Infectious Gastroenteritis

Diarrhea with Fever

Penelope H. Dennehy

J. Domachowske (ed.), *Introduction to Clinical Infectious Diseases*,
https://doi.org/10.1007/978-3-319-91080-2_15

15.1 Definition

Acute gastroenteritis (AGE) is an illness caused by viral, bacterial, or parasitic infection of the intestinal tract. The World Health Organization defines AGE as a clinical syndrome characterized by increased stool frequency (e.g., 3 or more loose or watery stools in 24 h or a number of loose/watery bowel movements that exceeds the usual number of daily bowel movements by two or more), with or without vomiting or fever [1]. A change in stool consistency versus previous stool consistency is more indicative of diarrhea than stool frequency. Symptoms of AGE usually last less than 7 days and not longer than 2 weeks.

15.2 Pathogenesis

Diarrhea can be classified as noninflammatory, inflammatory, or invasive based on the effect of the enteric pathogen on the intestinal mucosa (Table 15.1).

The noninflammatory or secretory diarrheas are characterized by low-grade or no fever and diffuse watery nonbloody stools. Secretory diarrhea is caused by enterotoxin-producing organisms such as *Vibrio cholerae* and enterotoxigenic *E. coli*, viruses, and parasites such as *Giardia lamblia*. Cholera is characterized by severe watery diarrhea due to changes in ion secretion and absorption resulting from the action of cholera toxin on electrolyte transport in the gut. Viruses infect enterocytes causing villus blunting or shortening of the villi. There is a decrease in the number of cells making up the villi, reducing the overall absorptive surface for nutrient uptake and damaging intestinal enzymes on the villus tips which lead to increased carbohydrate in the intestinal lumen with resultant increased osmolarity of the intestinal contents with malabsorption. Infection with *Giardia lamblia* causes the loss of brush border absorptive surfaces and diffuses shortening of villi, leading to secretory diarrhea.

Inflammatory diarrhea is often characterized by high fevers (greater than 40 °C), bloody stools, severe abdominal pain, and smaller volume stools. This type of diarrhea is caused by two groups of organisms—cytotoxin-producing, noninvasive bacteria (e.g., enteroaggregative *E.coli*, enterohemorrhagic *E. coli*, and *Clostridium difficile*) or invasive organisms (e.g. *Salmonella* spp., *Shigella* spp., *Campylobacter jejuni*, *Entamoeba histolytica*). Infection with both types of organisms causes damage to the intestinal mucosa. The cytotoxin-producing organisms adhere to the mucosa, activate cytokines, and stimulate the intestinal mucosa to release inflammatory mediators. Invasive organisms, which can also produce cytotoxins, invade the intestinal mucosa to induce an acute inflammatory reaction, involving the activation of cytokines and inflammatory mediators. Invasive organisms, such as *Salmonella* spp., may cause enteric fever by penetrating the intestinal epithelium, where the organisms gain access to the lymphoid tissue and disseminate via the lymphatic or hematogenous route. Enteric fever is characterized by severe systemic illness with fever and abdominal pain.

15.3 Epidemiology

Acute infectious gastroenteritis is a major cause of morbidity and mortality worldwide. In the United States, prior to the introduction of rotavirus vaccine in 2006, AGE was responsible for more than 1.5 million outpatient visits, 200,000 hospitalizations, and 300 deaths per year [2]. Despite significant reductions in AGE after the introduction of rotavirus vaccine, there are still more than 105,000 hospitalizations annually among children <5 years of age in the United States alone [3, 4].

Viral gastroenteritis is the most common cause of diarrheal illness seen both in the emergency department and in general practice. Viral pathogens are more common among children <5 years old than among older children or adults. Acute viral gastroenteritis can be transmitted by asymptomatic carriers as well as by symptomatic patients before the onset of symptoms. Viral AGE is generally transmitted by the fecal-oral route. Illness usually begins 12 h to 5 days after

Table 15.1 Gastrointestinal syndromes

	Characteristics of the stool	Mechanism of diarrhea	Site of infection	Examples
Secretory or watery diarrhea	Copious Watery No blood No pus	Noninflammatory (enterotoxin)	Proximal small bowel	*Vibrio cholerae* Enterotoxigenic *E.coli* *Rotavirus* *Giardia lamblia*
Dysentery or colitis	Scant Pus Blood	Inflammatory (invasion or cytotoxin production)	Colon	*Shigella* species *Campylobacter* species *Entamoeba histolytica*
Enteric fever	Often no diarrhea	Penetrating into the bloodstream	Distal small bowel	*Salmonella typhi* *Yersinia enterocolitica*

exposure and generally lasts for 3–7 days. Viral pathogens are detected more commonly during the winter months.

Bacterial enteritis typically affects adults and children older than 2 years of age and occurs through oral-fecal contamination and after exposure to poultry, other farm animals, or contaminated meat. Bacterial pathogens are detected more commonly during the summer months.

15.4 Etiologies of Infectious Gastroenteritis

There have been few comprehensive studies of the etiology of AGE in the United States [5–8]. Diagnostic testing available in clinical laboratories in the past was limited and the tests available had limited sensitivities for many of the enteric pathogens, especially those that more commonly infect children. With the recent development of molecular diagnostic tests that detect multiple enteric pathogens, it is now possible to characterize the etiology of AGE among hospitalized children and other cohorts of interest more completely [9].

A large study using a molecular panel that detects 23 enteric pathogens conducted at a regional children's hospital provides insights into the current etiology of AGE among children in in the United States [10]. In this study a pathogen was detected in 52% of AGE episodes. The most commonly detected pathogens included diarrheagenic *E. coli*, *Norovirus*, and enteric *Adenovirus*. Multiple pathogens were identified from 15% of submitted specimens.

Before universal rotavirus immunization was adopted in the United States, approximately one half of all hospitalizations for acute nonbacterial gastroenteritis in children were caused by *Rotaviruses* [11]. Despite the marked reduction in *Rotavirus*, other viral pathogens are detected frequently and account for more than half of all pathogens identified in children <5 years old. Currently *Noroviruses* are the most important cause of nonbacterial acute gastroenteritis in all ages [12]. Other viral pathogens that have been proven to cause acute gastroenteritis are shown in Table 15.2.

