Approach to the adult with acute diarrhea in resource-abundant settings

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INTRODUCTION

Diarrheal disease is one of the top ten leading causes of death worldwide and is a particular concern for children younger than five years old in resource-limited settings [1]. Among adults in resource-abundant settings, diarrhea is often a "nuisance disease" in the healthy individual.

Most cases of acute diarrhea in adults are of infectious etiology, and most cases resolve with symptomatic treatment alone. When clinicians care for adults with diarrhea, two important decision points are when to perform stool testing and whether to initiate empiric antimicrobial therapy. Our approach to adults with acute diarrhea will be reviewed here and generally focuses on distinguishing those infectious etiologies for which treatment is beneficial from other causes (algorithm 1).

In the United States, expert guidelines on the diagnosis and management of acute diarrhea include guidelines from the Infectious Diseases Society of America [2] and the American College of Gastroenterology [3]. Links to these and other guidelines can be found elsewhere. (See 'Society guideline links' below.)

The evaluation of persistent and chronic diarrhea, which is often of a noninfectious etiology, and specific causes of acute diarrhea and chronic diarrhea are discussed separately. (See

"Causes of acute infectious diarrhea and other foodborne illnesses in resource-abundant settings" and "Approach to the adult with chronic diarrhea in resource-abundant settings".)

Diarrhea in travelers in or returning from resource-limited settings and the approach to diarrhea in residents of resource-limited settings are discussed in detail elsewhere. (See "Travelers' diarrhea: Epidemiology, microbiology, clinical manifestations, and diagnosis" and "Travelers' diarrhea: Treatment and prevention" and "Approach to the adult with acute diarrhea in resource-limited settings".)

DEFINITIONS

Diarrhea is defined as the passage of loose or watery stools, typically at least three times in a 24-hour period [4]. It reflects increased water content of the stool, whether due to impaired water absorption and/or active water secretion by the bowel.

The following definitions have been suggested according to the duration of symptoms:

- Acute – 14 days or fewer in duration
- Persistent diarrhea – More than 14 but fewer than 30 days in duration
- Chronic – More than 30 days in duration

Invasive diarrhea, or dysentery, is defined as diarrhea with visible blood or mucus, in contrast to watery diarrhea. Dysentery is commonly associated with fever and abdominal pain.

ETIOLOGY

Most cases of acute diarrhea are due to infections and are self-limited. The major causes of acute infectious diarrhea include viruses (norovirus, rotavirus, adenoviruses, astrovirus, and others), bacteria (*Salmonella*, *Campylobacter*, *Shigella*, enterotoxigenic *Escherichia coli*, *Clostridioides difficile*, and others), and protozoa (*Cryptosporidium*, *Giardia*, *Cyclospora*, *Entamoeba*, and others) (table 1).

Taken together, most cases of acute infectious diarrhea are likely viral, as indicated by the observation that stool cultures are positive in only 1.5 to 5.6 percent of cases in most studies [2]. Among those with severe diarrhea, however, bacterial causes are responsible for more cases. As an example, in a study of 173 healthy adults with severe acute community-acquired diarrhea (defined in this study as ≥4 fluid stools per day for more than three days), a bacterial pathogen

was identified in 87 percent of cases [5]. Protozoa are less commonly identified as the etiologic agents of acute gastrointestinal illness.

Updated information on outbreaks may be found on websites maintained by the United States Centers for Disease Control and Prevention and the US Food and Drug Administration. The United States Foodborne Diseases Active Surveillance Network (FoodNet) conducts active population-based surveillance for laboratory-diagnosed enteric infections; in 2021, there were 8 percent fewer infections than the average during 2016 to 2018, which may reflect an effect of the coronavirus disease 2019 (COVID-19) pandemic [6].

Noninfectious etiologies become more common as the course of the diarrhea persists and becomes chronic. (See "Approach to the adult with chronic diarrhea in resource-abundant settings".)

Exact data on the frequency of different causes of acute diarrhea vary according to the definition used, the diagnostic technology available, and the population studied. In addition, the prevalence of an identifiable infectious agent is probably grossly underestimated since many patients do not seek medical attention and testing is often not performed when patients do contact their clinician. (See "Causes of acute infectious diarrhea and other foodborne illnesses in resource-abundant settings", section on 'Most common causes overall'.)

EVALUATION

General principles — Most adults with acute diarrhea do not present to medical care, since symptoms are often mild and/or transient.

Clinical evaluation for acute diarrhea is warranted for individuals with persistent fever, bloody diarrhea, severe abdominal pain, symptoms of volume depletion (eg, dark or scant urine, symptoms of orthostasis), or a history of inflammatory bowel disease. Hospitalization may be warranted in the presence of such concerns, in particular if there is a complex medical history of immunosuppression (eg, because of treatment for malignancy, history of transplantation, or advanced human immunodeficiency virus [HIV] infection) or significant vascular or cardiovascular disease.

History — The initial evaluation of patients who present to medical care with acute diarrhea should include a careful history to determine the duration of symptoms, the frequency and characteristics of the stool, and associated symptoms. Additionally, there should be an attempt to elicit evidence of extracellular volume depletion (eg, dark yellow or scant urine, decreased skin turgor, orthostatic hypotension). Questioning about potential exposures, such as food

history, residence, occupational exposure, recent and remote travel, pets, and hobbies, can also provide further diagnostic clues. These historical elements can be helpful to suggest the potential causative pathogens (table 1), which in turn can inform additional work-up and the decision to use empiric antibiotic therapy. (See 'Stool tests for bacterial pathogens' below and 'Additional testing in specific circumstances' below and 'Empiric antibiotic therapy' below.)

- **Character of symptoms** – In addition to informing the severity of disease, details on the frequency and nature of the stool can suggest whether the diarrhea is originating in the small or the large bowel, and thus can suggest certain pathogens (table 2). Diarrhea of small bowel origin is typically watery, of large volume, and associated with abdominal cramping, bloating, and gas [7]. Weight loss can occur if diarrhea becomes persistent. Fever is rarely a significant symptom and occult blood or inflammatory cells in the stool are rarely identified. In contrast, diarrhea of large intestinal origin often presents with frequent, regular, small volume, and often painful bowel movements. Fever and bloody or mucoid stools are common, and red blood cells and inflammatory cells can be seen routinely on stool microscopy.

  These inflammatory signs associated with large bowel infection (fever, bloody or mucoid stools) suggest invasive bacteria (eg, *Salmonella*, *Shigella*, or *Campylobacter*), enteric viruses (eg, cytomegalovirus [CMV] or adenovirus), *Entamoeba histolytica*, or a cytotoxic organism such as *C. difficile* [3]. Visibly bloody acute diarrhea is relatively uncommon and raises the possibility of Shiga toxin-producing *E. coli* (STEC) (eg, *E. coli* O157:H7) infection. Other bacterial causes of visibly bloody diarrhea are *Shigella*, *Campylobacter*, and *Salmonella* species. Bloody diarrhea can also reflect noninfectious etiologies such as inflammatory bowel disease or ischemic colitis. (See "Causes of acute infectious diarrhea and other foodborne illnesses in resource-abundant settings", section on 'Diarrhea'.)

