ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults

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Abstract

Acute diarrheal infections are a common health problem globally and among both individuals in the United States and traveling to developing world countries. Multiple modalities including antibiotic and non-antibiotic therapies have been used to address these common infections. Information on treatment, prevention, diagnostics, and the consequences of acute diarrhea infection has emerged and helps to inform clinical management. In this ACG Clinical Guideline, the authors present an evidence-based approach to diagnosis, prevention, and treatment of acute diarrhea infection in both US-based and travel settings.

Introduction

Acute diarrheal infection is a leading cause of outpatient visits, hospitalizations, and lost quality of life occurring in both domes- tic settings and among those traveling abroad. The Centers for Disease Control and Prevention has estimated 47.8 million cases occurring annually in the United States, at an estimated cost upwards of US$150 million to the health-care economy (1,2). Acute diarrhea can be defined as the passage of a greater number of stools of decreased form from the normal lasting <14 days. Some definitions require an individual to present with an abrupt onset 3 or more loose or liquid stools above baseline in a 24-h period to meet the criteria of acute diarrhea. Persistent diarrhea is typically defined as diarrhea lasting between 14 and 30 days, with chronic diarrhea generally considered as diarrheal symptoms lasting for greater than a month. Acute diarrhea of infectious etiology is generally associated with other clinical features suggesting enteric involvement including nausea, vomiting, abdominal pain and cramps, bloating, flatulence, fever, passage of bloody stools, tenesmus, and fecal urgency. Acute diarrheal infection is also often referred to as gastroenteritis, and some acute gastro- intestinal infections may cause a vomiting predominant illness with little or no diarrhea.

This guideline provides recommendations for the diagnosis, management, and prevention of acute gastrointestinal infection focusing primarily on immune-competent adult individuals and does not consider *Clostridium difficile*-associated infections, which has recently been reviewed in a separate American College of Gastroenterology (ACG) Clinical Guideline (3). It replaces a previously published ACG Guideline on the same topic (4), and supplements previously published Infectious Disease Society of America (IDSA) (5), and World Gastroenterology Organization guidelines (6). This guideline is structured into five sections of clinical focus to include epidemiology and population health, diagnosis, treatment of acute disease, evaluation of persisting symptoms, and prevention. To support the guideline development, a comprehensive literature search on acute diarrheal infection in adults was performed across multiple databases. A medical library information specialist searched the Ovid MEDLINE and EMBASE databases for relevant articles on 18 February 2015, using the following main

terms (with synonyms and closely related words): “diarrhea” AND “acute disease,” “infectious diarrhea”, “dysentery,” or “acute gastroenteritis.” The searches were limited to English language articles published in the past 10 years and excluded case reports, and child or animal studies. Details of the search methodologies are provided in the **Appendix**. Additional articles were obtained from review of references from retrieved articles, as well as articles that were known to authors.

Each section presents key recommendations followed by a summary of the evidence (**Figure 1** and **Table 1**). The GRADE system was used to grade the strength of our recommendations and the quality of the evidence (7). The strength of a recommendation is graded as “strong,” when the evidence shows the benefit of the intervention or treatment clearly outweighs any risk, and as “conditional,” when uncertainty exists about the risk–benefit ratio. The quality of the evidence is graded as follows: “high,” if further research is unlikely to change our confidence in the estimate of the effect; “moderate,” if further research is likely to have an important impact and may change the estimate; “low,” if further research is very likely to change the estimate; “very low,” if an effect is very uncertain (8).

