

# Acute Diarrhea in Adults

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Acute diarrhea in adults is a common problem encountered by family physicians. The most common etiology is viral gastroenteritis, a self-limited disease. Increases in travel, comorbidities, and foodborne illness lead to more bacteria-related cases of acute diarrhea. A history and physical examination evaluating for risk factors and signs of inflammatory diarrhea and/or severe dehydration can direct any needed testing and treatment. Most patients do not require laboratory workup, and routine stool cultures are not recommended. Treatment focuses on preventing and treating dehydration. Diagnostic investigation should be reserved for patients with severe dehydration or illness, persistent fever, bloody stool, or immunosuppression, and for cases of suspected nosocomial infection or outbreak. Oral rehydration therapy with early refeeding is the preferred treatment for dehydration. Antimotility agents should be avoided in patients with bloody diarrhea, but loperamide/simethicone may improve symptoms in patients with watery diarrhea. Probiotic use may shorten the duration of illness. When used appropriately, antibiotics are effective in the treatment of shigellosis, campylobacteriosis, *Clostridium difficile*, traveler's diarrhea, and protozoal infections. Prevention of acute diarrhea is promoted through adequate hand washing, safe food preparation, access to clean water, and vaccinations. (*Am Fam Physician*. 2014;89(3):180-189. Copyright © 2014 American Academy of Family Physicians.)

**CME** This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 173.

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► **Patient information:** A handout on this topic, written by the authors of this article, is available at <http://www.aafp.org/afp/2014/0201/p180-s1>.

Acute diarrhea is defined as stool with increased water content, volume, or frequency that lasts less than 14 days.<sup>1</sup> Diarrheal illness accounts for 2.5 million deaths per year worldwide.<sup>2</sup> In the United States, an estimated 48 million foodborne diarrheal illnesses occur annually, resulting in more than 128,000 hospitalizations and 3,000 deaths.<sup>3,4</sup> In the developing world, infectious causes of acute diarrhea are largely related to contaminated food and water supplies.<sup>5</sup> In the developed world, technological progress and an increase in mass production of food have paradoxically contributed to the persistence of foodborne illness, despite higher standards of food production.<sup>6</sup>

## Differential Diagnosis

Infectious causes of acute diarrhea include viruses, bacteria, and, less often, parasites. Noninfectious causes include medication adverse effects, acute abdominal processes, gastroenterologic disease, and endocrine disease.

Clinically, acute infectious diarrhea is classified into two pathophysiologic syndromes, commonly referred to as noninflammatory (mostly viral, milder disease) and inflammatory (mostly invasive or with toxin-producing bacteria, more severe disease).<sup>7,8</sup> *Table 1*

compares noninflammatory and inflammatory acute infectious diarrhea.<sup>7,8</sup>

Viral infections are the most common cause of acute diarrhea.<sup>9</sup> Bacterial infections are more often associated with travel, comorbidities, and foodborne illness. When a specific organism is identified, the most common causes of acute diarrhea in the United States are *Salmonella*, *Campylobacter*, *Shigella*, and Shiga toxin-producing *Escherichia coli* (enterohemorrhagic *E. coli*).<sup>10</sup> The Centers for Disease Control and Prevention provides a comprehensive list of foodborne illnesses at <http://www.cdc.gov/foodsafety/diseases>.

## History and Physical Examination

### HISTORY

The onset, duration, severity, and frequency of diarrhea should be noted, with particular attention to stool character (e.g., watery, bloody, mucus-filled, purulent, bilious). The patient should be evaluated for signs of dehydration, including decreased urine output, thirst, dizziness, and change in mental status. Vomiting is more suggestive of viral illness or illness caused by ingestion of a preformed bacterial toxin. Symptoms more suggestive of invasive bacterial (inflammatory) diarrhea include fever, tenesmus, and grossly bloody stool.<sup>11</sup>

**Table 1. Noninflammatory vs. Inflammatory Diarrheal Syndromes**

Factor	Noninflammatory	Inflammatory
Etiology	Usually viral, but can be bacterial or parasitic	Generally invasive or toxin-producing bacteria
Pathophysiology	More likely to promote intestinal secretion without significant disruption in the intestinal mucosa	More likely to disrupt mucosal integrity, which may lead to tissue invasion and destruction
History and examination findings	Nausea, vomiting; normothermia; abdominal cramping; larger stool volume; nonbloody, watery stool	Fever, abdominal pain, tenesmus, smaller stool volume, bloody stool
Laboratory findings	Absence of fecal leukocytes	Presence of fecal leukocytes
Common pathogens	Enterotoxigenic <i>Escherichia coli</i> , <i>Clostridium perfringens</i> , <i>Bacillus cereus</i> , <i>Staphylococcus aureus</i> , <i>Rotavirus</i> , <i>Norovirus</i> , <i>Giardia</i> , <i>Cryptosporidium</i> , <i>Vibrio cholerae</i>	<i>Salmonella</i> (non-Typhi species), <i>Shigella</i> , <i>Campylobacter</i> , Shiga toxin-producing <i>E. coli</i> , enteroinvasive <i>E. coli</i> , <i>Clostridium difficile</i> , <i>Entamoeba histolytica</i> , <i>Yersinia</i>
Other	Generally milder disease Severe fluid loss can still occur, especially in malnourished patients	Generally more severe disease

Information from references 7 and 8.