  Syndromes that begin with diarrhea but progress to fever and systemic complaints, such as headache and muscle aches, should raise the possibility of other etiologies, including a typhoidal illness (particularly in travelers from resource-limited settings) or infection with *Listeria* monocytogenes (particularly if a stiff neck is also present or the patient is a pregnant woman).

Other details that can provide clues to the microbiological diagnosis include (table 1):

- **Food history** – Consumption of unpasteurized dairy products, raw or undercooked meat or fish, or organic vitamin preparations may suggest certain pathogens. (See "Causes of acute infectious diarrhea and other foodborne illnesses in resource-abundant settings".)

Although it is often difficult to know which food exposure was the potential source, the timing of symptom onset following exposure to the suspected offending food can be an important clue to the diagnosis (table 3) [3]:

- Within six hours – Suggests ingestion of a preformed toxin of *Staphylococcus aureus* or *Bacillus cereus*, particularly if nausea and vomiting were the initial symptoms
- At 8 to 16 hours – Suggests infection with *Clostridium perfringens*
- At more than 16 hours – Suggests either viral or other bacterial infection (eg, contamination of food with enterotoxigenic or STEC or other pathogens)

- **Other exposures**
  - Exposure to animals (poultry, turtles, petting zoos) has been associated with *Salmonella* infection.
  - Travel to a resource-limited setting increases the risk of bacterial diarrhea and also informs the risk of certain parasitic infections. (See "Travelers' diarrhea: Epidemiology, microbiology, clinical manifestations, and diagnosis".)
  - Occupation in daycare centers has been associated with infections with *Shigella*, *Cryptosporidium*, and *Giardia*. Rotavirus is a potential consideration, but in countries that routinely immunize infants against rotavirus, infection due to rotavirus has decreased substantially.
- **Medical history** – It is also important to ask about recent antibiotic use (as a clue to the presence of *C. difficile* infection), other medications (such as proton pump inhibitors, which can increase the risk of infectious diarrhea), and to obtain a complete past medical history (eg, to identify an immunocompromised host or the possibility of nosocomial infection). As examples of medical history informing the likelihood of various pathogens, pregnancy increases the risk of listeriosis following consumption of contaminated meat products or unpasteurized dairy products approximately 20-fold, cirrhosis has been associated with *Vibrio* infection, and hemochromatosis has been associated with *Yersinia* infection.

Physical examination — The examination focuses on evaluating volume status and identifying complications.

Volume depletion can be suggested by dry mucous membranes, diminished skin turgor, postural or frank reductions in blood pressure, and altered sensorium. These signs can be mild

or absent with early hypovolemia. (See "Etiology, clinical manifestations, and diagnosis of volume depletion in adults", section on 'Physical examination'.)

The abdominal examination should evaluate for findings that can suggest ileus or peritonitis, including abdominal distension, pain with gentle percussion, abdominal rigidity, or rebound tenderness. (See "Evaluation of the adult with nontraumatic abdominal or flank pain in the emergency department", section on 'Physical examination'.)

General laboratory tests — Laboratory tests are not routinely warranted for most patients with acute diarrhea. If substantial volume depletion is present (suggested by signs or symptoms such as dark and concentrated urine), a basic metabolic panel should be performed to screen for hypokalemia or renal dysfunction. The complete blood count does not reliably distinguish bacterial etiologies of diarrhea from others but may be helpful in suggesting severe disease or potential complications. A low platelet count may prompt concern for the development of the hemolytic-uremic syndrome, and a leukemoid reaction is consistent with the diagnosis of *C. difficile* infection. Blood cultures should be obtained in patients with high fevers or who appear systemically ill.

Stool tests for bacterial pathogens

Indications — For most patients who do not have severe illness or high-risk comorbidities, it is reasonable to continue expectant management for several days without microbiologic stool testing (either stool cultures or multiplex molecular panel tests) [8].

We pursue microbiologic stool testing for patients with acute community-acquired diarrhea and the following features (algorithm 1) [2,3,9]:

- Severe illness
  - Hypovolemia
  - Passage of >6 unformed stools per 24 hours
  - Severe abdominal pain
- Other signs or symptoms concerning for inflammatory diarrhea
  - Bloody diarrhea
  - Passage of many small volume stools containing blood and mucus
  - Temperature ≥38.5°C (101.3°F)
- High-risk host features

- Age ≥70 years
- Comorbidities, such as cardiac disease, which may be exacerbated by hypovolemia or rapid infusion of fluid
- Immunocompromising condition (including advanced HIV infection)
- Inflammatory bowel disease
- Pregnancy

- Symptoms persisting for more than one week

- Public health concerns (eg, diarrheal illness in food handlers, health care workers, and individuals in day care centers)

The main reason for microbiologic stool testing in these patients with acute diarrhea is to identify a potential bacterial pathogen that would inform the potential for complications and treatment decisions.

We typically perform stool cultures for microbiologic stool testing, which can identify the most common bacterial causes of diarrhea. Many laboratories are also adopting multiplex molecular panels to perform microbiologic stool testing. These issues are further discussed below. (See 'Stool culture' below and 'Multipathogen molecular panels' below.)

If patients have exposures associated with certain other bacterial pathogens, special culture work-up may be warranted, as below. (See 'Additional testing in specific circumstances' below.)

Routine stool cultures are of little value in patients who develop diarrhea after being hospitalized for 72 hours or more [10]. Testing for *C. difficile* is more likely to be helpful [11]. (See "*Clostridioides difficile* infection in adults: Clinical manifestations and diagnosis".)

Performance

Stool culture — The optimal specimen for culture is a diarrheal stool specimen, which should be inoculated onto culture plates as quickly as possible. A routine stool culture will identify *Salmonella*, *Campylobacter*, and *Shigella*, the three most common causes of bacterial diarrhea in the United States. *E. coli* O157:H7 can be isolated on sorbitol-MacConkey plates or identified with antigen testing or polymerase chain reaction (PCR) of stool (see 'Bloody diarrhea' below). A stool culture that is positive for one of these pathogens in a patient with acute diarrheal symptoms can be interpreted as a true positive. If a stool specimen cannot be obtained promptly, a rectal swab culture can be obtained to accelerate the diagnosis [12], although some data suggest decreased sensitivity in adults [13,14].

The clinician may need to specify the bacteria of concern when submitting the stool to facilitate the appropriate processing of the stool in the microbiology laboratory; specific media, methods, or stains may be required to isolate or identify organisms of interest:

- Culture for *Campylobacter*, a fastidious organism, includes collection in transport media and culture on appropriate selective media at a particular temperature and incubation environment; this is routinely done by clinical laboratories.
- When *Aeromonas* and most strains of *Yersinia* are possible pathogens (eg, travelers' diarrhea or foodborne outbreaks, especially in infants), the laboratory needs to be notified; these organisms grow in routine culture but are frequently overlooked unless their isolation is specified.
- Isolation of *Vibrio* species from stool (suspected in seafood- or shellfish-associated disease, patients with cirrhosis, patients with profuse watery diarrhea, or patients who have traveled to a country with ongoing cholera transmission) generally requires a selective media, such as thiosulfate, citrate, bile salts, and sucrose, to suppress growth of other organisms.
- Gastroenteritis due to *Listeria* should be considered in outbreaks of febrile gastroenteritis with non-bloody diarrhea if routine cultures are negative.