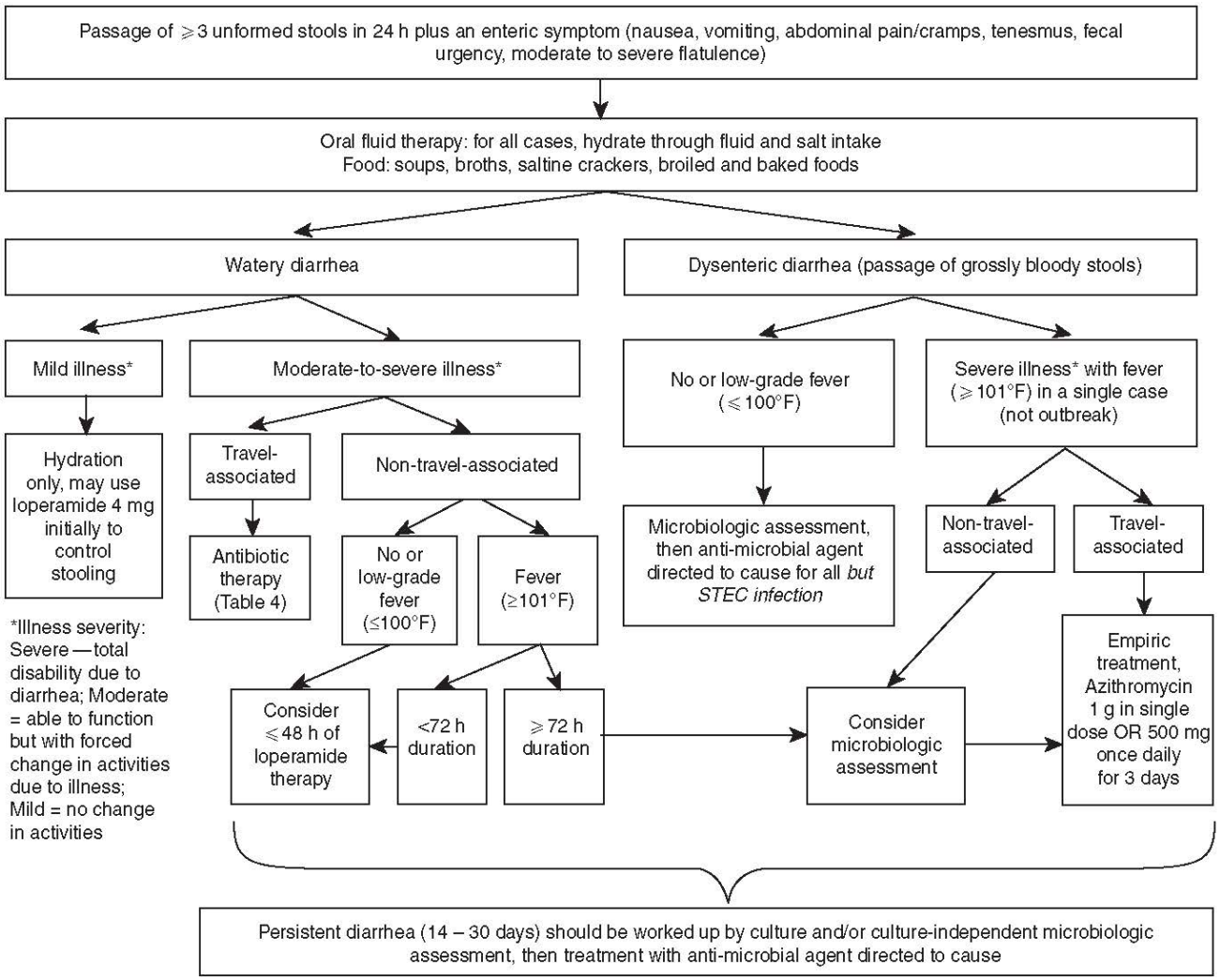

Figure 1. Approach to empiric therapy and diagnostic-directed management of the adult patient with acute diarrhea (suspect infectious etiology).