A food and travel history is helpful to evaluate potential exposures. Children in day care, nursing home residents, food handlers, and recently hospitalized patients are at high risk of infectious diarrheal illness. Pregnant women have a 12-fold increased risk of listeriosis,<sup>12</sup> which is primarily contracted by consuming cold meats, soft cheeses, and raw milk.<sup>13</sup> Recent sick contacts and use of antibiotics and other medications should be noted in patients with acute diarrhea. Sexual practices that include receptive anal and oral-anal contact increase the possibility of direct rectal inoculation and fecal-oral transmission.

The history should also include gastroenterologic disease or surgery; endocrine disease; radiation to the pelvis; and factors that increase the risk of immunosuppression, including human immunodeficiency virus infection, long-term steroid use, chemotherapy, and immunoglobulin A deficiency. History findings associated with causes of diarrhea are summarized in *Table 2*,<sup>1,7,8,14,15</sup> and clinical features by pathogen are summarized in *Table 3*.<sup>1,14</sup>

#### PHYSICAL EXAMINATION

The primary goal of the physical examination is to assess the patient's degree of dehydration. Generally ill appearance, dry mucous membranes, delayed capillary refill time, increased heart rate, and abnormal orthostatic vital signs can be helpful in identifying more severe dehydration. Fever is more suggestive of inflammatory

diarrhea. The abdominal examination is important to assess for pain and acute abdominal processes. A rectal examination may be helpful in assessing for blood, rectal tenderness, and stool consistency.

#### Diagnostic Testing

Because most watery diarrhea is self-limited, testing is usually not indicated.<sup>1,16</sup> In general, specific diagnostic investigation can be reserved for patients with severe dehydration, more severe illness, persistent fever, bloody stool, or immunosuppression, and for cases of suspected nosocomial infection or outbreak.

#### OCCULT BLOOD

It is unclear how much fecal occult blood testing affects pretest probability. Nevertheless, it is a rapid and inexpensive test, and when tests are positive for fecal occult blood in conjunction with the presence of fecal leukocytes or lactoferrin, the diagnosis of inflammatory diarrhea is more common.<sup>17</sup> Of note, fecal occult blood testing is 71% sensitive and 79% specific for inflammatory diarrhea in developed countries, but the sensitivity drops to 44% and specificity to 72% in developing countries.<sup>18</sup>

#### LEUKOCYTES AND LACTOFERRIN

Testing stool for leukocytes to screen for inflammatory diarrhea poses several challenges, including the handling of specimens and the standardization of laboratory processing and interpretation. There is a wide variability

**Table 2. Clues to the Diagnosis of Acute Diarrhea**

<i>History</i>	<i>Potential pathogen/etiology</i>
Afebrile, abdominal pain with bloody diarrhea	Shiga toxin–producing <i>Escherichia coli</i>
Bloody stools	<i>Salmonella</i> , <i>Shigella</i> , <i>Campylobacter</i> , Shiga toxin–producing <i>E. coli</i> , <i>Clostridium difficile</i> , <i>Entamoeba histolytica</i> , <i>Yersinia</i>
Camping, consumption of untreated water	<i>Giardia</i>
Consumption of food commonly associated with foodborne illness	
Fried rice	<i>Bacillus cereus</i>
Raw ground beef or seed sprouts	Shiga toxin–producing <i>E. coli</i> (e.g., <i>E. coli</i> O157:H7)
Raw milk	<i>Salmonella</i> , <i>Campylobacter</i> , Shiga toxin–producing <i>E. coli</i> , <i>Listeria</i>
Seafood, especially raw or undercooked shellfish	<i>Vibrio cholerae</i> , <i>Vibrio parahaemolyticus</i>
Undercooked beef, pork, or poultry	<i>Staphylococcus aureus</i> , <i>Clostridium perfringens</i> , <i>Salmonella</i> , <i>Listeria</i> (beef, pork, poultry), Shiga toxin–producing <i>E. coli</i> (beef and pork), <i>B. cereus</i> (beef and pork), <i>Yersinia</i> (beef and pork), <i>Campylobacter</i> (poultry)
Exposure to day care centers	<i>Rotavirus</i> , <i>Cryptosporidium</i> , <i>Giardia</i> , <i>Shigella</i>
Fecal-oral sexual contact	<i>Shigella</i> , <i>Salmonella</i> , <i>Campylobacter</i> , protozoal disease
Hospital admission	<i>C. difficile</i> , treatment adverse effect
Human immunodeficiency virus infection, immunosuppression	<i>Cryptosporidium</i> , Microsporida, <i>Isospora</i> , <i>Cytomegalovirus</i> , <i>Mycobacterium avium-intracellulare</i> complex, <i>Listeria</i>
Medical conditions associated with diarrhea	Endocrine: Hyperthyroidism, adrenocortical insufficiency, carcinoid tumors, medullary thyroid cancer Gastrointestinal: Ulcerative colitis, Crohn disease, irritable bowel syndrome, celiac disease, lactose intolerance, ischemic colitis, colorectal cancer, short bowel syndrome, malabsorption, gastrinoma, VIPoma, bowel obstruction, constipation with overflow Other: Appendicitis, diverticulitis, human immunodeficiency virus infection, systemic infections, amyloidosis, adnexitis
Medications or other therapies associated with diarrhea	Antibiotics (especially broad-spectrum), laxatives, antacids (magnesium- or calcium-based), chemotherapy, colchicine, pelvic radiation therapy Less common: Proton pump inhibitors, mannitol, nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, cholesterol-lowering medications, lithium
Persistent diarrhea with weight loss	<i>Giardia</i> , <i>Cryptosporidium</i> , <i>Cyclospora</i>
Pregnancy	<i>Listeria</i>
Recent antibiotic use	<i>C. difficile</i>
Receptive anal intercourse, with or without rectal pain or proctitis	Herpes simplex virus infection, chlamydia, gonorrhea, syphilis
Rectal pain or proctitis	<i>Campylobacter</i> , <i>Salmonella</i> , <i>Shigella</i> , <i>E. histolytica</i> , <i>C. difficile</i> , <i>Giardia</i>
Rice-water stools	<i>V. cholerae</i>
Several persons with common food exposure have acute onset of symptoms	Food poisoning with preformed toxins Onset of symptoms within 6 hours: <i>Staphylococcus</i> , <i>B. cereus</i> (typically causes vomiting) Onset of symptoms within 8 to 16 hours: <i>C. perfringens</i> type A (typically causes diarrhea)
Travel to a developing country	Enterotoxigenic <i>E. coli</i> is most common Many other pathogens (e.g., <i>Shigella</i> , <i>Salmonella</i> , <i>E. histolytica</i> , <i>Giardia</i> , <i>Cryptosporidium</i> , <i>Cyclospora</i> , enteric viruses) are possible because of poorly cleaned or cooked food, or fecal contamination of food or water