Performance of stool culture for the various gastrointestinal bacterial pathogens are discussed in the respective topic reviews.

Bacterial pathogens are generally excreted continuously, in contrast to ova and parasites, which are often shed intermittently. Thus, a negative culture is usually not a false negative, and repeat specimens are rarely required.

Multipathogen molecular panels — Some laboratories have access to multiplex stool tests; these use molecular techniques to test for a panel of many different pathogens (bacterial, viral, and parasitic) performed on diarrheal stool samples as well as rectal swabs in some cases. It is important for clinicians to understand which technology is being used for the diagnosis of diarrheal pathogens in their clinical laboratory, since test performance and result interpretation depend, in part, on the test employed.

Careful clinical correlation is necessary when interpreting results of molecular testing, since these assays detect genetic material (which does not always reflect infection with a viable organism), and identification of more than one pathogen is not uncommon [15]. Any specimens that test positive for a bacterial pathogen on a multiplex molecular panel (or other culture-

independent test) should be submitted for confirmatory culture; this is important for public health purposes and for susceptibility testing [2,3]. If the original specimen was a rectal swab, an additional stool specimen may be warranted to perform confirmatory culture.

Some evidence suggests that stool multiplex PCR tests can decrease health care utilization costs and antibiotic prescribing [16].

Additional testing in specific circumstances

Bloody diarrhea — For patients with bloody diarrhea, at least two potential pathogens, STEC and *Entamoeba*, warrant additional testing. In addition to culture, we check bloody stools for Shiga toxin and, if available, fecal leukocytes or lactoferrin; if the fecal leukocyte/lactoferrin test is negative, we test for amebiasis. The possibility of noninfectious etiologies may also warrant further evaluation.

- Because of the possibility of STEC as a cause of bloody diarrhea, such samples should undergo direct testing (with immunoassays or molecular tests) for Shiga toxin. Many laboratories will do this automatically with bloody specimens. Although *E. coli* O157:H7 can be isolated on sorbitol-MacConkey agar and identified with antigen testing, other strains of Shiga toxin producing *E. coli* cannot be identified in this way. Many multiplex molecular tests will also test for Shiga toxin as part of the panel. Clinicians should confirm with their clinical laboratory how the Shiga toxin test is performed (so that they can submit the sample optimally) and whether it is automatically performed or requires a specific request. (See "Shiga toxin-producing Escherichia coli: Clinical manifestations, diagnosis, and treatment", section on 'Evaluation and diagnosis'.)

- Bloody diarrhea can also be caused by intestinal amebiasis, particularly in extended (>1 month) travelers to or migrants from areas of the world where this infection is endemic (India, Africa, Mexico, and parts of Central and South America), men who have sex with men (MSM), or institutionalized individuals. The presence of bloody diarrhea in the absence of fecal leukocytes is suggestive of amebiasis, as these organisms destroy leukocytes. (See "Intestinal Entamoeba histolytica amebiasis", section on 'Diagnosis'.)

Noninfectious etiologies, in particular ischemic colitis and inflammatory bowel disease, can also present acutely with abdominal pain and bloody diarrhea. In patients who have risk factors for colonic ischemia, imaging with computed tomography and potentially endoscopy may be warranted. Endoscopy can be useful to evaluate patients with bloody diarrhea for inflammatory bowel disease if their symptoms do not resolve. (See "Colonic ischemia", section on 'Diagnosis' and "Endoscopic diagnosis of inflammatory bowel disease in adults".)

Persistent diarrhea — Work-up and management for patients with persistent diarrhea or diarrhea that does not respond to empiric treatment includes testing for parasitic organisms and other evaluation for noninfectious processes. (See "Approach to the adult with chronic diarrhea in resource-abundant settings", section on 'Initial evaluation'.)

Sending stool samples for ova and parasite testing is **not** cost effective for the majority of patients with acute diarrhea [17]. However, testing for parasitic organisms is reasonable in patients with persistent diarrhea, among whom parasites become more likely pathogens [3]. The spectrum of parasites associated with persistent diarrhea can vary based on exposures or populations. In general, *Giardia*, *Cryptosporidium*, and *E. histolytica* are the most common parasitic pathogens in patients with persistent diarrhea. Persistent diarrhea following travel to certain locations, such as Russia, Nepal, or mountainous regions, is associated with *Giardia*, *Cryptosporidium*, or *Cyclospora*. Persistent diarrhea with exposure to infants in daycare centers has been associated with *Giardia* and *Cryptosporidium*. Microsporidium should be a consideration in immunocompromised patients with persistent diarrhea.

Most of these pathogens can be diagnosed by microscopy for ova and parasites. Three specimens should be sent on consecutive days (or each specimen separated by at least 24 hours) for ova and parasite examination since parasite excretion may be intermittent. Routine microscopy does not detect cryptosporidia spores; if suspected, the laboratory should be alerted to the potential diagnosis, and specific stains (eg, modified acid fast or trichrome stains) for the organisms should be requested. *Giardia*, *Cryptosporidium*, and *Entamoeba* can also be detected by antigen or molecular testing. (See "Approach to stool microscopy" and "Giardiasis: Epidemiology, clinical manifestations, and diagnosis", section on 'Diagnosis' and "Cryptosporidiosis: Epidemiology, clinical manifestations, and diagnosis", section on 'Diagnosis' and "Intestinal Entamoeba histolytica amebiasis", section on 'Diagnosis' and "Cyclospora infection", section on 'Diagnosis'.)

Noninfectious etiologies also become more likely when acute diarrhea persists or does not respond to empiric therapy. The evaluation of patients for a noninfectious etiology should be pursued in those patients in whom evaluation fails to identify a pathogen (eg, bacterial, viral, or protozoal) and the diarrhea worsens or becomes chronic. In some cases, this will include endoscopy, for example, to distinguish inflammatory bowel disease from infectious diarrhea. (See "Approach to the adult with chronic diarrhea in resource-abundant settings" and "Endoscopic diagnosis of inflammatory bowel disease in adults".)

Antibiotic or health care exposures — For patients who are currently taking antibiotics, who have taken antibiotics within the past three months, or who have been hospitalized within the past three months prior to presentation with diarrhea, *C. difficile* colitis is a primary concern.

The approach to diagnosis of *C. difficile* in patients with clinically significant diarrhea is discussed elsewhere. (See "*Clostridioides difficile* infection in adults: Clinical manifestations and diagnosis", section on 'When to suspect and test for C. difficile infection'.)

Immunocompromised patients — Although the typical gastrointestinal pathogens are common causative organisms in immunocompromised patients with acute diarrhea, such patients have a higher risk of infections with less common gastrointestinal pathogens, in particular parasites and CMV. The likelihood of particular pathogens depends, in part, on the type of immune compromise. Noninfectious etiologies (eg, medications, graft versus host disease in stem cell transplant recipients) are also considerations. (See "Overview of infections following hematopoietic cell transplantation" and "Infection in the solid organ transplant recipient".)