In developed countries, bacterial pathogens account for 2–10% of cases of gastroenteritis [13, 14]. *Campylobacter* sp., *Salmonella* sp., *Shigella* sp., and enterohemorrhagic *E. coli* (EHEC) account for the majority of cases in the United States (Table 15.2). Cases of salmonellosis have been linked to exposure to farm animals, poultry, eggs, and household pets such as healthy-appearing turtles, snakes and lizards, and puppies or kittens with diarrhea. Campylobacteriosis cases can often be linked to exposure to farm animals, poultry, eggs, or consumption of raw milk. *Yersinia enterocolitica*, *Vibrio* sp. bacteria including *Vibrio cholerae* and non-01 cholera, *Aeromonas* sp., and *Plesiomonas* sp. are unusual etiologies of gastroenteritis in developed countries. *Yersinia enterocolitica* infections are often linked to the consumption of certain ethnic foods prepared using the intestines of pigs, especially during holiday times. Yersiniosis can cause mesenteric adenitis, mimicking the presentation of acute appendicitis, with or without symptoms of diarrhea. The diarrhea-causing *E. coli*, EIEC (enteroinvasive), and EPEC (enteropathogenic) are seen most often in developing countries (Table 15.3).

Table 15.2 Infectious causes of acute gastroenteritis in the United States

Viral	Bacterial	Parasitic
Rotavirus	*Campylobacter* spp.	*Giardia intestinalis*
Norovirus	*Salmonella* strains	*Cryptosporidium parvum*
Astrovirus	*E. coli*	
Enteric *Adenoviruses* (*Adenovirus* 40/41)	*Shigella* spp.	
Sapovirus	*Clostridium difficile*	
	Yersinia enterocolitica	

Table 15.3 Classification of *Escherichia coli* that is associated with gastroenteritis

E. coli type	Epidemiology	Stool characteristics
Enterohemorrhagic or Shiga-like toxin-producing (EHEC or STEC)	Hemorrhagic colitis associated with the development of hemolytic uremic syndrome	Bloody or non-bloody
Enteropathogenic (EPEC)	Acute and chronic endemic and epidemic diarrhea in infants	Watery
Enterotoxigenic (ETEC)	Infantile gastroenteritis in developing countries and traveler's diarrhea in all ages	Watery
Enteroinvasive (EIEC)	Diarrhea with fever in all ages	Bloody or non-bloody; dysentery
Enteroaggregative (EAEC)	Acute and chronic diarrhea in infants	Watery, occasionally bloody

Up to 35% of individuals who travel to developing countries may experience bouts of diarrhea during or immediately following the trip. Most cases occur within the first 2 weeks of travel and last about 4 days. Regions of travel associated with the highest risk are Africa, South Asia, Latin America, and the Middle East. Bacteria are the most frequent cause of traveler's diarrhea, and enterotoxigenic *E. coli* is the most commonly identified pathogen.

Parasitic causes of gastroenteritis are uncommon in healthy children in the United States accounting for 1–8% of cases of gastroenteritis. Parasitic infections occur more

frequently in recent immigrants, travelers, and backcountry campers, those with exposure to farm animals, and immunocompromised patients. *Giardia lamblia* and *Cryptosporidium parvum* infections are the most common causes of parasitic disease in the United States (Table 15.2).

15.5 Clinical Presentation

Non-bloody diarrhea, vomiting, and fever are the most common findings in patients with viral gastroenteritis. However the clinical presentation of bacterial gastroenteritis may overlap with viral disease and the two are often clinically indistinguishable. Clinical features that suggest bacterial gastroenteritis include age greater than 2 years, gross blood or mucus in the stool, high fever (greater than 40 °C), tenesmus, associated seizures, severe abdominal pain, and smaller volume stools. Patients with bacterial AGE are more likely to have identified risks such as international travel, exposure to poultry or other farm animals, and consumption of processed meat. Parasitic infections typically cause watery diarrhea, abdominal cramping, vomiting, and low-grade fever. Parasitic infections frequently cause more prolonged diarrhea often lasting well beyond 14 days.

15.6 Complications

As a direct consequence of diarrhea and vomiting:

- Hypovolemia/dehydration: Severe dehydration may lead to shock, multi-organ dysfunction, and death. Dehydration occurs predominantly among very young children and the extreme elderly. Young children are more susceptible to dehydration than older children because they have a higher body surface-to-volume ratio, a higher metabolic rate, and lower fluid reserves. Extreme elderly patients may be unable to maintain adequate oral hydration independently.
- Electrolyte abnormalities and acid-base disturbance including hypernatremia, hyponatremia, hypokalemia, and metabolic acidosis.
- Lactose intolerance due to damage to mature enterocytes on small intestinal villi containing lactase is uncommon.
- Irritant diaper dermatitis.

Other complications are shown in Table 15.4.

Table 15.4 Complications of infectious gastroenteritis

Complication	Associated etiologic agent(s)
Bacteremia	*Salmonella* spp., *Yersinia enterocolitica*
Seizures and fever	*Shigella* spp. (more common), *Campylobacter* and *Salmonella* spp. less likely
Encephalopathy	*Shigella* spp. (more common), with *Salmonella* sp. less likely
Extraintestinal infections	*Salmonella* sp. (more common), other bacteria less likely
Guillain-Barre syndrome	*Campylobacter jejuni*
Hemolytic-uremic syndrome	E. coli O157:H7 and other Shiga toxin-producing strains (STEC)
Meningitis	*Salmonella* spp. in neonates and extreme elderly
Reactive arthritis	*Salmonella* spp., *Shigella* spp., *Campylobacter* spp., and *Yersinia* spp.
Bowel perforation, toxic megacolon, secondary bacteremia	Any of the bacterial agents associated with invasive diarrhea; *C. difficile*
Pseudoappendicitis	*Yersinia enterocolitica*

15.7 Clinical Evaluation

The evaluation of children with acute gastroenteritis frequently begins with a telephone call from the caregiver. The focus of the conversation should be to assess the child's fluid status and the possibility of severe illness or a condition other than acute gastroenteritis that requires specific therapy.

