>
<td>Objective signs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse</td>
<td>Normal</td>
<td>Tachycardia</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Normal</td>
<td>Normal or decrease</td>
<td>10–20 mmHg systolic</td>
</tr>
<tr>
<td>Postural hypotension</td>
<td>No</td>
<td>Yes or no</td>
<td>Yes</td>
</tr>
<tr>
<td>Jugular venous pressure</td>
<td>Normal</td>
<td>Normal or slightly flat</td>
<td>Flat</td>
</tr>
<tr>
<td>Dry mucosa (mouth, tongue)</td>
<td>No</td>
<td>Slight</td>
<td>Severe</td>
</tr>
<tr>
<td>Skin turgor</td>
<td>Good</td>
<td>Fair</td>
<td>Poor</td>
</tr>
<tr>
<td>Sunken eye balls</td>
<td>No</td>
<td>Minimal</td>
<td>Sunken</td>
</tr>
</tbody>
</table>
and, if possible, weighed or accurately measured. In those patients who are not sick enough and still can go to toilets on their own, it may be difficult to estimate accurately the amount of deficit and ongoing loss. Where culturally acceptable the use of ‘cholera cots’ can be very helpful to monitor the amount of ongoing loss. If cholera cots are not available, it may be safer to replace twice the amount of estimated loss and closely monitor the status of hydration of the patient.

Antibiotics, when given to cholera patients, reduce stool volume loss and shorten the clinical course.25 If there is recent epidemiological data available, the empiric antibiotics should be given according to the sensitivity of Vibrio cholerae in the region. In cases where antibioticogram is not available, tetracycline 2 g daily for 3 days should be the treatment. Alternatively, doxycycline 300 mg as a single oral dose, or 100 mg twice daily for 3 days, and ciprofloxacin 500 mg twice daily for 3 days (especially in regions where resistance to tetracycline is greater than 20%), have all been recommended. For pregnant women, furazolidone 400 mg/day for 3 days has been suggested. Antidiarrheal drugs may be somewhat effective in reducing enteric symptoms, but they play a minor role in the treatment of watery diarrhea and cannot be routinely recommended. (Loperamide is not indicated for patients with severe watery diarrhea, for example cholera, but for watery diarrhea in travelers, loperamide can be very helpful). Treatment should rely only on rehydration therapy and antibiotics only. Recently the use of resistant starch has been shown to be of benefit in reducing stool volume loss and shortening the clinical course in adult patients with cholera.26

Watery diarrhea without dehydration

Patients in this group comprise the majority of cases of acute diarrhea in adults. They are often mild and are not accompanied with signs of dehydration. They represent acute gastroenteritis that are usually caused by enteric pathogens which have a self-limited course and generally does not need antibiotics (except in patients with extreme ages), for example Non-O1 vibrios, Vibrio parahemolyticus, Aeromonas spp., Plesiomonas spp., Edwardsiella spp., Salmonella spp. It may also include the milder and uncomplicated forms of diarrhea from Vibrio cholerae, Vibrio O139, Shigella boydii, Shigella sonnei, Campylobacter spp., Yersinia spp., and all groups of Escherichia coli.

In general, diarrhea is characterized by the passage of loose or loose watery stools with some food residue in the feces. These patients normally pass 4–8 stools a day without or with minimal signs of dehydration. There should be no gross blood or bloody mucoid material in the stool. Fever could be present but is often mild and does not last longer than two days. Abdominal pain and vomiting may be severe in the first few days but gradually subsides in the following days. Abdominal tenderness should be absent, both to light and deep palpation. If stool microscopic examination is available, it characteristically shows no ova or parasites, RBC or WBC. However, small numbers of RBC and WBC are sometimes present microscopically, but do not exceed 20 cells/HPF.27 These cases usually are not accompanied with fever.

**Treatment:** As dehydration is often mild, the need for fluid and electrolytes replacement may be less pressing than in the group with clinical dehydration. Nevertheless, rehydration remains the mainstay of treatment in this group of patients. As the disease is dynamic and mild dehydration may progress to more severe dehydration, early hydration with oral rehydration therapy (ORT) should be encouraged to prevent fluid deficits. Intravenous fluid replacement is often not needed. Administration of antibiotics is unnecessary and not recommended. Antidiarrheals can be allowed and loperamide has been recommended for use as self-medication in adults with mild acute diarrhea.28 (A brief review of scientific information regarding efficacy, side-effects and precautions for the use of these antidiarrheals follows.)

Particular attention should be paid to geriatric patients over the age of 65 years, immunocompromised patients, and patients with conditions predisposing to septicemia. Patients in these categories will need antibiotics, usually orally administered but sometimes systemically (see Appendix).

**Bloody diarrhea**

Most acute bloody diarrhea is caused by Shigella spp. and Campylobacter jejuni, Shigella dysenteriae and Shigella flexneri, often produce a more severe disease with high fever, while Shigella boydii and Shigella sonnei usually cause a milder disease. Other enteric pathogens producing bloody diarrhea include Salmonella enteritidis, Yersinia enterocolitica, Clostridium difficile, EHEC and EIEC. Sometimes Aeromonas hydrophila and Plesiomonas shigelloides that have severe enough diarrhea may also produce bloody diarrhea.29 Entamoeba histolytica infections commonly present as chronic diarrhea, but they may sometimes present as acute bloody diarrhea with or without fever.