For patients with acute diarrhea who have advanced HIV infection (CD4 cell count <200 cells/microL or other acquired immunodeficiency syndrome [AIDS]-defining condition) or other immunocompromising conditions, stool should be sent for culture as well as parasitic testing (microscopy for ova and parasites with special staining). This is discussed in detail elsewhere. (See "Evaluation of the patient with HIV and diarrhea".)

For patients who have concern for possible CMV infection (eg, patients with HIV infection with CD4 cell count <50 cells/microL, transplant recipients), endoscopy with biopsy is the best diagnostic approach. (See "AIDS-related cytomegalovirus gastrointestinal disease", section on 'Diagnosis and differential diagnosis' and "Approach to the diagnosis of cytomegalovirus infection", section on 'Gastrointestinal disease'.)

Neutropenic enterocolitis in patients with severe neutropenia (absolute neutrophil count <500 cells/microL) can present with diarrhea in addition to fever and abdominal pain. Imaging with computed tomography is warranted in such settings. (See "Neutropenic enterocolitis (typhlitis)".)

Outbreak settings — In the setting of a known community outbreak, additional testing may be warranted if patients with potential exposures present with diarrhea. As an example, community waterborne outbreaks or fecal-oral outbreaks have been associated with *Giardia*, *Cryptosporidium*, and norovirus, so testing for these parasitic and viral infections is appropriate in such settings. The evaluation of a waterborne outbreak requires a multidisciplinary approach for control. Any outbreak may require reporting of cases to the health department. (See "Approach to stool microscopy", section on 'Clinical approach' and "Giardiasis: Epidemiology, clinical manifestations, and diagnosis", section on 'Diagnosis' and "Cryptosporidiosis:

Epidemiology, clinical manifestations, and diagnosis", section on 'Diagnosis' and "Norovirus", section on 'Diagnosis'.)

Men who have sex with men — Receptive anal or oral-anal intercourse increases the risk of direct inoculation or fecal-oral transmission of bacterial and parasitic pathogens (in particular, *Shigella*, *Giardia* or *E. histolytica*). In addition to culture, stool from such patients should also be submitted for parasitic testing. These organisms can be detected by microscopy for ova and parasites (three specimens on consecutive days), by antigen testing, and by molecular methods. There are several nonpathogenic *Entamoeba* species (*Entamoeba dispar*, *Entamoeba hartmanni*, *Entamoeba coli*) that may be difficult to distinguish from *E. histolytica* and that may also be sexually transmitted in MSM. (See "Giardiasis: Epidemiology, clinical manifestations, and diagnosis", section on 'Diagnosis' and "Intestinal Entamoeba histolytica amebiasis", section on 'Diagnosis'.)

Acute diarrhea in MSM can also be a manifestation of proctitis, which can be caused by sexually transmitted infections (chlamydia, gonorrhea, syphilis, herpes simplex virus). Anoscopy can identify anorectal discharge or rectal mucosal friability, which are suggestive of proctitis. Testing for these sexually transmitted infections and empiric treatment for chlamydia and gonorrhea may be warranted in addition to stool culture. (See "Treatment of *Chlamydia trachomatis* infection", section on 'Proctitis and rectal infection' and "Clinical manifestations and diagnosis of *Chlamydia trachomatis* infections", section on 'Proctitis and rectal infection'.)

Indications for imaging — Abdominal imaging is not typically warranted in patients with acute diarrhea and rarely changes the clinical management [18]. However, for patients who have significant peritoneal signs or ileus, abdominal imaging (most typically computed tomography) can be important to identify potential complications, such as bowel perforation, abscess, fulminant colitis, toxic megacolon, or intestinal obstruction. (See "Evaluation of the adult with nontraumatic abdominal or flank pain in the emergency department".)

Radiographic findings of colonic wall thickening are characteristic of *C. difficile* infection but can also be seen with other causes of infectious (and non-infectious) colitis [19].

MANAGEMENT

The management of patients with acute diarrhea begins with general measures such as fluid repletion and nutrition maintenance, with adjustments in diet if necessary. Patients who have bothersome symptoms may benefit from symptomatic pharmacologic therapy. Antibiotic therapy is not indicated in most cases since the illness is usually self-limited. Nevertheless,

empiric and specific antibiotic therapy may be appropriate in certain situations, mainly in patients with severe disease, with symptoms and signs suggestive of invasive bacterial infection, or at high risk for complications (algorithm 1).

Fluid repletion — The most critical therapy in diarrheal illness is rehydration, preferably by the oral route, with solutions that contain water, salt, and sugar (table 4) [20-24]. Diluted fruit juices and flavored soft drinks along with saltine crackers and broths or soups may meet the fluid and salt needs in patients with mild illness [3]. The electrolyte concentrations of fluids used for sweat replacement (eg, Gatorade) are not equivalent to oral rehydration solutions, although they may be sufficient for the otherwise healthy patient with diarrhea who is not hypovolemic.

Oral rehydration solutions (ORS), including standard World Health Organization ORS or commercial ORS, such as Rehydralyte and Ceralyte, may be more appropriate in patients with more severe diarrheal disease. They should be used both to replete a volume depleted patient and also to maintain adequate volume status once replete. Composition of available ORS are discussed elsewhere. (See "Oral rehydration therapy", section on 'Commercial and standard oral rehydration solutions' and "Oral rehydration therapy", section on 'Oral rehydration solution properties for water absorption'.)

ORSs were developed following the realization that, in many small bowel diarrheal illnesses, intestinal glucose absorption via sodium-glucose cotransport remains intact. Thus, in diarrheal disease caused by any organism that depends on small bowel secretory processes, the intestine remains able to absorb water if glucose and salt are also present to assist in the transport of water from the intestinal lumen. Oral rehydration therapy is grossly underutilized in the US where health care providers tend to overuse intravenous hydration.

Adults with severe hypovolemia should initially receive intravenous fluid repletion. Once they are replete, they can be switched to oral rehydration solutions. (See "Maintenance and replacement fluid therapy in adults".)

Some UpToDate contributors also favor intravenous fluid administration in patients with bloody diarrhea and suspicion for Shiga-toxin producing *E. coli* infection. This is discussed in detail elsewhere. (See "Shiga toxin-producing Escherichia coli: Microbiology, pathogenesis, epidemiology, and prevention".)

Empiric antibiotic therapy — Given the lack of rapid diagnostic testing methods for enteric pathogens, most decisions on antibiotic therapy are often made empirically at the time of presentation. Indications and agent selection for empiric antibiotic therapy are discussed below.

Indications

- We generally withhold antibiotic therapy in the following circumstances:

  - For most patients with acute, nonbloody diarrhea (non-travel-associated), we recommend **not** administering empiric antibiotic therapy (algorithm 1). In most cases, the potential benefit of antibiotics (symptom reduction) does not outweigh the potential drawbacks (eg, toxicity, bacterial resistance, risk for *C. difficile* infection).