Table 1. Summary and strength of recommendations	
Epidemiology and public health	
1.	Diagnostic evaluation using stool culture and culture-independent methods if available should be used in situations where the individual patient is at high risk of spreading disease to others, and during known or suspected outbreaks. (Strong recommendation, low level of evidence)
Diagnosis	
2.	Stool diagnostic studies may be used if available in cases of dysentery, moderate–severe disease, and symptoms lasting >7 days to clarify the etiology of the patient's illness and enable specific directed therapy.(Strong recommendation, very low level of evidence)
3.	Traditional methods of diagnosis (bacterial culture, microscopy with and without special stains and immunofluorescence, and antigen testing) fail to reveal the etiology of the majority of cases of acute diarrheal infection. If available, the use of FDA-approved culture-independent methods of diagnosis can be recommended at least as an adjunct to traditional methods. (Strong recommendation, low level of evidence)
4.	Antibiotic sensitivity testing for management of the individual with acute diarrheal infection is currently not recommended. (Strong recommendation, very low level of evidence)
Treatment of acute disease	
5.	The usage of balanced electrolyte rehydration over other oral rehydration options in the elderly with severe diarrhea or any traveler with cholera-like watery diarrhea is recommended. Most individuals with acute diarrhea or gastroenteritis can keep up with fluids and salt by consumption of water, juices, sports drinks, soups, and saltine crackers. (Strong recommendation, moderate level of evidence)
6.	The use of probiotics or prebiotics for the treatment of acute diarrhea in adults is not recommended, except in cases of postantibiotic-associated illness. (Strong recommendation, moderate level of evidence)
7.	Bismuth subsalicylates can be administered to control rates of passage of stool and may help travelers function better during bouts of mild-to-moderate illness. (Strong recommendation, high level of evidence)
8.	In patients receiving antibiotics for traveler's diarrhea, adjunctive loperamide therapy should be administered to decrease duration of diarrhea and increase chance for a cure. (Strong recommendation, moderate level of evidence)
9.	The evidence does not support empiric anti-microbial therapy for routine acute diarrheal infection, except in cases of TD where the likelihood of bacterial pathogens is high enough to justify the potential side effects of antibiotics. (Strong recommendation, high level of evidence)
10.	Use of antibiotics for community-acquired diarrhea should be discouraged as epidemiological studies suggest that most community-acquired diarrhea is viral in origin (norovirus, rotavirus, and adenovirus) and is not shortened by the use of antibiotics. (Strong recommendation, very low-level evidence)

Table 1. Summary and strength of recommendations *continued*	
Evaluation of persisting symptoms	
11.	Serological and clinical lab testing in individuals with persistent diarrheal symptoms (between 14 and 30 days) are not recommended. (Strong recommendation, very low level of evidence)
12.	Endoscopic evaluation is not recommended in individuals with persisting symptoms (between 14 and 30 days) and negative stool work-up. (Strong recommendation, very low level of evidence)
Prevention	
13.	Patient level counseling on prevention of acute enteric infection is not routinely recommended but may be considered in the individual or close contacts of the individual who is at high risk for complications. (Conditional, very low level of evidence)
14.	Individuals should undergo pretravel counseling regarding high-risk food/beverage avoidance to prevent traveler's diarrhea. (Conditional, very low level of evidence)
15.	Frequent and effective hand washing and alcohol-based hand sanitizers are of limited value in preventing most forms of traveler's diarrhea but may be useful where low-dose pathogens are responsible for the illness as for an example during a cruise ship outbreak of norovirus infection, institutional outbreak, or in endemic diarrhea prevention. (Conditional recommendation, low level of evidence)
Prophylaxis	
16.	Bismuth subsalicylates have moderate effectiveness and may be considered for travelers who do not have any contraindications to use and can adhere to the frequent dosing requirements. (Strong recommendation, high level of evidence)
17.	Probiotics, prebiotics, and synbiotics for prevention of TD are not recommended. (Conditional recommendation, low level of evidence)
18.	Antibiotic chemoprophylaxis has moderate to good effectiveness and may be considered in high-risk groups for short-term use. (Strong recommendation, high level of evidence)
TD, traveler's diarrhea.	

Table 2. FDA-approved laboratory tests for enteric pathogens							
Manufacturer	**Test system**	**Platform**	**Pathogens detected**		**Detection time (h)**	**FDA-approved**	**Date-approved**
			Type	**No.**			
Luminex	GPP	xTAG	B, V, P	15	<5	Yes	15/01/13
Hologic/Gen-Probe	ProGastro SSCS	—	B	4	4	Yes	22/01/13
BD Diagnostics	EBP	BD MAX	B	4	3–4	Yes	02/04/13
Biofire Diagnostics	GI Panel	FilmArray	B, V, P	22	1–2	Yes	05/05/14
Nanosphere	EP	Verigene	B	6	2	Yes	24/06/14
B, bacteria; FDA, Food and Drug Administration; P, parasite; V, viral.							