Bloody diarrhea is often accompanied by fever that may persist for longer than 2 days and may be higher than 38.5°C. Initially, these patients may pass watery stools that rapidly progresses to bloody diarrhea and dysentery. Dysentery is characterized by the frequent passage (usually 10–30 times a day) of small-volume stools consisting of blood, mucus and pus; this diarrhea is accompanied by abdominal cramps and tenesmus, the painful straining at stool that may lead to rectal prolapse. Diagnosis is enhanced if microscopically RBC and WBC are found in the stool.27,30 It is essential to exclude amoebic colitis by examining fresh stool for trophozoites. Seizures are rare in adults with bloody diarrhea. Mild dehydration is common and severe dehydration is very rare. The hemolytic uremic syndrome rarely complicates bloody diarrhea. Bacteremia is associated with higher-than-usual mortality and is more common among elderly patients31–33 (see Appendix).
Treatment: The mild dehydration in bloody diarrhea can be readily corrected with ORT and intravenous therapy is often not needed. The use of antibiotics in most patients with bloody diarrhea reduces the duration of illness and can shorten the carrier stage. For practical purpose, after having excluded amoebic colitis and EHEC or STEC by careful stool examination, it is acceptable to start empiric therapy with antibiotics rather than waiting for stool culture results. If the local antibiogram of *Shigella* spp. is known, the preferred antibiotics can be selected. But if no information is available, one of the fluoroquinolones is preferred. Norfloxacin 800 mg/day, ciprofloxacin 1000 mg/day or levofloxacin 500 mg/day for 3–5 days should be adequate for healthy adults. For geriatric patients, or septicemic prone conditions, ofloxacin or ciprofloxacin is preferred. It is imperative not to administer antimotility agents, such as loperamide, diphenoxylate, atropine and codeine, as the drugs are suspected of enhancing the severity of disease by delaying excretion of organisms and thus facilitating further invasion of the mucosa.

Stool examination

Although fresh stool examination under light microscopy should be encouraged in every case, it may not always be practicable or possible. In real life situations, assessment of patients with acute diarrhea may have to rely solely on history and physical examination. Hence, in the algorithm, stool examination is recommended in patients with watery diarrhea with dehydration and in patients with bloody diarrhea, but not considered as essential in patients with watery diarrhea without dehydration. Depending on the availability, feasibility and local practice, stool examination may be done early in some cases and when it is done, the detection of microscopic RBC and WBC >20 cells/HPF by early stool examination may have some predictive value in detecting early cases of bloody diarrhea. In patients with gross bloody diarrhea, stool examination can provide essential information for differentiating shigellosis from amebiasis. In addition, dark-field microscopy (DFM) is strongly recommended in all patients with watery diarrhea with dehydration. A positive DFM for shooting bacteria should indicate the high possibility of *Vibrio* spp., especially *Vibrio cholerae*, and appropriate antibiotics to eradicate *Vibrio cholerae* should be promptly initiated. In situations in which DFM is not available, fine adjustment of light microscopic examination to look for active motile ‘shooting’ bacteria can be a helpful alternative to diagnose *Vibrio* spp. as a cause of diarrhea. Presence of stool ova and parasites in the stool should lead to appropriate therapy.

Stool culture

In general, stool culture is probably not necessary in patients who present to physicians with mild diarrhea without obvious signs of dehydration, and within the first few days of onset of illness. In most such individuals, the diarrhea will probably subside before the culture results become available. Stool culture is advisable in patients with bloody diarrhea, moderate to severe diarrhea with objective evidence of dehydration, and those with diarrhea that does not subside after a few days. In the situation of an outbreak, nosocomial diarrhea, or the specific conditions of acute diarrhea listed in Table 2, extensive work up with stool culture should be encouraged (see Appendix).

‘Routine’ culture techniques vary from country to country and hospital to hospital, depending on the availability, feasibility and local practice. When diarrhea is non-specific or indeterminate and there are limitations of resources and facilities, routine stool culture with MacConkey agar is the minimal requirement. Because most laboratories in the USA do not culture routinely for *Vibrio cholerae* or other *Vibrio* spp., clinicians should request appropriate cultures for clinically suspected cases. When *cholera* is suspected from a positive DFM or presence of shooting bacteria from light microscopy, thiosulfate-citrate- bile-salt-sucrose (TCBS) agar should be added to the routine MacConkey agar to detect *Vibrio* group organisms. Further identification for *Vibrio cholerae* serotype and serogrouping should be done, together with the identifications of *Vibrio* O139, Non-O1 *Vibrio cholerae* and *Vibrio parahaemolyticus*. When bloody diarrhea is suspected, selective media for *Shigella*, for example salmonella-shigella agar or XLD agar should be added to the routine MacConkey agar. Micro-aerophilic cultivation technique with inhibitory media to detect *Campylobacter* and special media for *Yersinia* should be added to the routine culture. If traveler’s diarrhea is diagnosed, culture for all bacterial causes should be performed. For suspected EHEC associated diarrhea, Sorbitol-MacConkey agar should be added to the routine culture.