Information from references 1, 7, 8, 14, and 15.

**Table 3. Clinical Features of Acute Diarrhea Caused by Select Pathogens**

Pathogen	Fever	Abdominal pain	Nausea, vomiting, or both	Fecal evidence of inflammation	Bloody stool	Heme-positive stools
<b>Bacterial</b>						
<i>Campylobacter</i>	Common	Common	Occurs	Common	Occurs	Variable
<i>Clostridium difficile</i>	Occurs	Occurs	Not common	Common	Occurs	Occurs
<i>Salmonella</i>	Common	Common	Occurs	Common	Occurs	Variable
Shiga toxin-producing <i>Escherichia coli</i>	Not common	Common	Occurs	Not common	Common	Common
<i>Shigella</i>	Common	Common	Common	Common	Occurs	Variable
<i>Vibrio</i>	Variable	Variable	Variable	Variable	Variable	Variable
<i>Yersinia</i>	Common	Common	Occurs	Occurs	Occurs	Occurs
<b>Parasitic</b>						
<i>Cryptosporidium</i>	Variable	Variable	Occurs	None to mild	Not common	Not common
<i>Cyclospora</i>	Variable	Variable	Occurs	Not common	Not common	Not common
<i>Entamoeba histolytica</i>	Occurs	Occurs	Variable	Variable	Variable	Common
<i>Giardia</i>	Not common	Common	Occurs	Not common	Not common	Not common
<b>Viral</b>						
Norovirus	Variable	Common	Common	Not common	Not common	Not common

Information from references 1 and 14.

in sensitivity and specificity. Therefore, this testing has fallen out of favor.<sup>18</sup>

Lactoferrin is a marker for leukocytes that is released by damaged or deteriorating cells, and increases in the setting of bacterial infections.<sup>19</sup> Commercially available immunoassay testing kits are a more precise and less variable method for specimen analysis compared with fecal leukocytes, with a sensitivity greater than 90% and a specificity greater than 70%.<sup>20</sup> Although there is some debate as to whether fecal lactoferrin is clearly superior to fecal leukocytes, the speed and simplicity of lactoferrin testing make it the preferred method to screen for the presence of leukocytes when indicated.<sup>21</sup>

### STOOL CULTURES

The indiscriminate use of stool cultures in the evaluation of acute diarrhea is inefficient (results are positive in only 1.6% to 5.6% of cases)<sup>1</sup> and expensive, with an estimated cost of \$900 to \$1,200 per positive stool culture.<sup>22</sup> Obtaining cultures only in patients with screening tests positive for leukocytes decreases the cost to \$150 per positive culture.<sup>23</sup> Obtaining cultures only in patients with grossly bloody stools increases the yield for positive culture results to greater than 30%.<sup>24</sup>

Although there is no consensus on which patients need a culture, it is reasonable to perform a culture if the patient has grossly bloody stool, severe dehydration, signs of inflammatory disease, symptoms lasting more than three to seven days, or immunosuppression.<sup>25,26</sup> Cultures are often obtained for traveler's diarrhea; however, empiric treatment is also an option.<sup>1,11</sup> In the hospital

setting, cultures should be reserved for the reasons listed above or if diarrhea begins more than three days after admission and there has been a nosocomial outbreak, the patient has human immunodeficiency virus infection or neutropenia, or the patient is older than 65 years with significant comorbidity (e.g., end-stage liver, renal, or pulmonary disease; leukemia hemiparesis caused by cardiovascular accident; inflammatory bowel disease).<sup>25</sup>

### CLOSTRIDIUM DIFFICILE TESTING

Testing for *Clostridium difficile* toxins A and B is recommended for patients who develop unexplained diarrhea after three days of hospitalization; the test will be positive in 15% to 20% of these patients.<sup>25,27</sup> Furthermore, the risk of contracting *C. difficile* infection increases by seven to 10 times throughout any period of antibiotic treatment and for the first month after antibiotic discontinuation, and this risk is still three times higher in the second and third months after antibiotic discontinuation.<sup>28</sup> Therefore, testing for *C. difficile* toxins is also suggested in patients who develop unexplained diarrhea while using antibiotics or within three months of discontinuing antibiotics. *C. difficile* testing can be considered in certain populations with significant comorbidities, including older persons and those who are immunocompromised.