Indications for a medical visit include the following [15, 16]:

- Age under 6 months or weight < 8 kg (17 lbs. 10 oz)
- Temperature ≥ 38 °C for infants <3 months or ≥ 39 °C for children 3–36 months
- Visible blood in stool
- Frequent and large amounts of diarrhea
- Diarrhea for more than 7 days or persistent vomiting
- Caregiver's report of symptoms of moderate to severe dehydration
- Multisystem compromise, cardiovascular instability (refer directly to the emergency department)
- Inability of the caregiver to administer or failure of the child to tolerate or respond to oral rehydration therapy at home
- Underlying immunodeficiency or condition complicating the treatment or course of illness, such as malnutrition, diabetes mellitus, or other metabolic diseases
- Social circumstances that make telephone assessment unreliable

The history and examination of children with symptoms and signs of gastroenteritis should focus on the following:

- Dehydration Assessment

The goal is to provide a starting point and determine the necessary intensity of intervention. Acute changes in body weight are the best measure. Decreased blood pressure is a late finding

Table 15.5 Clinical dehydration scale (CDS) for the assessment of children

	Points toward total assessment score		
	0	1	2
General appearance	Normal	Thirsty, restless, or lethargic but irritable when touched	Drowsy, limp, cold, sweaty, or coma
Eyes (periorbital skin turgor)	Normal	Slightly sunken	Extremely sunken
Mucous membranes (tongue)	Moist	Sticky	Dry
Tears	Tears	Decreased tears	Absent tears

Source [18]
A score of 0 represents no dehydration, a score of 1–4 represents some dehydration, and a score of 5–8 represents moderate/severe dehydration

Table 15.6 World Health Organization assessment for dehydration

	No dehydration (<5%)	Some dehydration (5–10%)	Severe dehydration (>10%)
Condition	Well, alert	Restless, irritable	Lethargic, unconscious
Eyes	Normal	Sunken	Sunken
Thirst	Drinks normally, not thirsty	Thirsty, drinks eagerly	Drinks poorly, not able to drink
Skin turgor/ capillary refill	Instant recoil	Delayed <2 seconds	Delayed >2 seconds

Source [41]

of hypovolemia in children that corresponds to greater than 10% of fluids losses and heralds cardiovascular collapse. Prior guidelines from the Centers for Disease Control and Prevention (1992) [16] and the American Academy of Pediatrics (1996) [17] grouped patients in three subgroups:

- Mild dehydration (3–5% fluid deficit)
- Moderate dehydration (6–9% fluid deficit)
- Severe dehydration (>10% fluid deficit)

New studies indicate that the first signs of dehydration in young children might not be evident until a 3–4% fluid loss has occurred. Severe dehydration signs are usually not seen until the patient has experienced 9–10% losses. Updated recommendations group patients with mild and moderate dehydration together (Table 15.5) [18]. The World Health Organization (WHO) recommends a simpler system for use by both physicians and lay health workers, which classifies dehydration as none, some, or severe (Table 15.6).

A meta-analysis of 13 separate studies looking at individual signs and symptoms of dehydration found that only capillary refill times of more than 2 s, decreased skin turgor, and abnormal respiratory pattern (hyperpnea) had statistically and clinically significant positive and negative likelihood ratios for detecting dehydration in children [19].

- Evaluation of the child for other causes of diarrhea and/or vomiting that requires specific therapy and can be confused with AGE in the first day or two of symptoms (e.g., meningitis, acute abdominal processes, diabetic ketoacidosis, toxic ingestions).

Hospitalization should be considered for all children with acute gastroenteritis in the following situations [15, 20]:

- Signs of severe dehydration are present.
- Caregivers are unable to manage oral rehydration or provide adequate care at home.
- Factors present necessitating closer observation, such as young age, decreased mental status, or uncertainty of diagnosis.

15.8 Diagnostic Testing

The diagnosis of acute gastroenteritis is made clinically. Laboratory studies such as serum electrolytes, blood urea nitrogen, creatinine, or urinalysis are not routinely necessary. Microbiologic testing is likewise unnecessary in immunocompetent hosts with uncomplicated gastroenteritis; however, microbiologic testing should be considered for [15, 21]:

- Outbreaks of gastroenteritis, particularly in an institution with a closed population such as a hospital, child-care center, or school
- Cohorting and isolation of hospitalized patients
- Patients with underlying conditions such as immune compromise, malignancy, or inflammatory bowel disease
- Patients with diarrhea of 7 days' duration or longer
- Uncertain diagnoses

Blood cultures should be obtained from infants less than 3 months of age and from any patient with a toxic appearance or other clinical signs of sepsis, patients in whom enteric fever is suspected, those who are immunocompromised, and those who traveled to or have had contact with travelers from enteric fever-endemic areas [22].

Stool testing should be performed for *Salmonella* sp., Shigella sp., *Campylobacter* sp., *Yersinia* sp., and STEC in patients with diarrhea accompanied by fever, bloody or mucoid stools, severe abdominal cramping or tenderness, or signs of sepsis [22] since they may require antimicrobial therapy tailored to the infecting organism.

Table 15.7 Pathogens detected by commercially available gastroenteritis multiplex polymerase chain reaction diagnostic panels

Bacteria and bacterial toxins	Viruses	Protozoa
Aeromonas spp.	*Astroviruses*	*Cryptosporidium* spp.
Campylobacter spp.	Enteric *adenoviruses* 40/41	*Cyclospora* spp.
C. difficile toxins A/B	*Noroviruses*	*Entamoeba histolytica*
E.coli O157	*Rotaviruses*	*Giardia lamblia*
EAEC	*Sapoviruses*	
EPEC		
ETEC toxins		
Plesiomonas shigelloides		
Salmonella spp.		
STEC toxins		
Shigella sp./EIEC		
Vibrio spp.		
Vibrio cholera toxin		
Yersinia enterocolitica		

Historically, the microbiologic diagnoses of acute gastroenteritis have been made using microscopy, rapid antigen tests, stool culture, and, occasionally, real-time polymerase chain reaction (PCR) assays. A combination of these tests was often required because each type of test evaluates for different subsets of etiologies, and it's often impossible to distinguish between possible groups of infectious etiologies based on the clinical presentation alone. Recently, multiplex molecular assays have been developed for the detection of gastrointestinal pathogens directly from stool samples. These panels allow for the detection and identification of up to 23 pathogens with a laboratory turnaround time as short as 1 h (Table 15.7). Three multiplex real-time PCR assays are now licensed in the United States and are rapidly replacing traditional tests for the detection of enteric pathogens.