Unresolved diarrhea

All patients who do not improve after rehydration, with or without antidiarrheals and/or empiric antibiotics, should require re-evaluation after 3–5 days, depending on the severity of the continuing illness. Such patients should be informed to bring along his or her ‘fresh’ stool specimen for microscopic re-examination and/or re-culture at their next visit. They should be advised to observe their stool. They should also be advised to consult their physician for re-evaluation if the stool character changes and becomes more watery or bloody, if they develop high fever (> 38.5°C), if their stage of
clinical dehydration does not improve, or if their abdominal pain becomes more intense or persistent. When the patient comes for the second visit, stool examination and culture should be done especially if they were not performed in the first visit. In cases of bloody diarrhea without an identifiable pathogen, which do not improve after empiric treatment, further investigation by doing sigmoidoscopy or colonoscopy together with biopsy is usually necessary.

### Sigmoidoscopy/colonoscopy

Patients who were managed along the scheme of the algorithm or have bloody diarrhea in spite of empiric antibiotics, and did not improve, should be further investigated by sigmoidoscopy or colonoscopy. Colonic biopsy together with culture should be performed even though the mucosa may look normal endoscopically.45

### Selective antibiotics for known pathogens

Whenever stool examination and culture results are available, treatment should be as selective and specific as possible. Selection of antibiotics for corresponding enteropathogens should follow the antibacterial sensitivity of the pathogen that was isolated. In situations where an antibiogram is not available, antibiotics selection should follow the available local or regional data regarding antibiotic susceptibility in that region or country. If no such information is available, the use of conventional recommended antibiotics (as shown in Table 5) is recommended. It must be noted that antibiotics are not recommended for some enteropathogens, as there is no information to confirm the efficacy of antibiotic use or the available information suggests that antibiotic use in this particular situation may actually be deleterious. Again, it should be stressed that dehydration needs to be properly corrected in all cases, no matter the result of the stool culture.

### Oral rehydration

In this article, the term ORS (Oral Rehydration Salts Solution) and ORT (Oral Rehydration Therapy) are used. To avoid confusion, clarification of these terms are presented below.

### Table 5  Recommended antibiotics against specific enteric pathogens

<table>
<thead>
<tr>
<th>Organism</th>
<th>Suggested antibiotics</th>
<th>Alternative antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Vibrio cholera</em> O1</td>
<td>Tetracycline, 500 mg q.i.d. × 3 d</td>
<td>Doxycycline, 300 mg single dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TMP-SMZ, 160–800 mg b.i.d. × 3 d</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluoroquinolone* × 3 d</td>
</tr>
<tr>
<td><em>Vibrio</em> O139</td>
<td>Tetracycline, 500 mg q.i.d. × 3 d</td>
<td>Doxycycline, 300 mg single dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TMP-SMZ, 160–800 mg b.i.d. × 3 d</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluoroquinolone* × 3 d</td>
</tr>
<tr>
<td>Other non-O1 Vibriosp.46</td>
<td>Antibiotics are usually not required, except in certain situations.</td>
<td>Doxycycline, 300 mg single dose</td>
</tr>
<tr>
<td></td>
<td>Tetracycline, 500 mg q.i.d. × 3 d</td>
<td>Fluoroquinolone* × 3 d</td>
</tr>
<tr>
<td><em>Vibrio parahemolyticus</em>47</td>
<td>Antibiotics are usually not required, except in certain situations.</td>
<td>Doxycycline, 300 mg single dose</td>
</tr>
<tr>
<td></td>
<td>Tetracycline, 500 mg q.i.d. × 3 d</td>
<td>Fluoroquinolone* × 3 d</td>
</tr>
<tr>
<td><em>Shigella</em> species</td>
<td>Fluoroquinolone* × 3 d</td>
<td>Ceftriaxone#, 1 g b.i.d. × 5–7 d</td>
</tr>
<tr>
<td>Non-typhoidal species of <em>Salmonella</em></td>
<td>Antibiotics are usually not required, except in certain situations.</td>
<td>Ceftriaxone#, 1 g b.i.d. × 5–7 d</td>
</tr>
<tr>
<td></td>
<td>Fluoroquinolone* × 5–7 d</td>
<td>TMP-SMZ, 160–800 mg b.i.d. × 3 d</td>
</tr>
<tr>
<td><em>Aeromonas</em> species</td>
<td>Antibiotics are usually not required, except in certain situations.</td>
<td>Ceftriaxone#, 1 g b.i.d. × 7–14 d</td>
</tr>
<tr>
<td></td>
<td>Fluoroquinolone* × 3 d</td>
<td>TMP-SMZ, 160–800 mg b.i.d. × 3 d</td>
</tr>
<tr>
<td><em>Plesiomonas</em> species</td>
<td>Antibiotics are usually not required, except in certain situations.</td>
<td>Ceftriaxone#, 1 g b.i.d. × 5–7 d</td>
</tr>
<tr>
<td></td>
<td>Fluoroquinolone* × 3 d</td>
<td>TMP-SMZ, 160–800 mg b.i.d. × 3 d</td>
</tr>
<tr>
<td>Enterotoxigenic <em>Escherichia coli</em></td>
<td>Antibiotics are usually not required, but may be required in certain situations.</td>
<td>TMP-SMZ, 160–800 mg b.i.d. × 3 d</td>
</tr>
</tbody>
</table>
### Table 5 (continued)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Suggested antibiotics</th>
<th>Alternative antibiotics</th>
</tr>
</thead>
</table>
| Enteropathogenic *Escherichia coli* | Antibiotics have no established therapeutic value and are usually not required, except in certain situations.  

| Enteroinvasive *Escherichia coli*   | Antibiotics are usually not required, except in certain situations.  

| Enterohaemorrhagic *Escherichia coli* (STEC) | Role of antibiotics is unclear and administration should be avoided as they may be harmful.  

| Campylobacter species                | Antibiotics are usually not required, except in certain situations.  

| Yersinia species                     | Antibiotics are usually not required, except in certain situations.  

| Toxigenic *Clostridium difficile*    | Offending antibiotics should be withdrawn if possible.  