  - For most stable patients with concern for Shiga toxin-producing *E. coli* (STEC) infection, including *E. coli* O157:H7 (eg, bloody diarrhea in the setting of an outbreak, absence of fever), we withhold empiric antibiotic therapy pending stool testing to rule out STEC infection or Shiga toxin production (algorithm 1). Antibiotics do not reduce symptoms or complications of STEC infection and have been associated with development of hemolytic uremic syndrome [25].

    The association between STEC and HUS is discussed separately. (See "Shiga toxin-producing Escherichia coli: Clinical manifestations, diagnosis, and treatment" and "Shiga toxin-producing Escherichia coli: Microbiology, pathogenesis, epidemiology, and prevention".)

  Despite the efficacy of antibiotics in reducing the duration of diarrheal symptoms in some settings, this benefit does not outweigh the drawbacks of potential side effects, promotion of bacterial resistance, eradication of normal flora (and increased risk of *C. difficile* infection), and cost for individuals with a short-lived illness.

- We favor empiric antibiotic therapy in the following circumstances (algorithm 1):

  - Severe illness (fever ≥38.5°C [101.3°F], hypovolemia, ≥6 unformed stools per 24 hours, severe abdominal pain)

  - Features of inflammatory diarrhea (bloody diarrhea, small volume mucous stools, fever)

  - High-risk host features (age ≥70 years, cardiac disease, immunocompromising condition, inflammatory bowel disease, pregnancy)

    In these circumstances, the benefits of antibiotic therapy likely outweigh the low risk of potential complications from treating STEC.

Choice of agent — When the decision to treat acute diarrhea has been made, we suggest azithromycin or a fluoroquinolone (table 5):

- Azithromycin – Azithromycin is preferred for patients with fever or dysentery (bloody or mucoid diarrhea) and in other patients suspected to be at risk for a fluoroquinolone-resistant pathogen (eg, in patients with diarrhea after travel to Southeast Asia, or during outbreaks of resistant pathogens) [3]. Azithromycin can be given as a single 1 g dose (for patients without dysentery) or as 500 mg once daily for three days (for patients with or without dysentery).

- Fluoroquinolones – Fluoroquinolones include ciprofloxacin (a single 750 mg dose or 500 mg twice daily for three to five days) or levofloxacin (500 mg as a single dose or given once daily for three to five days).

The single-dose regimens are associated with greater nausea than the multidose regimens.

Specific circumstances may warrant empiric treatment for particular pathogens. These include the following:

- For patients with severe diarrhea in the setting of recent antibiotic therapy (within the preceding three months), empiric treatment for *C. difficile* is reasonable if the clinical suspicion is high. (See "*Clostridioides difficile* infection in adults: Treatment and prevention".)

- For pregnant women with diarrhea accompanied by fever or systemic illness who had potential exposure to *Listeria* monocytogenes, empiric therapy often includes antibiotics with activity against this organism. (See "Treatment and prevention of Listeria monocytogenes infection", section on 'Pregnant patients'.)

- For patients with profuse watery diarrhea and potential exposure to cholera (eg, travel to an endemic or epidemic setting), empiric antibiotic coverage of *Vibrio cholerae* is reasonable given the potential for very severe disease. (See "Cholera: Treatment and prevention".)

- For patients with severe illness and suspected shigellosis who are at risk for drug resistant infection (including men who have sex with men, international travelers, people with HIV infection and people experiencing homelessness), empiric treatment should consist of a carbapenem pending results of antibiotic susceptibility testing. (See "Shigella infection: Treatment and prevention in adults".)

Symptomatic therapy — For patients who want symptomatic therapy, the antimotility agent loperamide (Imodium) can be used cautiously in patients in whom fever is absent or low grade

and the stools are not bloody. The dose of loperamide is two tablets (4 mg) initially, then 2 mg after each unformed stool for ≤2 days, with a maximum of 16 mg/day.

We avoid antimotility agents in patients with clinical features suggestive of dysentery (fever, bloody or mucoid stools) unless antibiotics are also given because of concerns that antimotility agents can prolong disease in such infections or lead to more severe illness. In such patients, bismuth salicylate (Pepto-Bismol, 30 mL or two tablets every 30 minutes for eight doses) is an acceptable alternative, although it is somewhat less effective and there is the potential for salicylate toxicity (especially in those who take aspirin for any reason and pregnant women). Another antisecretory agent, racecadotril, is an effective option for symptomatic therapy, if available (not in the US).

Antimotility agents are effective but should be taken with caution. In several randomized controlled studies, loperamide decreased the number of liquid bowel movements or the time to cessation of diarrhea compared with placebo (generally by approximately one day) [26,27]. The addition of loperamide to antibiotics also decreases the time to symptom resolution compared with antibiotics alone [28]. Diphenoxylate (Lomotil) is an alternative antimotility agent, but it has not been as well studied and may cause central opiate or cholinergic side effects. The dose of diphenoxylate is two tablets (5 mg) four times daily for ≤2 days. Patients should be cautioned that treatment with antimotility agents may mask the amount of fluid lost, since fluid may pool in the intestine. Thus, fluids should be used aggressively when antimotility agents are employed. Furthermore, there continues to be some concern that antimotility agents can prolong the duration of fever, diarrhea, and excretion of the organism in some types of dysenteric illnesses (eg, *Shigella*) [29], and so are avoided in such cases.

When compared with placebo, bismuth subsalicylate significantly reduced the number of unformed stools and increased the proportion of patients free of symptoms at the end of treatment trials [30-32]. However, in studies that compared bismuth subsalicylate with loperamide, loperamide brought significantly faster relief [30,33,34]. A role for bismuth subsalicylate may be in patients with significant fever and dysentery, conditions in which loperamide should be avoided. If used, the total dose of bismuth salicylate should be monitored, especially in pregnant women, to prevent salicylate toxicity.

If available, racecadotril, an enkephalinase inhibitor, has been demonstrated in several studies to reduce the output and duration of diarrhea, and in some studies, leads to more rapid improvement with fewer adverse effects compared with loperamide [35-37].

Dietary guidance — The benefit of specific dietary recommendations other than oral hydration has not been well established in controlled trials. However, adequate nutrition during an

episode of acute diarrhea is important to facilitate enterocyte renewal [23]; if patients are anorectic or have nausea and vomiting, a short period of consuming only liquids will not be harmful. Boiled starches and cereals (eg, potatoes, noodles, rice, wheat, and oat) with salt are indicated in patients with watery diarrhea; crackers, bananas, soup, and boiled vegetables may also be consumed [3]. Foods with high fat content should be avoided until the gut function returns to normal after a severe bout of diarrhea.

Dairy products (except yogurt) may be difficult to digest in the presence of diarrheal disease. This is due to secondary lactose malabsorption, which is common following infectious enteritis and may last for several weeks to months. Thus, temporary avoidance of lactose-containing foods is reasonable. (See "Lactose intolerance and malabsorption: Clinical manifestations, diagnosis, and management".)

No role for probiotics — Probiotic use in adults with acute infectious gastroenteritis is unproven. This issue is discussed further separately. (See "Probiotics for gastrointestinal diseases", section on 'Infectious diarrhea'.)