### OVA AND PARASITES

Routine analysis for ova and parasites in patients with acute diarrhea is not cost-effective, especially in developed countries.<sup>29</sup> Indications for ova and parasite testing

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include persistent diarrhea lasting more than seven days, especially if associated with infants in day care or travel to mountainous regions; diarrhea in persons with AIDS or men who have sex with men; community waterborne outbreaks; or bloody diarrhea with few fecal leukocytes.<sup>11</sup> The benefit of sending multiple samples to increase the test yield is debatable.

### ENDOSCOPY

The role of endoscopy in the diagnosis and management of acute diarrhea is limited. Endoscopic evaluation may be considered if the diagnosis is unclear after routine blood and stool tests, if empiric therapy is ineffective, or if symptoms persist.<sup>30</sup> Specifically, lower endoscopy with colonic biopsy and culture can be helpful in patients with diarrhea and suspected tuberculosis or diffuse colitis (as in *C. difficile* colitis) and in determining noninfectious causes of acute diarrhea, such as inflammatory bowel disease, ischemic colitis, enteropathy related to nonsteroidal anti-inflammatory drug use, and cancer.<sup>31</sup>

### Treatment

Figure 1 provides an algorithm for the treatment of acute diarrhea.<sup>1,14,20</sup>

### REHYDRATION THERAPY

The first step to treating acute diarrhea is rehydration, preferably oral rehydration.<sup>1</sup> The accumulated fluid deficit (calculated roughly as the difference between the patient's normal weight and his or her weight at presentation with diarrheal illness) must first be addressed. Next, the focus should turn to the replacement of ongoing losses and the continuation of maintenance fluids. An oral rehydration solution (ORS) must contain a mixture of salt and glucose in combination with water to best use the intestine's sodium-glucose coupled cellular transport mechanism.

In 2002, the World Health Organization endorsed an ORS with reduced osmolarity (250 mOsm per L or less compared with the prior standard of 311 mOsm per L). The reduced osmolarity ORS decreases stool outputs, episodes of emesis, and the need for intravenous rehydration,<sup>32</sup> without increasing hyponatremia, compared with the standard ORS.<sup>33</sup> A reduced osmolarity ORS can be roughly duplicated by mixing 1/2 teaspoon of salt, 6 teaspoons of sugar, and 1 liter of water. If oral rehydration is not feasible, intravenous rehydration may be necessary.

### FEEDING

Early refeeding decreases intestinal permeability caused by infections, reduces illness duration, and improves

nutritional outcomes.<sup>34,35</sup> This is particularly important in developing countries where underlying preexisting malnutrition is often a factor. Although the BRAT diet (bananas, rice, applesauce, and toast) and the avoidance of dairy are commonly recommended, supporting data for these interventions are limited. Instructing patients to refrain from eating solid food for 24 hours also does not appear useful.<sup>36</sup>

### ANTIDIARRHEAL MEDICATIONS

The antimotility agent loperamide (Imodium) may reduce the duration of diarrhea by as much as one day and increase the likelihood of clinical cure at 24 and 48 hours when given with antibiotics for traveler's diarrhea.<sup>37,38</sup> A loperamide/simethicone combination has demonstrated faster and more complete relief of acute nonspecific diarrhea and gas-related discomfort compared with either medication alone.<sup>39</sup>

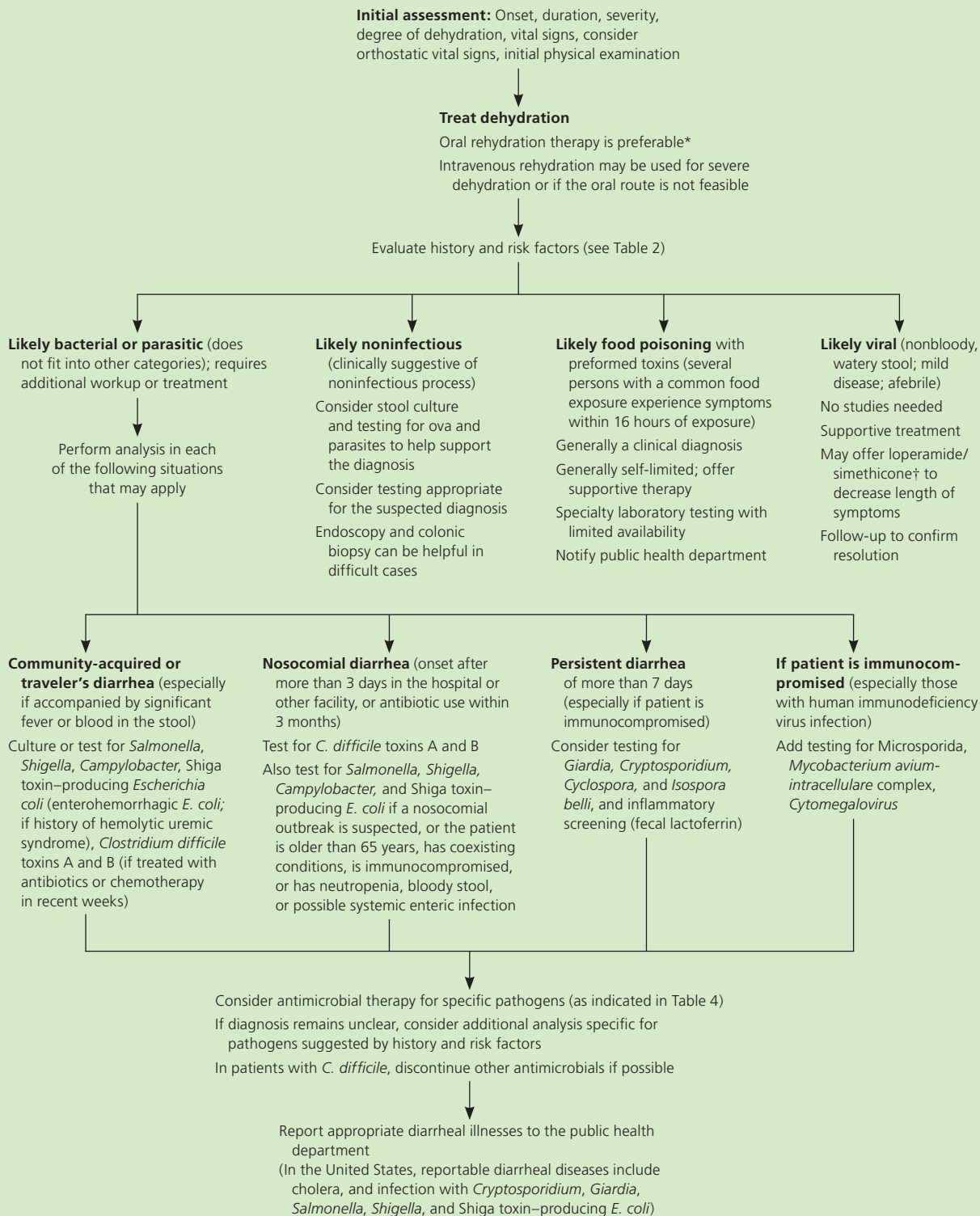
Loperamide may cause dangerous prolongation of illness in patients with some forms of bloody or inflammatory diarrhea and, therefore, should be restricted to patients with nonbloody stool.<sup>40</sup> The antisecretory drug bismuth subsalicylate (Pepto-Bismol) is a safe alternative in patients with fever and inflammatory diarrhea. There is inadequate evidence to recommend the use of the absorbents kaolin/pectin, activated charcoal, or attapulgite (no longer available in the United States). The antisecretory drug racecadotril, widely used in Europe but unavailable in the United States, appears to be more tolerable and as effective as loperamide.<sup>41</sup>