**Notes:**
- *fluoroquinolone, for example 300 mg ofloxacin, 400 mg norfloxacin, or 500 mg ciprofloxacin b.i.d.
- #antibiotics for suspected septicemic cases

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**Oral rehydration salts solution (ORS)**

Oral rehydration salts solution refers to the oral rehydration salts formula that is recommended by WHO. It contains sodium chloride 3.5 g, sucrose 40 g (or glucose 20 g), trisodium citrate dihydrate 2.9 g (or sodium bicarbonate 2.5 g) and potassium chloride 1.5 g in one litre of clean drinking water. This combination should give the concentration of sodium 90 mEq/L, potassium 20 mEq/L, chloride 80 mEq/L, HCO₃ 30 mEq/L and glucose 111 mmol/L.⁴⁹

**Oral rehydration therapy (ORT)**

Oral rehydration therapy in the context of these guidelines refers to the use of informal oral rehydration formulas or electrolyte packages with lower sodium concentration than the one recommended by WHO. It also refers to non-ORS measures of rehydration, including various natural or formulated electrolyte containing drinks.⁵⁰

Adult patients with watery diarrhea and clinical dehydration should receive the proper WHO-recommended ORS formula to correct their dehydration, especially in endemic areas of cholera. In other parts of the world where cholera is not a problem, a milder formula may be accepted. Patients with mild dehydration or patients with all types of diarrhea without obvious evidence of clinical dehydration can also use the WHO ORS formula in conjunction with intermittent free water drinking. In adults, the chance of having hyponatremia or hypernatremia may be much greater in the elderly.³¹ Hence, ORT or usage of lower sodium concentration of ORS, may be more appropriate in elderly patients. In geriatric patients, periodic assessment of serum electrolytes may be necessary. The super ORS, which
contain glycine or starch (cereal-based formulations) are receiving increased attention.\textsuperscript{51} Because of their lower osmolarity, they may reduce stool output and better enhance electrolytes absorption. The use of resistant starch to provide colonic short chain fatty acids may also be of importance.\textsuperscript{51}

In general, ORS or ORT should be taken by mouth slowly and intermittently by 'sipping' little by little, not 'drinking' in large amount in a short period of time. The amount to be taken should be approximately 1.5–2 times the estimated amount of deficit plus concurrent loss.

**Intravenous fluid replacement**

For initial management of severely dehydrated or hypovolemic shock patients, immediate intravenous fluid replacement is essential. Patients with moderate or milder degree of dehydration may also need intravenous fluid replacement if they have severe vomiting and are unable to drink ORS properly. Patients with dull consciousness, who may harbor the risk of aspiration, should also be rehydrated intravenously. Ringer's lactate is best recommended for all forms of acute diarrhea in adults, as it contains potassium 4 mEq/L, which can be replaced rapidly in large amounts according to the severity of deficit. The total fluid deficit in severely dehydrated patients can be replaced safely within the first 4 h of therapy, half within the first hour.\textsuperscript{52} The volume of fluid to be administered is determined by the rate of stool losses and the degree of pre-existing dehydration. Meanwhile, oral therapy usually can be initiated with the goal of maintaining fluid intake equal to the ongoing loss. However, patients with continued large-volume diarrhea might require prolonged intravenous treatment to keep up with gastrointestinal fluid losses. It should also be used with additional potassium supplements by mouth. The oral route of rehydration and potassium replacement is safer than the intravenous route and is physiologically regulated by thirst and urine output.

**Antidiarrheal drugs**

While every effort should be made to identify and correct the specific causes of diarrhea, in many cases, causes that are specific and potentially treatable are often not identifiable. Identification is not possible and symptomatic therapy alone is commonly indicated.

Although most diarrheas are self-limited, some antidiarrheal drugs may help in reducing amount of fluid loss, frequency and consistency of stool, or shorten the clinical course of diarrhea. The addition of antidiarrheal drugs improves the quality of life to a certain extent at the financial cost of the drugs. The cost-benefit ratio of using various antidiarrheal agents has not been properly studied. As acute diarrhea is a very common condition affecting large numbers of people, the routine usage of antidiarrheals could mean a great financial burden to countries, especially in the developing world, where diarrhea is very prominent. In industrialized countries, the antidiarrheal compounds may be cost effective and useful in returning people more quickly to work and school during a bout of diarrhea.