FOLLOW-UP

In general, follow-up stool testing is not necessary, even if it was initially positive. In some locations, a negative stool test following infection with certain bacterial infections (eg, *Salmonella*, *Shigella*, Shiga toxin-producing *E. coli*) is mandated for occupations with a high risk of transmission (eg, food handling or direct patient care) before returning to work after a diarrheal illness. Clinicians should consult with local public health officials regarding any such requirements.

If diarrhea resolves or responds rapidly to therapy, no further work-up or treatment is necessary. If diarrhea becomes persistent, the search for an etiology should be expanded to try to isolate a treatable process or pathogen or identify a noninfectious etiology. (See 'Persistent diarrhea' above and "Approach to the adult with chronic diarrhea in resource-abundant settings".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Acute diarrhea in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Diarrhea in teens and adults (The Basics)" and "Patient education: E. coli diarrhea (The Basics)")
- Beyond the Basics topic (see "Patient education: Acute diarrhea in adults (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Etiology** − Most cases of acute diarrhea are infectious. Overall, most cases of infectious diarrhea are likely viral; however, bacterial causes are responsible for most cases of severe diarrhea. (See 'Etiology' above.)
- **Evaluation**
  - **History and physical examination** − Most adults with acute diarrhea do not present to medical care because of the mild or transient nature of the symptoms.

    For those who present to medical care, the initial evaluation should assess for extracellular volume depletion (eg, dark yellow urine or scant amount of urine, decreased skin turgor, orthostatic hypotension) and determine the duration of symptoms, the frequency and characteristics of the stool, and associated symptoms (eg, fever and peritoneal signs). (See 'History' above and 'Physical examination' above.)

- **Diagnostic clues** − Inflammatory features (eg, fever, or bloody or mucoid stool) suggest infection of the large bowel, which is associated with pathogens distinct from small bowel infection (table 2). Potential exposures, such as food history, residence, occupational exposure, recent and remote travel, pets, and hobbies, can also provide further diagnostic clues as to potential microbiologic etiology (table 1). (See 'History' above.)

- **Indications for stool testing** − We obtain a stool sample for testing (stool culture and/or multiplex molecular testing) in the following circumstances (algorithm 1):

  - Severe illness (fever ≥38.5°C [101.3°F], hypovolemia, ≥6 unformed stools per 24 hours, severe abdominal pain, or hospitalization)

  - Features of inflammatory diarrhea (bloody diarrhea, small volume mucous stools, fever)

  - High-risk host features (age ≥70 years, cardiac disease, immunosuppression, inflammatory bowel disease, pregnancy)

  - Symptoms persisting >1 week

  - Public health concerns (eg, diarrheal illness in food handlers, health care workers, and individuals in day care centers)

  For most other patients, it is reasonable to continue expectant management for several days without performing stool testing. (See 'Stool tests for bacterial pathogens' above.)

- **Additional diagnostic workup** − Further diagnostic testing depends on the presenting features. Grossly bloody diarrhea warrants testing for Shiga toxin (to identify Shiga toxin-producing *Escherichia coli* [STEC]) and fecal leukocytes or lactoferrin, if available. Testing for *Clostridioides difficile* should be performed in cases of recent antibiotic use or health care exposure. Testing for parasites is not warranted in the majority of patients with acute diarrhea. It is useful, however, in patients with persistent diarrhea, in men who have sex with men, in immunocompromised hosts, during a community waterborne outbreak (associated with *Giardia* and *Cryptosporidium*), or with bloody diarrhea with few or no fecal leukocytes (associated with intestinal amebiasis). Parasitic tests include microscopy for ova and parasites as well as antigen or molecular testing for specific organisms. (See 'Additional testing in specific circumstances' above.)

- **Management**

- **Fluid repletion** – We assess volume status in all patients. The treatment priority for patients with diarrhea is volume repletion. We prefer oral rehydration solutions that contain water, salt, and sugar (table 4). Patients with severe hypovolemia should receive initial intravenous fluid repletion, followed by ongoing maintenance with oral fluids. (See 'Fluid repletion' above.)

- **Role of empiric antibiotics** − We withhold empiric antibiotic therapy in the following circumstances (see 'Indications' above):

  - For most patients with acute, nonbloody diarrhea (non-travel-associated), we recommend **not** administering empiric antibiotic therapy (algorithm 1) (**Grade 1B**). In most cases, the potential benefit of antibiotics (symptom reduction) does not outweigh the potential drawbacks (eg, toxicity, bacterial resistance, risk for *C. difficile* infection).

  - For most stable patients with concern for Shiga toxin-producing *E. coli* (STEC) infection, including *E. coli* O157:H7 (eg, bloody diarrhea in the setting of an outbreak, absence of fever), we withhold empiric antibiotic therapy pending stool testing to rule out STEC infection (algorithm 1). Antibiotics do not reduce symptoms or complications of STEC infection and have been associated with development of hemolytic uremic syndrome.

  We suggest empiric antibiotic therapy in the following circumstances (algorithm 1) (**Grade 2B**):

  - Severe illness (fever ≥38.5°C [101.3°F], hypovolemia, ≥6 unformed stools per 24 hours, severe abdominal pain)

  - Features of inflammatory diarrhea (bloody diarrhea, small volume mucous stools, fever)

  - High-risk host features (age ≥70 years, cardiac disease, immunocompromising condition, inflammatory bowel disease, pregnancy)

    In these circumstances, the benefits of antibiotic therapy likely outweigh the low risk of potential complications from treating STEC.

- **Choice of antibiotic agent** − For most patients with nonbloody diarrhea who warrant empiric antibiotic therapy, we suggest treatment with a fluoroquinolone or azithromycin (table 5) (**Grade 2B**); these agents are well tolerated and active against most infectious causes of diarrhea. We use azithromycin for patients with fever or

dysentery (bloody or mucoid diarrhea) and for patients suspected to be at risk for a fluoroquinolone-resistant pathogen (eg, during outbreaks of resistant pathogens). (See 'Choice of agent' above.)

- **Pathogen-directed treatment** − Even if a bacterial pathogen is identified, not all patients warrant antimicrobial therapy, and STEC specifically should **not** be treated with antibiotics. Indications for and selection of antimicrobial therapy for specific intestinal pathogens are discussed in detail in the appropriate topic reviews. (See "Nontyphoidal Salmonella: Gastrointestinal infection and asymptomatic carriage", section on 'Antimicrobial therapy' and "Shigella infection: Treatment and prevention in adults", section on 'Management' and "Campylobacter infection: Clinical manifestations, diagnosis, and treatment", section on 'Treatment' and "Shiga toxin-producing Escherichia coli: Microbiology, pathogenesis, epidemiology, and prevention".)

- **Antidiarrheal agents, diet, and probiotics**

  - **Antidiarrheal agents** − For patients with nonbloody diarrhea (in the setting of absent or low-grade fever), the antimotility agent loperamide may be used cautiously for ≤2 days. However, for patients with clinical features suggestive of dysentery (fever, bloody or mucoid stools), we suggest **avoiding** antimotility agents unless antibiotics are also given (**Grade 2C**), due to concern for prolonging disease; in such patients who are not candidates for loperamide, bismuth salicylate is an alternative. (See 'Symptomatic therapy' above.)