### ANTIBIOTIC THERAPY

Because acute diarrhea is most often self-limited and caused by viruses, routine antibiotic use is not recommended for most adults with nonsevere, watery diarrhea. Additionally, the overuse of antibiotics can lead to resistance (e.g., *Campylobacter*), harmful eradication of normal flora, prolongation of illness (e.g., superinfection with *C. difficile*), prolongation of carrier state (e.g., delayed excretion of *Salmonella*), induction of Shiga toxins (e.g., from Shiga toxin-producing *E. coli*), and increased cost.

However, when used appropriately, antibiotics are effective for shigellosis, campylobacteriosis, *C. difficile*, traveler's diarrhea, and protozoal infections. Antibiotic treatment of traveler's diarrhea (usually a quinolone) is associated with decreased severity of illness and a two- or three-day reduction in duration of illness.<sup>1,42</sup> If the patient's clinical presentation suggests the possibility of Shiga toxin-producing *E. coli* (e.g., bloody diarrhea, history of eating seed sprouts or rare ground beef, proximity

# Treatment of Acute Diarrhea



\*—Use the new World Health Organization reduced-osmolarity oral rehydration solution or a substitute. It can be roughly duplicated by mixing 1/2 teaspoon of salt, 6 teaspoons of sugar, and 1 liter of water.

†—Dosing for loperamide/simethicone: 2 tablets (2 mg of loperamide/125 mg of simethicone per tablet) followed by 1 additional tablet after each unformed stool, up to 4 tablets in 24 hours (3 doses).

**Figure 1.** Algorithm for the treatment of acute diarrhea.

Information from references 1, 14, and 20.

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to an outbreak), antibiotic use should be avoided because it may increase the risk of hemolytic uremic syndrome.<sup>43</sup> Conservative management without antibiotic treatment is less successful for diarrhea lasting more than 10 to 14 days, and testing and treatment for protozoal infections should be considered.<sup>1</sup> Antibiotics may be considered in patients who are older than 65 years, immunocompromised, severely ill, or septic. *Table 4* summarizes antibiotic therapy for acute diarrhea.<sup>1,14,16,44,45</sup>

### PROBIOTICS

Probiotics are thought to work by stimulating the immune system and competing for binding sites on intestinal epithelial cells. Their use in children with acute diarrhea is associated with reduced severity and duration of illness (an average of about one less day of illness).<sup>46</sup> Although many species are generally categorized as probiotics, even closely related strains may have different clinical effects. Effects of strain-specific probiotics need to be verified in adult studies before a specific evidence-based recommendation can be made.<sup>16</sup>

### ZINC SUPPLEMENTATION

Research in children suggests that zinc supplementation (20 mg per day for 10 days in children older than two months) may play a crucial role in treating and preventing acute diarrhea, particularly in developing countries. Studies demonstrate a decrease in the risk of dehydration, and in the duration and severity of the diarrheal episode by an estimated 20% to 40%.<sup>47</sup> Additional research is needed to evaluate potential benefits of zinc supplementation in the adult population.