There is a wide variety of antidiarrheal drugs available on the market. Physicians in each region of the world will have to keep in mind the cost-risk-benefit ratios and make their own judgment in selecting or recommending the antidiarrheals. In the following paragraphs the evidence supporting the use of each antidiarrheal drug is briefly reviewed, so that physicians can decide which to use by judging from their efficacy, side-effects, indications and contra-indications based on the available literature. Antidiarrheal drugs are grouped and discussed under the following topics.

**Antiperistaltics or antimotility drugs**

Most available antiperistaltic agents act by altering intestinal motility. Some also may have mild proabsorptive or antisecretory activity. They include loperamide, diphenoxylate, codeine, tincture opium and other opiates. They may be helpful in secretory diarrhea of mild to moderate severity by reducing the frequency and volume of stools.\textsuperscript{53–55} Among all antimotility drugs, loperamide is the most commonly recommended agent for use in uncomplicated diarrhea.\textsuperscript{28,56} However, such antimotility agents are contraindicated in diarrhea caused by invasive pathogens because the induced intestinal stasis may enhance tissue invasion by the organisms or delay their clearance from the bowel. Hence, bloody diarrhea with high fever, immunocompromised host and septicemic prone conditions with diarrhea should not be given this group of drugs.

Some of these drugs may cause addiction, if they are to be administered for a long period. Suppression of respiration is significant in children and may be harmful in elderly people with chronic lung disease. The newer loperamide preparation, loperamide oxide, may be the drug in this group with the least side-effects.\textsuperscript{57} Response to loperamide can vary from one person to another. The aim should be to reduce the frequency of diarrhea, not to 'stop' diarrhea.

**Anticholinergics**

They include atropine, hyoscine, hyoscyamine and dicyclomine. They are not effective in reducing the frequency and volume of stools, but may have some value in selected cases in reducing pain from abdominal cramps.\textsuperscript{58} High dose of anticholinergics may cause dry mouth, urinary retention, blurred vision, palpitation, ileus and exacerbation of glaucoma.

**Adsorbents**

There are a variety of drugs in this group, for example activated charcoal, kaolin, pectin, dioctahedral smectite, attapulgite (anhydrous aluminum silicate), aluminum hydroxide and tannic acid. Theoretically these medications adsorb toxins produced by toxigenic bacteria and
Acute diarrhea in adults is a common everyday condition all over the world. Besides acute infectious diarrhea, the definition also encompasses many intestinal conditions that may present as acute diarrhea. Stool examination and culture results are often not available, and proper hydration together with empiric treatment has to be initiated. A practical approach for the management of adult patients with acute diarrhea is presented in an algorithmic diagram. After careful history taking and a physical examination to exclude other conditions that may present as acute diarrhea, and other specific situations of acute diarrhea that deserve to be approached differently, patients are classified as having predominately diarrhea or predominately vomiting. The diarrhea predominant group is further classified into watery diarrhea and bloody diarrhea subgroups by their gross stool appearance. The watery diarrhea subgroup with clinical dehydration will have to exclude cholera by stool examination with dark field microscopy confirmed later by stool culture. The watery diarrhea without clinical dehydration subgroup is managed by ORT with or without antidiarrheals. The bloody diarrhea subgroup is controlling motility and secretion of the gut. As 5HT is also a neurotransmitter found in the brain and the enteric nervous system (ENS). The antagonists of 5HT3 receptor were found to inhibit extrinsic sensory neuron stimulation (which can inhibit nausea, vomiting, stomach pain and bloating) and reduce peristalsis and secretory reflex. As a result, they help to reduce stool volume and improve stool consistency. Another newer antisecretory agent is oral enkephalinase inhibitor (Racecadotril). It prevents the degradation of endogenous opioids (enkephalins), thereby reducing hypersecretion of water and electrolytes into the intestinal lumen. Clinical trials that show the efficacy of these drugs in the management of acute diarrhea in children and adults are being validated. Octreotide, which is a long-acting synthetic analog of somatostatin, has a significant antisecretory effect. It is expensive and has to be administered subcutaneously. It is more reasonable to prescribe in otherwise refractory cases of chronic diarrhea.

**Probiotics**

Probiotics are non-pathogenic organisms, for example Lactobacillus acidophilus and Saccharomyces boulardii, which multiply in the patient’s intestine and produce metabolites, which increase acidity of stool and prohibit the growth of enteropathogens. They prevent the invasion of bacteria in intestine tissue, and produce short chain fatty acids that are beneficial for intestine recovery, and increase the rate of fluid and electrolyte absorption. In children, there are studies which show that the use of probiotics could reduce the clinical course of acute diarrhea. In adults, they are used mainly in chronic diarrhea and relapse of antibiotic associated enterocolitis.

**Antisecretory drugs**

There are many drugs in everyday use that have antisecretory effects in vitro, for example phenothiazine, chlorpromazine, aspirin, indomethacin, lithium carbonate, and calmodulin-inhibitors. They work by a variety of different mechanisms including inhibition of prostaglandins and effects on cyclic AMP, calmodulin inhibition, inhibition of gut hormones and encephalinase inhibition of chloride channels. But some of these drugs have to be administered in very high doses to give effective antisecretory effects in vivo. Hence, their drug-related side-effects preclude them from being used effectively. This group of drugs is more physiologic in approach and may become the ideal agents for use in acute diarrhea. Bismuth salts preparations, according to their mode of action, are also an antisecretory agents. They are found to be as effective as loperamide, and reduce the number of stools passed by about 50%, with improvement in other associated symptomatology. The untoward side-effects of bismuth preparations are blackened stool, blackened tongue, tinnitus and fecal impaction.