  - **Diet** − Dietary modification may be helpful. For patients with watery diarrhea, encourage consumption of boiled starches and cereals (eg, potatoes, noodles, rice, wheat, and oat) with salt; crackers, bananas, soup, and boiled vegetables are also reasonable options. Avoid foods with high fat content. (See 'Dietary guidance' above.)

    Temporary avoidance of many lactose-containing foods may be helpful; dairy products (except yogurt) may be difficult to digest due to secondary lactose malabsorption, which may last for several weeks to months. (See "Lactose intolerance and malabsorption: Clinical manifestations, diagnosis, and management".)

  - **Probiotics** – Use of probiotics in adults with acute infectious gastroenteritis is unproven. (See "Probiotics for gastrointestinal diseases", section on 'Infectious diarrhea'.)

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REFERENCES

1. GBD 2016 Diarrhoeal Disease Collaborators. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of diarrhoea in 195 countries: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Infect Dis 2018; 18:1211.
2. Shane AL, Mody RK, Crump JA, et al. 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea. Clin Infect Dis 2017; 65:e45.
3. Riddle MS, DuPont HL, Connor BA. ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults. Am J Gastroenterol 2016; 111:602.
4. Guerrant RL, Van Gilder T, Steiner TS, et al. Practice guidelines for the management of infectious diarrhea. Clin Infect Dis 2001; 32:331.
5. Dryden MS, Gabb RJ, Wright SK. Empirical treatment of severe acute community-acquired gastroenteritis with ciprofloxacin. Clin Infect Dis 1996; 22:1019.
6. Collins JP, Shah HJ, Weller DL, et al. Preliminary Incidence and Trends of Infections Caused by Pathogens Transmitted Commonly Through Food - Foodborne Diseases Active Surveillance Network, 10 U.S. Sites, 2016-2021. MMWR Morb Mortal Wkly Rep 2022; 71:1260.
7. Wanke CA. Small intestinal infections. Curr Opin Gastroenterol 1994; 10:59.
8. Clark SD, Sidlak M, Mathers AJ, et al. Clinical Yield of a Molecular Diagnostic Panel for Enteric Pathogens in Adult Outpatients With Diarrhea and Validation of Guidelines-Based Criteria for Testing. Open Forum Infect Dis 2019; 6:ofz162.
9. Thielman NM, Guerrant RL. Clinical practice. Acute infectious diarrhea. N Engl J Med 2004; 350:38.
10. Rohner P, Pittet D, Pepey B, et al. Etiological agents of infectious diarrhea: implications for requests for microbial culture. J Clin Microbiol 1997; 35:1427.
11. Savola KL, Baron EJ, Tompkins LS, Passaro DJ. Fecal leukocyte stain has diagnostic value for outpatients but not inpatients. J Clin Microbiol 2001; 39:266.

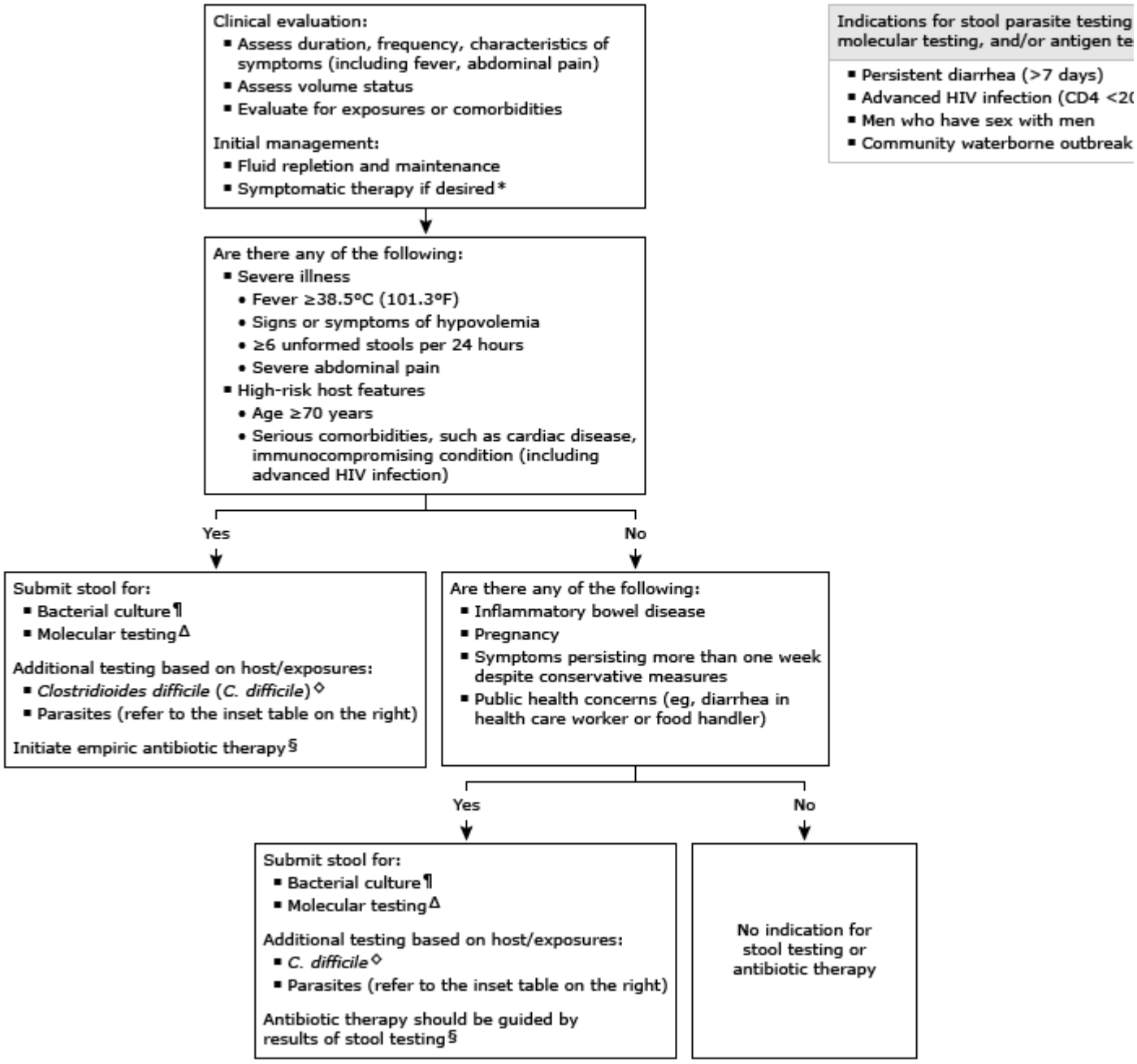
12. Jean S, Yarbrough ML, Anderson NW, Burnham CA. Culture of Rectal Swab Specimens for Enteric Bacterial Pathogens Decreases Time to Test Result While Preserving Assay Sensitivity Compared to Bulk Fecal Specimens. J Clin Microbiol 2019; 57.
13. Kotar T, Pirš M, Steyer A, et al. Evaluation of rectal swab use for the determination of enteric pathogens: a prospective study of diarrhoea in adults. Clin Microbiol Infect 2019; 25:733.
14. Kotton CN, Lankowski AJ, Hohmann EL. Comparison of rectal swabs with fecal cultures for detection of Salmonella typhimurium in adult volunteers. Diagn Microbiol Infect Dis 2006; 56:123.
15. Binnicker MJ. Multiplex Molecular Panels for Diagnosis of Gastrointestinal Infection: Performance, Result Interpretation, and Cost-Effectiveness. J Clin Microbiol 2015; 53:3723.
16. Axelrad JE, Freedberg DE, Whittier S, et al. Impact of Gastrointestinal Panel Implementation on Health Care Utilization and Outcomes. J Clin Microbiol 2019; 57.
17. Siegel DL, Edelstein PH, Nachamkin I. Inappropriate testing for diarrheal diseases in the hospital. JAMA 1990; 263:979.
18. Aisenberg GM, Grimes RM. Computed tomography in patients with abdominal pain and diarrhoea: does the benefit outweigh the drawbacks? Intern Med J 2013; 43:1141.
19. Guerri S, Danti G, Frezzetti G, et al. Clostridium difficile colitis: CT findings and differential diagnosis. Radiol Med 2019; 124:1185.
20. Avery ME, Snyder JD. Oral therapy for acute diarrhea. The underused simple solution. N Engl J Med 1990; 323:891.
21. Carpenter CC, Greenough WB, Pierce NF. Oral-rehydration therapy--the role of polymeric substrates. N Engl J Med 1988; 319:1346.
22. Santosham M, Burns B, Nadkarni V, et al. Oral rehydration therapy for acute diarrhea in ambulatory children in the United States: a double-blind comparison of four different solutions. Pediatrics 1985; 76:159.
23. Duggan C, Santosham M, Glass RI. The management of acute diarrhea in children: oral rehydration, maintenance, and nutritional therapy. Centers for Disease Control and Prevention. MMWR Recomm Rep 1992; 41:1.
24. de Zoysa I, Kirkwood B, Feachem R, Lindsay-Smith E. Preparation of sugar-salt solutions. Trans R Soc Trop Med Hyg 1984; 78:260.
25. Wong CS, Jelacic S, Habeeb RL, et al. The risk of the hemolytic-uremic syndrome after antibiotic treatment of Escherichia coli O157:H7 infections. N Engl J Med 2000; 342:1930.