### Prevention

Good hygiene, hand washing, safe food preparation, and access to clean water are key factors in preventing diarrheal illness.<sup>48</sup> Public health interventions to promote hand washing alone can reduce the incidence of diarrhea by about one-third.<sup>49</sup> Vaccine development remains a high priority for disease prevention,

**Table 4. Summary of Antibiotic Therapy for Acute Diarrhea**

<i>Organism</i>	<i>Therapy effectiveness</i>	<i>Preferred medication</i>
<b>Bacterial</b>		
<i>Campylobacter</i>	Proven in dysentery and sepsis Possibly effective in enteritis	Azithromycin (Zithromax), 500 mg once per day for 3 to 5 days
<i>Clostridium difficile</i>	Proven	Metronidazole (Flagyl), 500 mg three times per day for 10 days
Enteropathogenic/enteroinvasive <i>Escherichia coli</i>	Possible	Ciprofloxacin, 500 mg twice per day for 3 days
Enterotoxigenic <i>E. coli</i>	Proven	Ciprofloxacin, 500 mg twice per day for 3 days
<i>Salmonella</i> , non-Typhi species	Doubtful in enteritis Proven in severe infection, sepsis, or dysentery	—
Shiga toxin-producing <i>E. coli</i>	Controversial	No treatment
<i>Shigella</i>	Proven in dysentery	Ciprofloxacin, 500 mg twice per day for 3 days, or 2-g single dose
<i>Vibrio cholerae</i>	Proven	Doxycycline, 300-mg single dose
<i>Yersinia</i>	Not needed in mild disease or enteritis Proven in severe disease or bacteremia	—
<b>Protozoal</b>		
<i>Cryptosporidium</i>	Possible	Therapy may not be necessary in immunocompetent patients with mild disease or in patients with AIDS who have a CD4 cell count greater than 150 cells per mm <sup>3</sup>
<i>Cyclospora</i> or <i>Isoospora</i>	Proven	TMP/SMX DS, 160/800 mg twice per day for 7 to 10 days AIDS or immunosuppression: TMP/SMX DS, 160/800 mg twice to four times per day for 10 to 14 days, then three times weekly for maintenance
<i>Entamoeba histolytica</i>	Proven	Metronidazole, 750 mg three times per day for 5 to 10 days, plus paromomycin, 25 to 35 mg per kg per day in 3 divided doses for 5 to 10 days
<i>Giardia</i>	Proven	Metronidazole, 250 to 750 mg three times per day for 7 to 10 days
Microsporidia	Proven	Albendazole (Albenza), 400 mg twice per day for 3 weeks

DS = double strength; TMP/SMX = trimethoprim/sulfamethoxazole.

Information from references 1, 14, 16, 44, and 45.

Alternative medications	Comments
Erythromycin, 500 mg four times per day for 3 to 5 days Ciprofloxacin (Cipro), 500 mg twice per day for 5 to 7 days	Consider prolonged treatment if the patient is immunocompromised
Vancomycin, 125 mg four times per day for 10 days	If an antimicrobial agent is causing the diarrhea, it should be discontinued if possible
TMP/SMX DS, 160/800 mg twice per day for 3 days	—
TMP/SMX DS, 160/800 mg twice per day for 3 days Azithromycin, 500 mg per day for 3 days	Enterotoxigenic <i>E. coli</i> is the most common cause of traveler's diarrhea
Options for severe disease: Ciprofloxacin, 500 mg twice per day for 5 to 7 days TMP/SMX DS, 160/800 mg twice per day for 5 to 7 days Azithromycin, 500 mg per day for 5 to 7 days	In addition to patients with severe disease, it is appropriate to treat patients younger than 12 months or older than 50 years, and patients with a prosthesis, valvular heart disease, severe atherosclerosis, malignancy, or uremia Patients who are immunocompromised should be treated for 14 days
No treatment	The role of antibiotics is unclear; they are generally avoided because of their association with hemolytic uremic syndrome Antimotility agents should be avoided
Azithromycin, 500 mg twice per day for 3 days TMP/SMX DS, 160/800 mg twice per day for 5 days Ceftriaxone (Rocephin), 2- to 4-g single dose	Use of TMP/SMX is limited because of resistance Patients who are immunocompromised should be treated for 7 to 10 days
Azithromycin, 1-g single dose Tetracycline, 500 mg four times per day for 3 days TMP/SMX DS, 160/800 mg twice per day for 3 days	Doxycycline and tetracycline are not recommended in children because of possible tooth discoloration
Options for severe disease: Doxycycline combined with an aminoglycoside TMP/SMX DS, 160/800 mg twice per day for 5 days Ciprofloxacin, 500 mg twice per day for 7 to 10 days	—
Option for severe disease: Nitazoxanide (Alinia), 500 mg twice per day for 3 days (may offer longer treatment for refractory cases in patients with AIDS)	Highly active antiretroviral therapy, which achieves immune reconstitution, is adequate to eradicate intestinal disease in patients with AIDS
—	—
Tinidazole (Tindamax), 2 g per day for 3 days, plus paromomycin, 25 to 35 mg per kg per day in 3 divided doses for 5 to 10 days	If the patient has severe disease or extraintestinal infection, including hepatic abscess, serology will be positive
Tinidazole, 2-g single dose	Relapses may occur
—	Highly active antiretroviral therapy, which achieves immune reconstitution, is adequate to eradicate intestinal disease in patients with AIDS



## SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	References
In patients with acute diarrhea, stool cultures should be reserved for grossly bloody stool, severe dehydration, signs of inflammatory disease, symptoms lasting more than three to seven days, immunosuppression, and suspected nosocomial infections.	C	25, 26
Testing for <i>Clostridium difficile</i> toxins A and B should be performed in patients who develop unexplained diarrhea after three days of hospitalization.	C	25, 27
Routine testing for ova and parasites in acute diarrhea is not necessary in developed countries, unless the patient is in a high-risk group (i.e., diarrhea lasting more than seven days, especially if associated with infants in day care or travel to mountainous regions; diarrhea in patients with AIDS or men who have sex with men; community waterborne outbreaks; or bloody diarrhea with few fecal leukocytes).	C	11, 29
The first step to treating acute diarrhea is rehydration, preferably oral rehydration.	C	1
Combination loperamide/simethicone may provide faster and more complete relief of acute nonspecific diarrhea and gas-related discomfort than either medication alone.	B	39
Antibiotics (usually a quinolone) reduce the duration and severity of traveler's diarrhea.	A	42

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort>.

particularly for those in the developing world. Effective and safe vaccines exist for rotavirus, typhoid fever, and cholera, and are under investigation for *Campylobacter*, enterotoxigenic *E. coli*, and *Shigella* infections. To contain disease outbreaks, designated diseases should be reported to public health authorities. In the United States, reportable diarrheal illnesses include those caused by *Vibrio cholerae*, *Cryptosporidium*, *Giardia*, *Salmonella*, *Shigella*, and Shiga toxin-producing *E. coli*.