The major advantages of multiplex molecular assays are lower detection limits, higher sensitivity for common pathogens such as *Rotavirus* and *Shigella* spp., and the ability to detect uncultivatable pathogens such as *Noroviruses* [23]. Studies have demonstrated that the use of these multiplex panels will increase the positivity rates of enteric pathogens by two- to fourfold compared to conventional methods.

As use of these multiplex molecular assays becomes more commonplace, several new challenges will likely emerge for the clinician [23, 24]. First, these assays do not provide antimicrobial sensitivity data for bacterial organisms detected, so empiric antibiotic selection will need to be based upon prior known sensitivity patterns from the community or from the general literature. In addition these assays detect microbial DNA or RNA, not viable organisms, and therefore do not distinguish an active symptomatic infection from asymptomatic infection, colonization, or previous infection with continued shedding of the pathogen alive or dead. Pathogens such as *Norovirus*, *Rotavirus*, and *Salmonella* spp. have been shown to be present in the stool of asymptomatic individuals or shed for long periods following the resolution of disease and may be detected in those settings as well as in symptomatic disease. Organisms such as EAEC, EPEC, and *Sapovirus* that have not been routinely tested for in the past may be detected. This may present a challenge for the clinician to interpret the clinical significance of test results showing the detection of these pathogens. The rate of reported coinfections is likely to increase with the use of these panels as well [25]. Insufficient data are available to guide clinicians on how to interpret such findings. Further research on use and interpretation of results from these highly sensitive assays is necessary [26–28].

15.9 Differential Diagnosis

Extraintestinal infections which may present with diarrhea and/or vomiting include staphylococcal and streptococcal toxic shock syndrome, meningitis, bacterial sepsis, bacterial pneumonia including legionellosis, urinary tract infection, and otitis media. These infections can usually be differentiated from acute gastroenteritis by their extraintestinal manifestations and/or early results of laboratory testing.

A number of noninfectious conditions can also present with symptoms that mimic those of infectious gastroenteritis. These include inflammatory bowel diseases, intussusception, appendicitis, food allergies, and lactase deficiency.

15.10 Clinical Management

The current mainstay of the clinical management and treatment for acute infectious gastroenteritis consists of oral rehydration and early reintroduction of food [15, 16, 20, 22, 29, 30]. Intravenous rehydration should be reserved for cases where oral fluid correction is not tolerated or when the severity of fluid losses has already led to impending hypovolemic shock.

The objectives of treatment include the following:

- Prevention of dehydration, if there are no signs of dehydration.
- Treatment of dehydration, when present.
- Prevention of nutritional sequelae, by continued feeding during and after diarrhea.
- Reduction of the duration and severity of diarrhea.

No specific antiviral therapy is available for viral gastroenteritis. Anti-infective options are available for the treatment

of bacterial and parasitic causes of gastroenteritis, but their use is not always indicated, frequently unnecessary, and, in some instances, should be specifically avoided. Symptomatic therapy for AGE with watery diarrhea and/or vomiting consists of replacing fluid losses and correcting electrolyte disturbances through oral and/or intravenous fluid administration.

15.10.1 Oral Rehydration Therapy

The American Academy of Pediatrics (AAP), the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN), and the World Health Organization (WHO) all recommend oral rehydration solution (ORS) as the treatment of choice for children with mild-to-moderate gastroenteritis in both developed and developing countries, based on the results of many randomized, controlled trials and several large meta-analyses [16, 17, 19, 31].

Oral rehydration takes advantage of a specific sodium-glucose transporter (SGLT-1) in the intestinal brush border of the intestine to increase the reabsorption of sodium, which leads to the passive reabsorption of water. This transport remains intact even during severe gastroenteritis.

Rehydration solutions with low osmolarity and 1:1 ratio of glucose to sodium perform optimally. Solutions with high concentrations of glucose, such as juice, soft drinks, and sports drinks, have higher osmolarity thereby impairing optimal water/sodium transport from the gut into the bloodstream. Their use is discouraged during oral rehydration therapy, a point that should be used when discussing home strategies with parents who may assume otherwise.

WHO programs focusing on the treatment of dehydration with ORS have substantially decreased deaths from cholera and other gastroenteritis in developing countries. In the United States, the absence of cholera and the generally high level of nutrition and generous total body sodium levels in children have led to the development of a consensus for use of ORS containing less sodium than is currently included in the WHO-recommended ORS recipe. ORS available in the United States include Pedialyte, Infalyte, and Naturalyte. Both the WHO ORS and solutions containing less sodium have been shown to be safe and effective in treating dehydration associated with acute gastroenteritis.

The full benefits of oral rehydration therapy (ORT) have not been realized in the United States. One of the reasons for the low use of ORT is the ingrained, habitual use of intravenous therapy for most children who are hospitalized and many who are brought to the emergency department. Up to 49% of pediatricians report that they always use intravenous fluids to treat moderate dehydration and 33% use intravenous fluids to treat mild dehydration despite recommendations for the use of ORS in these clinical situations [24].

Hydration status in children can be assessed on the basis of easily observed signs and symptoms (Tables 15.5 and 15.6). Children with AGE who are not thirsty have moist mucous membranes, and wet diapers and tears are not dehydrated and do not require ORS. If the child is breastfed, the mother should be encouraged to breastfeed more frequently than usual and for longer at each feed. If the child is not exclusively breastfed, then oral maintenance fluids should be given at a rate of approximately 500 mL/day for children younger than 2 years, 1000 mL/day for children aged 2–10 years, and 2000 mL/day for children older than 10 years. In addition, ongoing fluid losses should be replaced with 10 mL/kg body weight of additional ORS for each loose stool and 2 mL/kg body weight of additional ORS for each episode of emesis (both for breastfed and non-breastfed children). A study by Freedman et al. found that patients with mild gastroenteritis and minimal dehydration experienced fewer treatment failures when offered half-strength apple juice followed by their preferred drinks compared with children given ORS [32].

Children who are mildly or moderately dehydrated should receive 50 to 100 ml/kg of ORS over 4 h and should be reevaluated often for changes in hydration. Additional ORS is given to replace ongoing losses (10 mL/kg body weight for each stool and 2 mL/kg body weight for each episode of emesis). After the initial rehydration phase, patients may be transitioned to maintenance fluids.