Recently, drugs that affect 5-hydroxytryptamine (5HT) or serotonin were found to have a pivotal role in...
treated with antibiotics either empirically or after stool examination and culture to rule out EHEC or STEC. If patients do not improve after the first visit and specific pathogens causing diarrhea are identified, specific antibiotics should be administered according to the sensitivity results or data from the community. Further investigation by repeating stool examination and culture together with sigmoidoscopy or colonoscopy are essential if the patient does not get better. There are special situations in acute diarrhea that require special considerations and these are discussed in detail.

REFERENCES


Acute diarrhea in adults


Acute diarrhea in the elderly

Acute diarrhea that occurs in patients aged over 65 years is associated with higher mortality. Diarrhea is a common problem among the elderly that can have catastrophic results. Atherosclerosis predisposes older adults to morbidity sequelae from dehydration resulting from diarrhea. Ischemic colitis is a serious differential diagnosis especially in developed countries. Deaths related to diarrheal illnesses are recognized among older adults living in the community as well as among those confined to nursing homes. Outbreaks have most often been associated with excess deaths from diarrhea among nursing-home patients. Although most cases of dehydration from diarrhea result from gastrointestinal infections, non-infectious causes of diarrhea related to prescription of laxatives, side-effects of medications and use of enteral feedings are common. *Clostridium difficile* infection is particularly common among older adults in hospitals and nursing homes, and relapsing disease in these groups may be more frequent than among younger adults. The approach to an elderly patient with diarrhea is to ensure proper hydration using available oral rehydration solutions, proceed with diagnostic tests likely to yield a positive result, avoid the use of harmful antiperistaltic drugs, and provide adequate follow-up of the nutritional state. Antibiotics should be administered in acute diarrhea due to invasive bacteria, especially salmonella.

**Traveler’s diarrhea**

This is a specific entity that occurs after a person has traveled from an industrialized country to a developing country and experienced acute diarrhea. The risk increases if the traveler consumes food from street vendors rather than from a restaurant or a hotel. Symptoms and severity depend on the prevalence of common pathogens endemic in the developing country.
The common causes of acute traveler’s diarrhea vary from one geographical area to another.78–84 The most frequently identified pathogen causing traveler’s diarrhea is toxigenic Escherichia coli, although in some parts of the world (notably North Africa and South–East Asia), Campylobacter infections appear to predominate. Other common causative organisms include enteroga-gregative E. coli, Salmonella spp., Shigella spp., rotavirus and the Norwalk agent. Except for giardiasis, cryptosporidium and cyclosporidium, parasitic infections are uncommon causes of traveler’s diarrhea.

The disease is usually short-lived, self-limited, however, many of them are amenable to antibiotics. Choice of antibiotics depends on epidemiologic data. The same principle should apply in correcting dehydration from other types of diarrhea. Antidiarrheal drugs can be given in conjunction with antibiotics. A growing problem for travelers is the development of antibiotic resistance in many bacterial pathogens; examples include strains of Campylobacter resistant to quinolones and strains of E. coli, Shigella, and Salmonella resistant to trimethoprim-sulfamethoxazole.

**Antibiotic associated enterocolitis**

Diarrhea that occurs as a result of administered antibiotics which alter the normal intestinal flora and increase the proliferation of Clostridium difficile, produce enterotoxin A and B that cause enterocolitis and pseudomembrane formation.85 Positive history of antibiotics usage prior to the development of diarrhea may raise the possibility of antibiotic associated enterocolitis, however, the use after the onset of diarrhea usually does not suggest antibiotic associated enterocolitis. Onset of symptoms occurs either during antimicrobial administration or within four weeks after treatment. While all antimicrobials may cause the syndrome, some drugs cause it more commonly than others and some only rarely. The common causes of antibiotic associated enterocolitis include clindamycin, ampicillin, and the cephalosporins. The rare causes of antibiotic associated enterocolitis are vancomycin, metronidazole, and the aminoglycosides.

The clinical spectrum of antibiotics-associated entero-colitis is diverse. It ranges from mild loose watery diarrhea to severe colitis causing bloody or dysentery-like diarrhea in the later course of the disease. In the first week, diarrhea is usually watery, voluminous and without gross blood or mucus. Later, it becomes bloody. Other symptoms also vary considerably. At one end of the spectrum are many patients with annoying diarrhea with no severe systemic toxicity; while at the other end are those with high and prolonged fever with abdominal pain. Abdominal pain can be severe with cramping, especially at the left iliac fossa. Vomiting is uncommon and dehydration is often mild except in very severe cases. Examination of stool may reveal large numbers of red blood cells and some leukocytes. Stool culture for C. difficile needs anaerobic conditions and may take several days to perform. It is usually more practical to perform cytotoxin assay in the stool using ELISA, or tissue culture assay technique in confirming diagnosis. Sigmoidoscopy or colonoscopy may reveal normal, minimally erythematous colonic mucosa with some edema, or granular, friable, or hemorrhagic mucosa with typical pseudomembrane formation.