**Data Sources:** A literature search was completed in Medline via Ovid, EBSCOhost, DynaMed, Essential Evidence Plus, and the Cochrane Database of Systematic Reviews. Keywords were acute diarrhea, evaluation of acute diarrhea, *Clostridium difficile*, testing in acute diarrhea, and diagnostic testing in acute diarrhea. Search dates: March to April 2011, and December 2013.

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## REFERENCES

- Guerrant RL, Van Gilder T, Steiner TS, et al.; Infectious Diseases Society of America. Practice guidelines for the management of infectious diarrhea. *Clin Infect Dis*. 2001;32(3):331-351.
- Kosek M, Bern C, Guerrant RL. The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. *Bull World Health Organ*. 2003;81(3):197-204.
- Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States. *Emerg Infect Dis*. 2011;17(1):7-15.
- Scallan E, Griffin PM, Angulo FJ, Tauxe RV, Hoekstra RM. Foodborne illness acquired in the United States—unspecified agents. *Emerg Infect Dis*. 2011;17(1):16-22.
- DuPont HL. Diarrheal diseases in the developing world. *Infect Dis Clin North Am*. 1995;9(2):313-324.
- Hedberg CW, MacDonald KL, Osterholm MT. Changing epidemiology of food-borne disease: a Minnesota perspective. *Clin Infect Dis*. 1994;18(5):671-680.
- Aranda-Michel J, Giannella RA. Acute diarrhea: a practical review. *Am J Med*. 1999;106(6):670-676.
- Turgeon DK, Fritsche TR. Laboratory approaches to infectious diarrhea. *Gastroenterol Clin North Am*. 2001;30(3):693-707.
- Jones TF, Bulens SN, Gettner S, et al. Use of stool collection kits delivered to patients can improve confirmation of etiology in foodborne disease outbreaks. *Clin Infect Dis*. 2004;39(10):1454-1459.
- Centers for Disease Control and Prevention. Preliminary FoodNet data on the incidence of infection with pathogens transmitted commonly through food—10 states, 2009. *MMWR Morb Mortal Wkly Rep*. 2010; 59(14):418-422.
- DuPont HL. Guidelines on acute infectious diarrhea in adults. The Practice Parameters Committee of the American College of Gastroenterology. *Am J Gastroenterol*. 1997;92(11):1962-1975.
- Hof H. History and epidemiology of listeriosis. *FEMS Immunol Med Microbiol*. 2003;35(3):199-202.
- Janakiraman V. Listeriosis in pregnancy: diagnosis, treatment, and prevention. *Rev Obstet Gynecol*. 2008;1(4):179-185.
- Thielman NM, Guerrant RL. Clinical practice. Acute infectious diarrhea. *N Engl J Med*. 2004;350(1):38-47.
- Ilnyckyj A. Clinical evaluation and management of acute infectious diarrhea in adults. *Gastroenterol Clin North Am*. 2001;30(3):599-609.
- Farthing M, Salam MA, Lindberg G, et al.; World Gastroenterology Organisation. Acute diarrhea in adults and children: a global perspective. *J Clin Gastroenterol*. 2013;47(1):12-20.