Table 3. Randomized double-blind placebo-controlled trials evaluating probiotics in treatment effectiveness of acute diarrhea

Study author	Year	Location	Clinical Setting	N	Eligibility	Intervention	Outcomes	Ref.
Bruno	1981	Italy	In-patient	49	Acute enteritis (non-typhoid)	*Enterococcus* LAB SF68 (Bioflorin: ≥75×10^6 three times daily for 10 days). Placebo comparator	•[P] diarrhea ≥4 days: EXP 2/25 vs. PLAC 11/24 •[P] diarrhea ≥3 days: EXP 6/25 vs. 17/24	(84)
Bruno	1983	Italy	In-patient	21	Acute febrile enteritis (non-typhoid)	*Enterococcus* LAB SF68 (Bioflorin: ≥75×10^6 three times daily for 10 days). Placebo comparator	•[P] diarrhea ≥4 days: EXP 1/10 vs. PLAC 7/11 •[P] diarrhea ≥3 days: EXP 3/10 vs. PLAC 7/11	(85)
Buydens	1996	Belgium	In-patient and outpatient	185	Acute watery diarrhea	*Enterococcus* LAB SF68 (Bioflorin: ≥75×10^6 three times daily for ≥6 days). Placebo comparator	•[P] diarrhea ≥4 days: EXP 7/93 vs. PLAC 61/92 •[P] diarrhea ≥3 days: EXP 57/93 vs. PLAC 88/92 •Mean (s.d.) freq. on day 3: EXP 1.1(0.3) vs. PLAC 2.5 (1.3)	(86)
Hochter	1990	Germany	Outpatient	92	Acute diarrhea (exclusion; no antibiotics)	S. boulardii (600 mg/day for 2 days then 300 mg/day on days 3 to 7. Placebo comparator	•Mean (s.d.) freq. on day 3: EXP 2.4 (2.1) vs. PLAC 3.0 (2.8)	(89)
Mitra	1990	Bangladesh	Not described	183	V. cholera (n=114) or ETEC (n=41) infection	Streptococcus faecium SF68 containing 1×10(9) of live SF68 or capsules of placebo containing killed SF68 (non-placebo) once every 8 h for 3 days.	V. cholera •Duration (h): EXP 80 vs. PLAC 80, P=0.96 •Cumulative volume 48 h (ml/kg body wt) EXP 395.5 vs. PLAC 286.5, P=0.13 ETEC •Duration (h): EXP 24 vs. PLAC 24, P=0.62 •Cumulative volume 48 h (ml/kg body wt) EXP 57.5 vs. PLAC 76.4, P=0.42	(88)
Wunderlich	1989	Switzerland and Lichtenstein	Not described	78	Acute diarrhea (exclusions not stated)	*Enterococcus* LAB SF68 (Bioflorin: 225×10^6 three times daily for 7 days). Placebo comparator	•[P] diarrhea ≥4 days: EXP11/40 vs. PLAC 23/38 •[P] diarrhea ≥3 days: EXP 19/40 vs. PLAC 27/38	(87)

ETEC, enterotoxigenic E. coli; EXP, active treatment group; [P], probability; PLAC, placebo group; s.d., standard deviation.

Table 4. Acute diarrhea antibiotic treatment recommendations		
Antibiotic[a]	**Dose**	**Treatment duration**
Levofloxacin	500 mg by mouth	Single dose[b] or 3-day course
Ciprofloxacin	750 mg by mouth or	Single dose[b]
	500 mg by mouth	3-day course
Ofloxacin	400 mg by mouth	Single dose[b] or 3-day course
Azithromycin[c,d]	1,000 mg by mouth or	Single dose[b]
	500 mg by mouth	3-day course[d]
Rifaximin[e]	200 mg by mouth three times daily	3-days

ETEC, Enterotoxigenic Escherichia coli.
[a]Antibiotic regimens may be combined with loperamide, 4 mg first dose, and then 2 mg dose after each loose stool, not to exceed 16 mg in a 24-h period.
[b]If symptoms are not resolved after 24 h, complete a 3-day course of antibiotics.
[c]Use empirically as first line in Southeast Asia and India to cover fluoroquinolone-resistant Campylobacter or in other geographical areas if Campylobacter or resistant ETEC are suspected.
[d]Preferred regimen for dysentery or febrile diarrhea.
[e]Do not use if clinical suspicion for Campylobacter, Salmonella, Shigella, or other causes of invasive diarrhea.