The course is highly variable. In patients with clinically mild disease, withdrawal of offending antibiotics usually leads to prompt resolution of symptoms. Those who have more protracted diarrhea usually need specific therapy. Oral rehydration therapy is the mainstay treatment to correct dehydration. Intravenous fluid may be required in severe cases. Empiric metronidazole 250–500 mg four times daily should be administered while waiting for the result of a cytotoxin study, and should be continue for 10–14 days. If cytotoxin study is positive and the patient does not get better after a week of metronidazole, then vancomycin 125–250 mg/day should be substituted. Relapses or reinfections are common and occur in as many as 20% of cases. These patients can be treated with the same treatment as given for the primary infection. Subsequent recurrences of antibiotic associated enterocolitis are best managed with vancomycin plus rifampicin.

Antidiarrheal drugs have no advantage in treating antibiotic-associated enterocolitis, except cholestyramine and probiotics, which can be helpful in chronic or relapsing disease.

**Hemorrhagic colitis (due to Enterohaemorrhagic E. coli, EHEC or Shiga Toxin Producing E. coli, STEC)**

Hemorrhagic colitis, caused by enterohaemorrhagic Escherichia coli (EHEC), should always be a differential diagnosis in patients who present with acute bloody diarrhea, especially during an outbreak of food-borne illness. Patients who present with non-bloody diarrhea that progresses to bloody diarrhea should also raise the possibility of EHEC diarrhea. Other prominent complaints include striking abdominal pain and tenderness often in the absence of fever. In an outbreak situation, some patients with EHEC infection may be asymptomatic and are only recognized during epidemiologic surveillance in association with symptomatic cases. In general, the mortality rate is 1–2%,86 although it may be substantially higher in the young and the elderly.87

The most worrisome complication of EHEC infection is the hemolytic–uremic syndrome (HUS),88 which most frequently involves children between the ages of 5–10 years.89 Hemolytic-uremic syndrome is characterized by the triad of acute renal failure, microangiopathic hemolytic anemia, and thrombocytopenia. Patients who also have fever and neurologic symptoms are considered to have the related disorder thrombotic thrombocyto-penic purpura (TTP), which has also been associated with E. coli O157:H7 infection.89,90 Hemolytic-uremic syndrome usually begins 5–10 days after the onset of diarrhea.86,90 The incidence of subclinical renal dysfunction is substantially higher, particularly in patients with prolonged anuria during the initial presentation.92,93 Stool culture using sorbitol-MacConkey agar
should be done in all suspected EHEC diarrhea. The Centers for Disease Control and Prevention (CDC) has recommended that all stools from patients with a history of bloody diarrhea should be screened for *E. coli* O157:H7 or Shiga toxin by direct stool examination. All *E. coli* O157:H7 and Shiga toxin-positive stools should be sent to a reference laboratory for confirmation. A number of newer diagnostic approaches for EHEC infection focuses on direct detection of Shiga toxins in stool, or the use of DNA probes for detecting the toxin genes in fecal isolates. One such assay, the Premier EHEC assay, utilizes an enzyme-linked immunosorbent assay (ELISA) to detect both Shiga toxin 1 and Shiga toxin 2 in stool.

The only current treatment of EHEC infection is supportive, with monitoring for the development of microangiopathic complications such as HUS. The impact of antibiotic therapy on the duration of diarrhea or on the subsequent occurrence of systemic complications is controversial. The use of antibiotics may actually increase the risk of HUS, perhaps by increasing production or release of toxin. A number of newer approaches to therapy of EHEC infection are currently being evaluated, but are not yet proven effective nor available routinely. These include: toxin-binding resins given orally and hyperimmune antitoxin antisera.

### Nosocomial diarrhea

Nosocomial diarrhea, that is acute diarrhea that occurs in hospitalized patients, is an important problem in hospitals, and in critical care units in particular. Hospital-acquired diarrhea may be on an infectious or non-infectious basis. Common non-infectious causes of nosocomial diarrhea include food intolerance, drug induced diarrhea, drug-induced changes in the fecal flora, or changes secondary to enteral hyperalimentation. Infectious causes of nosocomial diarrhea are due to eating food contaminated with enteric pathogens or in outbreak situations. However, the major cause of sporadic (non-epidemic) nosocomial diarrhea is *Clostridium difficile.* All cases of nosocomial diarrhea should be properly investigated with stool examination, culture and *C. difficile* cytotoxin assay. Proper hydration together with dietary adjustment should immediately be employed. If possible, discontinuation of offending drugs or antibiotics should be considered. Empiric metronidazole can be started in patients with a possibility of antibiotic associated enterocolitis. (See antibiotic associated enterocolitis for details of this infection). Systemic antibiotics may be necessary in immunocompromised patients.

### Outbreak diarrhea

Acute diarrhea that occurs in two or more persons from the same exposure, assumed to be caused by the same pathogens, is considered an outbreak. In the situation in which there is a known outbreak of an epidemiologically important enteric pathogen, for example cholera, salmonella, shigella, campylobacter, EHEC (STEC), any acute diarrheas that occur in the outbreak area should be managed as if they are caused by the ‘outbreak pathogen’, no matter the severity of diarrhea. As in an outbreak situation, the disease spectrum is often highly variable, ranging from very mild to very severe. All acute diarrhea in the outbreak area should be reported to the Area Health Authority and proper epidemiologic investigation should be employed. Rapid testing or a kit that is helpful in identifying the ‘outbreak pathogen’ should be used in the field and further confirmation can be done later in a reference center. Antibiotics that are known to be effective in eradicating the pathogen should be empirically administered to all acute diarrhea cases in the outbreak area. The purpose is to contain the spreading of the disease, not necessarily to shorten the clinical course of diarrhea in that particular case. Epidemiologic surveillance is necessary until the outbreak completely subsides.