Children who are severely dehydrated with changes in vital signs or mental status require emergency intravenous fluid resuscitation. Hypotension is a late manifestation of shock in children. Mental status, heart rate, and perfusion, as assessed by capillary refill time, are better indicators of severe dehydration and incipient shock. After initial treatment with IV fluids, these children can be given oral rehydration.

Children who are vomiting generally tolerate ORS. ORS is contraindicated in the child who is obtunded or at risk for aspiration. When oral hydration therapy is complete, regular feeding should be resumed.

15.10.2 Early Refeeding

Early refeeding is recommended in managing acute gastroenteritis because luminal contents are a known growth factor for enterocytes and help facilitate mucosal repair following injury [33]. Introducing a regular diet within a few hours of rehydration or continuing the diet during gastroenteritis without dehydration has been shown to shorten the duration of the disease. Early refeeding has not been associated with increased morbidity such as electrolyte disturbance or a need for intravenous therapy.

Almost all infants with acute gastroenteritis can tolerate breastfeeding. For formula-fed infants, diluted formula does not provide any benefit over full-strength formula. Infants with the most severe gastroenteritis may require lactose-free formula until mucosal recovery, a healing process that is usually complete after 2 weeks.

Older children can consume a regular age-appropriate diet. Foods that contain complex carbohydrates (e.g., rice, wheat, potatoes, bread, and cereals), lean meats, fruits, and vegetables are encouraged. Fatty foods and simple carbohydrates should be avoided. No data suggests that a diet consisting of only bananas, rice, applesauce, and toast (the BRAT diet) speeds recovery from gastroenteritis, although those foods are appropriate to be included in a more varied diet. Exclusive use of the BRAT diet may lead to suboptimum nutrition. Lactose restriction is not usually necessary but may help to reduce diarrheal frequency in some children as an optional, short-term, and temporary dietary change during their convalescence.

15.10.3 The Use of Antimicrobials

Patients with uncomplicated gastroenteritis should not routinely be given antibiotics, including otherwise healthy individuals with salmonellosis who are older than 6 months of age. Antimicrobial treatment for gastroenteritis proven to be caused by bacteria other than *Salmonella* spp. or a parasite can be considered for patients who continue to have symptoms at the time the laboratory results become available, but is not always necessary [15, 20, 22]. Available data suggest that patients with hemorrhagic colitis secondary to EHEC, including E. coli O157:H7, who are treated with antibiotics are more likely to develop the complication of hemolytic uremic syndrome. As such, antibiotic use should generally be avoided in these patients unless they appear toxic or develop a secondary bacteremia while their colon is inflamed.

Certain patients do require antimicrobial therapy for infectious gastroenteritis because treatment reduces their risk for developing complications and accelerates their recovery. Individuals with suspected or confirmed sepsis, with extraintestinal spread of bacterial disease, who are younger than 6 months and found to have salmonella gastroenteritis, who are malnourished or immunocompromised with salmonella gastroenteritis, and those with *Clostridium difficile*-associated pseudomembranous enterocolitis, giardiasis, dysenteric shigellosis, dysenteric amebiasis, or cholera should receive antimicrobials [21]. Table 15.8 details antimicrobial treatment for specific pathogens causing infectious diarrhea.

15.10.4 Adjunctive Management

Antidiarrheal (i.e., kaolin-pectin) and antimotility agents (i.e., loperamide) are contraindicated in the treatment of acute gastroenteritis in children because of their lack of benefit and increased risk of adverse effects, including ileus, drowsiness, and nausea. Antimotility agents can, however, be particularly helpful as adjunctive therapy in adolescents and adults with traveler's diarrhea secondary to ETEC.

The antinausea and antiemetic drug ondansetron may be given to facilitate tolerance of oral rehydration in children older than 4 years of age and to help control nausea and vomiting associated with acute gastroenteritis in adolescents and adults. A review of seven randomized, controlled trials found that oral ondansetron reduced vomiting and the need for intravenous rehydration and hospital admission [34]. Over-the-counter antiemetics are not recommended due to associated drowsiness because that side effect impairs oral rehydration efforts.

Probiotics are supplements containing live microbes, usually bacteria or yeast that are sometimes used to prevent or treat symptoms of infectious diarrhea. Possible mechanisms of action for probiotics include synthesis of antimicrobial substances, competition with pathogens for nutrients, modification of toxins, and/or stimulation of nonspecific immune responses to pathogens that facilitate their clearance. Two meta-analyses support the use of probiotics (especially ***Lactobacillus***) in the treatment of acute infectious diarrhea in children [35, 36]. A recent meta-analysis found probiotics may be especially effective for the prevention of *C. difficile*-associated diarrhea in patients receiving antibiotics [37]. Despite the observation that probiotics help to prevent *Clostridium difficile*-associated diarrhea (CDAD), there is no evidence that they can be used effectively to treat CDAD or that they provide any added benefit as adjunctive therapy when combined with standard antibiotic treatment regimens.

15.11 Prevention of Infectious Gastroenteritis

Prevention remains a key strategy for reducing the overall burden of infectious gastroenteritis. Effective strategic measures shown to prevent the spread of enteric pathogens include proper sanitation methods for food processing and preparation, sanitary water supplies, pasteurization of milk, proper hand hygiene, sanitary sewage disposal, exclusion of infected people from handling food or providing health care, and exclusion of people with gastroenteritis from use of public recreational water facilities including swimming pools, lakes, and ponds.

Eggs and other foods of animal origin should be cooked thoroughly. Raw eggs and food-containing raw eggs should not be consumed. Hand hygiene after handling raw poultry, washing cutting boards and utensils with soap and water after contact with raw poultry, avoiding contact of fruits and vegetables with the juices of raw poultry, and thorough cooking of poultry are critical. Thorough hand hygiene after having contact with human or animal feces, particularly from puppies and kittens with gastroenteritis, is important and makes good common sense.