17. Guerrant RL, Shields DS, Thorson SM, Schorling JB, Gröschel DH. Evaluation and diagnosis of acute infectious diarrhea. *Am J Med.* 1985; 78(6B):91-98.
18. Gill CJ, Lau J, Gorbach SL, Hamer DH. Diagnostic accuracy of stool assays for inflammatory bacterial gastroenteritis in developed and resource-poor countries. *Clin Infect Dis.* 2003;37(3):365-375.
19. Chen CC, Chang CJ, Lin TY, Lai MW, Chao HC, Kong MS. Usefulness of fecal lactoferrin in predicting and monitoring the clinical severity of infectious diarrhea. *World J Gastroenterol.* 2011;17(37):4218-4224.
20. Choi SW, Park CH, Silva TM, Zaenker EI, Guerrant RL. To culture or not to culture: fecal lactoferrin screening for inflammatory bacterial diarrhea. *J Clin Microbiol.* 1996;34(4):928-932.
21. Hayakawa T, Jin CX, Ko SB, Kitagawa M, Ishiguro H. Lactoferrin in gastrointestinal disease. *Intern Med.* 2009;48(15):1251-1254.
22. Guerrant RL, Wanke CA, Barrett LJ, Schwartzman JD. A cost effective and effective approach to the diagnosis and management of acute infectious diarrhea. *Bull N Y Acad Med.* 1987;63(6):484-499.
23. Gangarosa RE, Glass RI, Lew JF, Boring JR. Hospitalizations involving gastroenteritis in the United States, 1985: the special burden of the disease among the elderly. *Am J Epidemiol.* 1992;135(3):281-290.
24. Talan D, Moran GJ, Newdow M, et al.; EMERGency ID NET Study Group. Etiology of bloody diarrhea among patients presenting to United States emergency departments: prevalence of *Escherichia coli* O157:H7 and other enteropathogens. *Clin Infect Dis.* 2001;32(4):573-580.
25. Bauer TM, Lalvani A, Fehrenbach J, et al. Derivation and validation of guidelines for stool cultures for enteropathogenic bacteria other than *Clostridium difficile* in hospitalized adults. *JAMA.* 2001;285(3):313-319.
26. Manatsathit S, Dupont HL, Farthing M, et al.; Working Party of the Program Committee of the Bangkok World Congress of Gastroenterology 2002. Guideline for the management of acute diarrhea in adults. *J Gastroenterol Hepatol.* 2002;17(suppl):S54-S71.
27. Rohner P, Pittet D, Peppey B, Nije-Kinge T, Auckenthaler R. Etiological agents of infectious diarrhea: implications for requests for microbial culture. *J Clin Microbiol.* 1997;35(6):1427-1432.
28. Centers for Disease Control and Prevention. Vital signs: preventing *Clostridium difficile* infections. *MMWR Morb Mortal Wkly Rep.* 2012;61(9):157-162.
29. Siegel DL, Edelman PH, Nachamkin I. Inappropriate testing for diarrheal diseases in the hospital. *JAMA.* 1990;263(7):979-982.
30. Shen B, Khan K, Ikenberry SO, et al.; ASGE Standards of Practice Committee. The role of endoscopy in the management of patients with diarrhea. *Gastrointest Endosc.* 2010;71(6):887-892.
31. Bellaiche G, Le Pennec MP, Slama JL, et al. The value of rectosigmoidoscopy and the bacteriologic culture of colon biopsies in the etiologic diagnosis of acute diarrhea of adults. A prospective study of 65 patients [in French]. *Ann Gastroenterol Hepatol (Paris).* 1996;32(1):11-17.
32. Hahn S, Kim Y, Garner P. Reduced osmolarity oral rehydration solution for treating dehydration due to diarrhoea in children: systematic review. *BMJ.* 2001;323(7304):81-85.
33. Alam NH, Yunus M, Faruque AS, et al. Symptomatic hyponatremia during treatment of dehydrating diarrheal disease with reduced osmolarity oral rehydration solution. *JAMA.* 2006;296(5):567-573.
34. Duggan C, Nurko S. "Feeding the gut": the scientific basis for continued enteral nutrition during acute diarrhea. *J Pediatr.* 1997;131(6):801-808.
35. Gadewar S, Fasano A. Current concepts in the evaluation, diagnosis and management of acute infectious diarrhea. *Curr Opin Pharmacol.* 2005;5(6):559-565.
36. De Bruyn G. Diarrhea in adults (acute). *Am Fam Physician.* 2008;78(4):503-504.
37. Taylor DN, Sanchez JL, Candler W, Thornton S, McQueen C, Echeverria P. Treatment of travelers' diarrhea: ciprofloxacin plus loperamide compared with ciprofloxacin alone. A placebo-controlled, randomized trial. *Ann Intern Med.* 1991;114(9):731-734.
38. Riddle MS, Arnold S, Tribble DR. Effect of adjunctive loperamide in combination with antibiotics on treatment outcomes in traveler's diarrhea: a systematic review and meta-analysis. *Clin Infect Dis.* 2008;47(8):1007-1014.
39. Hanauer SB, DuPont HL, Cooper KM, Laudadio C. Randomized, double-blind, placebo-controlled clinical trial of loperamide plus simethicone versus loperamide alone and simethicone alone in the treatment of acute diarrhea with gas-related abdominal discomfort. *Curr Med Res Opin.* 2007;23(5):1033-1043.
40. DuPont HL, Hornick RB. Adverse effect of lomotil therapy in shigellosis. *JAMA.* 1973;226(13):1525-1528.
41. Matheson AJ, Noble S. Racecadotril. *Drugs.* 2000;59(4):829-835.
42. De Bruyn G, Hahn S, Borwick A. Antibiotic treatment for travellers' diarrhoea. *Cochrane Database Syst Rev.* 2000;(3):CD002242.
43. Wong CS, Jelacic S, Habeeb RL, Watkins SL, Tarr PI. The risk of the hemolytic-uremic syndrome after antibiotic treatment of *Escherichia coli* O157:H7 infections. *N Engl J Med.* 2000;342(26):1930-1936.
44. Casburn-Jones AC, Farthing MJ. Management of infectious diarrhoea. *Gut.* 2004;53(2):296-305.
45. McMahan ZH, DuPont HL. Review article: the history of acute infectious diarrhoea management—from poorly focused empiricism to fluid therapy and modern pharmacotherapy. *Aliment Pharmacol Ther.* 2007;25(7):759-769.
46. Allen SJ, Martinez EG, Gregorio GV, Dans LF. Probiotics for treating acute infectious diarrhoea. *Cochrane Database Syst Rev.* 2010;(11):CD003048.
47. Bhutta ZA, Bird SM, Black RE, et al. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. *Am J Clin Nutr.* 2000;72(6):1516-1522.
48. World Health Organization. The treatment of diarrhoea. A manual for physicians and other senior health workers. 2005. <http://whqlib.doc.who.int/publications/2005/9241593180.pdf>. Accessed October 1, 2013.
49. Ejemot RI, Ehiri JE, Meremikwu MM, Critchley JA. Hand washing for preventing diarrhoea. *Cochrane Database Syst Rev.* 2008;(1):CD004265.