### Institutional diarrhea

This is acute diarrhea that occurs in persons who stay in an institution where there is a uniform population with the same clinical or social setting, for example a nursing home, a day-care center, a refugee camp, etc.

Any single case of acute diarrhea that occurs in an institution should all be investigated by stool examination and culture, as there is risk of spreading among inhabitants in the same institution and may progress to an established outbreak of diarrhea. Apart from the routine correction of dehydration, there should also be isolation of the patient and an improvement of hygiene and sanitation in the institution. Early empiric treatment with antibiotics may help to contain the suspected enteropathogens. In patients with diarrhea due to salmonella, empiric antibiotic treatment may increase the time of shedding of the organism by one to three weeks. Antibiotics are usually not given to otherwise healthy patients with milder forms of non-typhoid salmonellosis. The young or the elderly and patients with immunocompromised are usually given antimicrobials in intestinal salmonellosis. In confirmed groups, other organisms may produce illness in individuals or as outbreaks. The cause of the illness generally requires laboratory study for identification.

### Acute diarrhea in immunocompromised patients

Acute diarrhea that occurs in an immunocompromised host, who has been treated with immunosuppressive agents or chemotherapy, or those with HIV infection, autoimmune diseases, malignancy, especially hematologic malignancy, and acute graft-versus-host condition are a special entity. Acute diarrhea that occurs in
Acute diarrhea in adults

these patients may easily lead to septicemia, hence early antibiotic therapy during their course of diarrhea should be instituted, no matter the type or severity of the diarrhea. Apart from the hemodynamic support, parenteral antibiotics are often needed. Bloody diarrhea in immunocompromised patients may also be caused by cytomegalovirus enteric infection.

Acute and chronic diarrhea that occurs in an HIV-infected person should receive special attention in terms of investigation and management. HIV-infected persons, who are not yet immunocompromised or having CD4 count > 500 cell/mm³, can be managed as in the suggested algorithm (Fig. 1). But HIV-infected persons who are immunocompromised or their CD4 counts are < 500 cell/mm³, apart from doing routine stool culture and examination, stool staining for AFB, modified AFB, modified trichrome staining and C. difficile cytotoxin assay should also be employed. Blood cultures should be performed since enteropathogens and Mycobacterium-avium intracellulare often produce bacteremia in immunocompromised patients. Empiric treatment can be considered if the nature of enteropathogens infecting these patients is known. Specific treatment with antibiotics, if being administered, should be given in a more prolonged course to ensure the complete eradication of the pathogen and prevent early relapse. Nutritional management is also required in this group of patients.

Gay bowel syndrome

This is a specific syndrome of acute diarrhea that occurs in homosexual men who may or may not be infected with HIV. Homosexual people are a unique group of patients who are prone to diarrhea due to their sexual activity, which is the primary method of transmission for several important enteric parasitic diseases. The majority of parasitic sexually transmitted diseases involve protozoan pathogens; however, nematode and arthropod illnesses are also included in this group. Oral-anal and oral-genital sexual practices predispose male homosexuals to infection with many enteric pathogens, including parasitic protozoans and helminths. The most common of these parasitic infections are amebiasis, caused by Entamoeba histolytica, and giardiasis caused by Giardia lamblia. Both entities may cause acute or chronic diarrhea, as well as other abdominal symptoms. Most gay men with amebiasis are asymptomatic, and invasive disease in this group is extremely rare. Both amebiasis and giardiasis can be diagnosed on the basis of microscopic examination of stool specimens, although duodenal aspiration is occasionally necessary to confirm a diagnosis of giardiasis. Metronidazole is efficacious in the treatment of both amoebiasis and giardiasis. Other common causes of diarrhea in homosexual males include the spread of the organisms by the fecal oral route (e.g., shigella, campylobacter, salmonella) and those spread by receptive anal intercourse (e.g., Neisseria gonorrhoeae, Chlamydia trachomatis, Herpes simplex and Treponema pallidum.)

Acute diarrhea in septicemic prone conditions

Acute diarrhea that occurs in a person who is prone to septicemia due to the presence of some underlying conditions that are not truly immunocompromised conditions but were reported to have related higher incidence of septicemia with diarrhea, or complications when diarrhea occurs, for example cirrhosis, especially alcoholic cirrhosis, uncontrolled diabetes mellitus, patients with heart valves, prosthesis, severe atherosclerosis with aortic aneurysm, malignancy and uremia. There are several reports of Non-O1 Vibrios septicemia in patients with cirrhosis. Uncontrolled diabetes mellitus patients with diarrhea are prone to gram negative septicemia. Patients with heart valve, prosthesis, severe atherosclerosis are prone to salmonella septicemia and lodging of salmonella infection at the diseased heart valve and prosthesis. These patients should be aware of the possibility of septicemia and an early empiric parenteral antibiotic should be administered from the first presentation.