The single most important intervention that can be used to minimize fecal-oral transmission in at-risk areas such as restaurants, medical office settings, hospitals, schools, child-care facilities, community gatherings, campgrounds, fund

Table 15.8 Antimicrobial treatment of bacterial gastroenteritis

Bacterial pathogen	Who to treat	Recommended therapy	Alternative therapy	Comments
Aeromonas hydrophila	Those who remain symptomatic	Ciprofloxacin for 5 days or azithromycin for 3 days	TMP/SMX for 5 days	Not all strains produce enterotoxins or diarrhea
Campylobacter jejuni (and other species)	Children with dysentery	Erythromycin for 5 days or azithromycin for 3 days	Doxycycline or ciprofloxacin	Early treatment shortens the duration of illness and prevents relapse
Clostridium difficile (antibiotic-associated colitis)	Moderate to severe cases All immunocompromised patients	Oral metronidazole or oral vancomycin for 7 days	Relapse: several options including oral vancomycin taper and fecal transplant	Vancomycin more effective for severe disease
Enterohemorrhagic *E. coli* (EHEC, STEC, *E. coli* O157:H7)	Not recommended May increase the risk of hemolytic uremic syndrome (HUS)	Only for patients who appear toxic or are bacteremic	Antibiotics, if used, should be based on susceptibility results of the pathogen	Antibiotics have not been shown to decrease illness severity
Enteropathogenic *E. coli* (EPEC)	Those who remain symptomatic	Neomycin for 5 days (intraluminal agent, not absorbed)	None	Most strains are not toxogenic or invasive May cause prolonged postinfectious diarrhea
Salmonella spp., non-typhoid strains	Patients at risk for invasive disease Enteric fever	Susceptible strains use azithromycin for 3 days, cefixime for 5–7 days, or TMP-SMX for 14 days	Ceftriaxone or ciprofloxacin for resistant strains; 5-day course	Not indicated for noninvasive AGE with nontyphoidal strains May prolong carriage
Salmonella typhi Cause of typhoid fever	All patients, symptomatic or not	Susceptible strains use azithromycin or ceftriaxone for 5 days, cefixime for 14 days, or TMP-SMX for 14 days	Ciprofloxacin for 5 days	Increasing cephalosporin resistance being described
Shigella spp.	Those who remain symptomatic	Susceptible strains use cefixime for 5 days, azithromycin for 3 days, or ciprofloxacin for 3–5 days	Alternatives for susceptible strains use TMP-SMX for 5 days or ampicillin (not amoxicillin) Ceftriaxone for 2–5 days for resistant strains	Shortens the duration of diarrhea Eradicates the organism from the stool Resistance to antibiotics is common
Traveler's diarrhea (ETEC)	Those who remain symptomatic	Azithromycin or cefixime or ciprofloxacin for 3 days	Rifaximin for those 12 yrs. and older, TMP-SMX	Most illnesses brief and self-limited Resistance increasing worldwide; check country-specific susceptibility data
Vibrio cholerae	Confirmed or suspected case by travel history	Doxycycline or furazolidone for 3 days	Ciprofloxacin or TMP-SMX (if susceptible)	Close attention to replacement of losses
Yersinia enterocolitica	Severe disease or immunocompromised host Not necessary for mild disease in healthy patients	TMP-SMX or ciprofloxacin	Ceftriaxone or gentamicin	High rates of resistance to ampicillin

TMP/SMX is trimethoprim plus sulfamethoxazole

raising events involving the preparation of food and drink, and picnic settings is frequent hand hygiene measures combined with staff training and monitoring of staff procedures, where appropriate. Hand hygiene using alcohol-based sanitizers can be helpful in many settings but should not be used to clean hands that are visibly soiled and do not reduce transmission of *C. difficile* spores or non-enveloped viruses such as *Norovirus*, *Rotavirus*, or *Adenoviruses*.

15.11.1 Vaccines

The prevention of acute gastroenteritis through immunization is now available for some enteric pathogens. Two oral rotavirus vaccines, a monovalent attenuated human rotavirus vaccine and a pentavalent bovine-human reassortant vaccine, are now available for use in many parts of the world, including the United States [38, 39]. In the years following their introduction in the United States, vaccine use reduced the burden of rotavirus-related hospitalizations by 60–93% depending on overall vaccine coverage, age group studied, and the specific *Rotavirus* season evaluated. Reductions in all-cause gastroenteritis or diarrhea-related hospitalizations, emergency visits, and outpatient/physician office visits have also been observed [40].

Vaccines for cholera and typhoid fever have been developed for use in countries where these diseases are endemic or epidemic. Research is also underway to develop vaccines for other pathogens such as *Norovirus* and *C. difficile*.

15.12 Exercises

Please refer to the supplementary information section for answers to these exercises.

Complications	Etiologies
1. Pseudoappendicitis	A. *Campylobacter jejuni*
2. Seizures and fever	B. *E. coli* O157:H7
3. Guillain-Barre syndrome	C. *Salmonella* spp. in neonates
4. Hemolytic-uremic syndrome	D. *Shigella* spp.
5. Meningitis	E. *Yersinia enterocolitica*

Questions related to case scenarios:

Case 1. A 19-year-old young man presents with a history of diarrhea, abdominal cramps, and fever a few days after acquiring a pet turtle. What is the likely cause of his diarrhea?

A. *Campylobacter jejuni*
B. *E. coli O157:H7*
C. *Salmonella* spp
D. *Shigella* spp
E. *Yersinia enterocolitica*

Case 2. A 2-year-old child who attends day care presents with abdominal cramps and severe bloody diarrhea which has been present for 2 days. He has no fever. What is the likely etiology of his illness?

A. *E. coli 0157:H7*
B. *Giardia lamblia*
C. *Norovirus*
D. *Rotavirus*
E. *Salmonella* spp

Case 3. A previously healthy 32-year-old woman develops bloody diarrhea and fever. She visits the emergency department where a stool culture is obtained. Twenty-four hours later, the culture is reported as positive for *Salmonella* spp. She is still having diarrhea and low-grade fever. Of the following options, which treatment is preferred?

A. Ampicillin
B. Ceftriaxone
C. Ciprofloxacin
D. No antibiotic
E. Trimethoprim-sulfamethoxazole

Case 4a. A 6-month-old boy presents with a 2-day history of mild fever and vomiting and watery diarrhea with 8–10 stools per day. Vital signs include a temperature of 38 °C, pulse of 120 beats per minute, and respiratory rate of 40 breaths per minute. He is lethargic but arousable and has slightly decreased periorbital skin turgor, "sticky" mucous membranes, and decreased tears. What is this the child's clinical dehydration score?

A. 0
B. 3
C. 4
D. 5
E. 8

Case 4b. For the 6-month-old boy described in case 4a, which is the most appropriate *next* step in management?

A. Administer a bolus of intravenous fluid
B. Administer an oral rehydration solution
C. No therapy needed
D. Give a single dose of loperamide
E. Give a single dose of ondansetron

References

1. World Health Organization. Diarrheal disease, fact sheet 2017. http://who.int/news-room/fact-sheets/detail/diarrhoeal-disease.
2. Glass RI, Kilgore PE, Holman RC, Jin S, Smith JC, Woods PA, et al. The epidemiology of rotavirus diarrhea in the United States: surveillance and estimates of disease burden. J Infect Dis. 1996;174(Suppl 1):S5–11.
3. Cortes JE, Curns AT, Tate JE, Cortese MM, Patel MM, Zhou F, et al. Rotavirus vaccine and health care utilization for diarrhea in U.S. children. N Engl J Med. 2011;365(12):1108–17.
4. Curns AT, Steiner CA, Barrett M, Hunter K, Wilson E, Parashar UD. Reduction in acute gastroenteritis hospitalizations among US children after introduction of rotavirus vaccine: analysis of hospital discharge data from 18 US states. J Infect Dis. 2010;201(11):1617–24.

5. Cohen MB, Nataro JP, Bernstein DI, Hawkins J, Roberts N, Staat MA. Prevalence of diarrheagenic Escherichia coli in acute childhood enteritis: a prospective controlled study. J Pediatr. 2005;146(1):54–61.
6. Nataro JP, Mai V, Johnson J, Blackwelder WC, Heimer R, Tirrell S, et al. Diarrheagenic Escherichia coli infection in Baltimore, Maryland, and New Haven, Connecticut. Clin Infect Dis. 2006;43(4):402–7.
7. Denno DM, Shaikh N, Stapp JR, Qin X, Hutter CM, Hoffman V, et al. Diarrhea etiology in a pediatric emergency department: a case control study. Clin Infect Dis. 2012;55(7):897–904.
8. Klein EJ, Boster DR, Stapp JR, Wells JG, Qin X, Clausen CR, et al. Diarrhea etiology in a Children's Hospital Emergency Department: a prospective cohort study. Clin Infect Dis. 2006;43(7):807–13.
9. Platts-Mills JA, Operario DJ, Houpt ER. Molecular diagnosis of diarrhea: current status and future potential. Curr Infect Dis Rep. 2012;14(1):41–6.
10. Stockmann C, Pavia AT, Graham B, Vaughn M, Crisp R, Poritz MA, et al. Detection of 23 gastrointestinal pathogens among children who present with diarrhea. J Pediatric Infect Dis Soc. 2017;6(3):231–8.
11. Malek MA, Curns AT, Holman RC, Fischer TK, Bresee JS, Glass RI, et al. Diarrhea- and rotavirus-associated hospitalizations among children less than 5 years of age: United States, 1997 and 2000. Pediatrics. 2006;117(6):1887–92.
12. Payne DC, Vinje J, Szilagyi PG, Edwards KM, Staat MA, Weinberg GA, et al. Norovirus and medically attended gastroenteritis in U.S. children. N Engl J Med. 2013;368(12):1121–30.
13. Elliott EJ. Acute gastroenteritis in children. BMJ. 2007;334(7583):35–40.
14. Vernacchio L, Vezina RM, Mitchell AA, Lesko SM, Plaut AG, Acheson DW. Diarrhea in American infants and young children in the community setting: incidence, clinical presentation and microbiology. Pediatr Infect Dis J. 2006;25(1):2–7.
15. Guarino A, Ashkenazi S, Gendrel D, Lo Vecchio A, Shamir R, Szajewska H, et al. European Society for Pediatric Gastroenterology, hepatology, and nutrition/European Society for Pediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe: update 2014. J Pediatr Gastroenterol Nutr. 2014;59(1):132–52.
16. King CK, Glass R, Bresee JS, Duggan C. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. MMWR Recomm Rep. 2003;52(RR-16):1–16.
17. American Academy of Pediatrics. Provisional committee on quality improvement, subcommittee on acute gastroenteritis. Practice parameter: the management of acute gastroenteritis in young children. American Academy of Pediatrics, provisional committee on quality improvement, subcommittee on acute gastroenteritis. Pediatrics. 1996;97(3):424–35.
18. Friedman JN, Goldman RD, Srivastava R, Parkin PC. Development of a clinical dehydration scale for use in children between 1 and 36 months of age. J Pediatr. 2004;145(2):201–7.
19. Steiner MJ, DeWalt DA, Byerley JS. Is this child dehydrated? JAMA. 2004;291(22):2746–54.
20. Acute Gastroenteritis Guideline Team-Cincinnati Children's Hospital Medical Center. Evidence-based Care Guideline: Prevention and Management of Acute Gastroenteritis (AGE) in children age 2 mo to 18 yrs; 2011. p. 1–20. Available from: https://www.cincinnatichildrens.org/-/media/cincinnati%20childrens/home/service/j/anderson-center/evidence-based-care/recommendations/type/gastroenteritis-care-guideline.
21. National Collaborating Centre for Women's and Children's Health (UK). Diarrhoea and Vomiting Caused by Gastroenteritis: Diagnosis, Assessment and Management in Children Younger than 5 Years. London: National Institute for Health and Clinical Excellence: Guidance; 2009.
22. Shane AL, Mody RK, Crump JA, Tarr PI, Steiner TS, Kotloff K, et al. 2017 Infectious Diseases Society of America clinical practice guidelines for the diagnosis and Management of Infectious Diarrhea. Clin Infect Dis. 2017;65(12):1963–73.
23. Ramanan P, Bryson AL, Binnicker MJ, Pritt BS, Patel R. Syndromic panel-based testing in clinical microbiology. Clin Microbiol Rev. 2018;31(1):e00024–17.
24. Fang FC, Patel R. 2017 Infectious Diseases Society of America infectious diarrhea guidelines: a view from the clinical laboratory. Clin Infect Dis. 2017;65(12):1974–6.
25. Wessels E, Rusman LG, van Bussel MJ, Claas EC. Added value of multiplex Luminex gastrointestinal pathogen panel (xTAG(R) GPP) testing in the diagnosis of infectious gastroenteritis. Clin Microbiol Infect. 2014;20(3):O182–7.
26. Binnicker MJ. Multiplex molecular panels for diagnosis of gastrointestinal infection: performance, result interpretation, and cost-effectiveness. J Clin Microbiol. 2015;53(12):3723–8.
27. Corcoran MS, van Well GT, van Loo IH. Diagnosis of viral gastroenteritis in children: interpretation of real-time PCR results and relation to clinical symptoms. Eur J Clin Microbiol Infect Dis. 2014;33(10):1663–73.
28. Freeman K, Mistry H, Tsertsvadze A, Royle P, McCarthy N, Taylor-Phillips S, et al. Multiplex tests to identify gastrointestinal bacteria, viruses and parasites in people with suspected infectious gastroenteritis: a systematic review and economic analysis. Health Technol Assess. 2017;21(23):1–188.
29. Lo Vecchio A, Vandenplas Y, Benninga M, Broekaert I, Falconer J, Gottrand F, et al. An international consensus report on a new algorithm for the management of infant diarrhoea. Acta Paediatr. 2016;105(8):e384–9.
30. Piescik-Lech M, Shamir R, Guarino A, Szajewska H. Review article: the management of acute gastroenteritis in children. Aliment Pharmacol Ther. 2013;37(3):289–303.
31. Sandhu BK. Practical guidelines for the management of gastroenteritis in children. J Pediatr Gastroenterol Nutr. 2001;33(Suppl 2):S36–9.
32. Freedman SB, Willan AR, Boutis K, Schuh S. Effect of dilute apple juice and preferred fluids vs electrolyte maintenance solution on treatment failure among children with mild gastroenteritis: a randomized clinical trial. JAMA. 2016;315(18):1966–74.
33. Sandhu BK. Rationale for early feeding in childhood gastroenteritis. J Pediatr Gastroenterol Nutr. 2001;33(Suppl 2):S13–6.
34. Fedorowicz Z, Jagannath VA, Carter B. Antiemetics for reducing vomiting related to acute gastroenteritis in children and adolescents. Cochrane Database Syst Rev. 2011;9:CD005506.
35. Allen SJ, Okoko B, Martinez E, Gregorio G, Dans LF. Probiotics for treating infectious diarrhoea. Cochrane Database Syst Rev. 2004;2:CD003048.
36. Szajewska H, Guarino A, Hojsak I, Indrio F, Kolacek S, Shamir R, et al. Use of probiotics for management of acute gastroenteritis: a position paper by the ESPGHAN working Group for Probiotics and Prebiotics. J Pediatr Gastroenterol Nutr. 2014;58(4):531–9.
37. Johnston BC, Ma SS, Goldenberg JZ, Thorlund K, Vandvik PO, Loeb M, et al. Probiotics for the prevention of Clostridium difficile-associated diarrhea: a systematic review and meta-analysis. Ann Intern Med. 2012;157(12):878–88.
38. Committee on Infectious Diseases of the American Academy of Pediatrics. Prevention of rotavirus disease: updated guidelines for use of rotavirus vaccine. Pediatrics. 2009;123(5):1412–20.
39. Cortese MM, Parashar UD. Prevention of rotavirus gastroenteritis among infants and children: recommendations of the advisory committee on immunization practices (ACIP). MMWR Recomm Rep. 2009;58(RR-2):1–25.
40. Dennehy PH. Rotavirus infection: an update on management and prevention. Adv Pediatr Infect Dis. 2012;59(1):47–74.
41. WHO. The Treatment of diarrhoea: a manual for physicians and other senior health workers. 4th rev. edn; 2005. Geneva, Switzerland: World Health Organization. http://whqlibdoc.who.int/publications/2005/9241593180.pdf.

Recommended Additional Reading and Other Available Resources Including Clinical Practice Guidelines Grouped by Subtopic

Management of AGE

Shane AL, Mody RK, Crump JA, Tarr PI, Steiner TS, Kotloff K, Langley JM, Wanke C, Warren CA, Cheng AC, Cantey J, Pickering LK. 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the diagnosis and management of infectious diarrhea. Clinical Infect Dis. 2017;65(12):e45–80. https://doi.org/10.1093/cid/cix669.

Guarino A, Ashkenazi S, Gendrel D, Lo Vecchio A, Shamir R, Szajewska H. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/European Society for Pediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe: update 2014. J Pediatr Gastroenterol Nutr. 2014;59:132–52.

Acute Gastroenteritis Guideline Team, Cincinnati Children's Hospital Medical Center. Evidence-based care guideline: prevention and management of acute gastroenteritis (AGE) in children age 2 mo to 18 yrs. 2011. Available from: https://www.cincinnatichildrens.org/-/media/cincinnati%20childrens/home/service/j/anderson-center/evidence-based-care/recommendations/type/gastroenteritis-care-guideline.

National Collaborating Centre for Women's and Children's Health. Diarrhoea and vomiting caused by gastroenteritis: diagnosis, assessment and management in children younger than 5 years. Commissioned by the National Institute for Health and Clinical Excellence, 2009; available: https://www.nice.org.uk/guidance/cg84.

King CK, Glass R, Bresee JS, Duggan C. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. MMWR Recomm Rep. 2003;52:1–16.

American Academy of Pediatrics, Provisional Committee on Quality Improvement, Subcommittee on Acute Gastroenteritis. Practice parameter: the management of acute gastroenteritis in young children. Pediatrics. 1996;97:424.

Use of Ondansetron for Infectious Gastroenteritis

National Collaborating Centre for Women's and Children's Health. Management of vomiting in children and young people with gastroenteritis: Ondansetron. Commissioned by the National Institute for Health and Clinical Excellence; available: https://www.nice.org.uk/advice/esuom34/chapter/Key-points-from-the-evidence.

Cheng A. Emergency department use of oral ondansetron for acute gastroenteritis-related vomiting in infants and children. Paediatr Child Health. 2011;16(3):177–9.

Use of Probiotics for Infectious Gastroenteritis

Szajewska H. What are the indications for using probiotics in children? Arch Dis Child. 2016;101:398–403.

Thomas DW, Greer FR, American Academy of Pediatrics Committee on Nutrition; American Academy of Pediatrics Section on Gastroenterology, Hepatology, and Nutrition. Probiotics and prebiotics in pediatrics. Pediatrics. 2010;126:1217–31.