26. Petruccelli BP, Murphy GS, Sanchez JL, et al. Treatment of traveler's diarrhea with ciprofloxacin and loperamide. J Infect Dis 1992; 165:557.
27. Murphy GS, Bodhidatta L, Echeverria P, et al. Ciprofloxacin and loperamide in the treatment of bacillary dysentery. Ann Intern Med 1993; 118:582.
28. 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; 47:1007.
29. DuPont HL, Hornick RB. Adverse effect of lomotil therapy in shigellosis. JAMA 1973; 226:1525.
30. Steffen R. Worldwide efficacy of bismuth subsalicylate in the treatment of travelers' diarrhea. Rev Infect Dis 1990; 12 Suppl 1:S80.
31. Graham DY, Estes MK, Gentry LO. Double-blind comparison of bismuth subsalicylate and placebo in the prevention and treatment of enterotoxigenic Escherichia coli-induced diarrhea in volunteers. Gastroenterology 1983; 85:1017.
32. DuPont HL, Sullivan P, Pickering LK, et al. Symptomatic treatment of diarrhea with bismuth subsalicylate among students attending a Mexican university. Gastroenterology 1977; 73:715.
33. DuPont HL, Flores Sanchez J, Ericsson CD, et al. Comparative efficacy of loperamide hydrochloride and bismuth subsalicylate in the management of acute diarrhea. Am J Med 1990; 88:15S.
34. Johnson PC, Ericsson CD, DuPont HL, et al. Comparison of loperamide with bismuth subsalicylate for the treatment of acute travelers' diarrhea. JAMA 1986; 255:757.
35. Salazar-Lindo E, Santisteban-Ponce J, Chea-Woo E, Gutierrez M. Racecadotril in the treatment of acute watery diarrhea in children. N Engl J Med 2000; 343:463.
36. Eberlin M, Chen M, Mueck T, Däbritz J. Racecadotril in the treatment of acute diarrhea in children: a systematic, comprehensive review and meta-analysis of randomized controlled trials. BMC Pediatr 2018; 18:124.
37. Fischbach W, Andresen V, Eberlin M, et al. A Comprehensive Comparison of the Efficacy and Tolerability of Racecadotril with Other Treatments of Acute Diarrhea in Adults. Front Med (Lausanne) 2016; 3:44.

Topic 2717 Version 58.0

GRAPHICS

Approach to acute nonbloody diarrhea in adults in resource-rich settings



This algorithm outlines an approach to the workup and initial management of acute diarrhea acquired in resource-rich settings, with a focus on infectious etiologies, which are the most common causes. Refer to UpToDate content on acute diarrhea in resource-rich settings for more details.

HIV: human immunodeficiency virus.

* Loperamide and bismuth salicylates are both effective in reducing the duration and frequency of diarrhea; loperamide is somewhat more effective. Loperamide is often avoided when *C. difficile* is suspected. Patients taking loperamide should be cautioned not to exceed the maximum daily dose.

¶ Routine stool culture identifies *Salmonella*, *Campylobacter*, and *Shigella*. If other bacterial organisms (such as *Vibrio*, *Listeria*, *Yersinia*, or *Aeromonas*) are suspected based on exposures, the laboratory should be notified for specific plating of the specimen.

Δ Some laboratories perform multiplex molecular stool testing for multiple organisms simultaneously; the indications for such testing are similar to those for stool cultures. Any specimens that test positive for a bacterial pathogen on a multiplex molecular panel (or other culture-independent test) should be submitted for confirmatory culture; this is important for susceptibility testing and for public health purposes.

◇ Testing for *C. difficile* is warranted for individuals who have had antibiotic use or hospitalization within the prior three months; in addition, testing for *C. difficile* is often performed in patients with inflammatory bowel disease.

§ For most patients with non-travel-associated diarrhea, we do not administer empiric antibiotic therapy routinely, since the potential benefits do not outweigh potential drawbacks in most patients with acute diarrhea. For select patients with severe or persistent disease or high-risk host features, empiric antibiotic treatment is reasonable since symptom reduction may have a greater relative benefit in such patients. In such cases, we suggest treatment with azithromycin or a fluoroquinolone. We favor azithromycin for patients with fever and in patients suspected to be at risk for a fluoroquinolone-resistant pathogen (eg, in patients with diarrhea after travel to Southeast Asia, or during outbreaks of resistant pathogens). Empiric antibiotic therapy should be tailored to stool culture results when available.

Graphic 68348 Version 13.0

Causes of acute infectious diarrhea in adults in resource-rich settings

	Likely pathogens	Mean incubation period	Classic/common food sources	Other epidemiolc clues
Watery diarrhea	Norovirus	24 to 48 hours	Shellfish, prepared foods, vegetables, fruit	▪ Outbreaks in: • Restaurants • Health care facilities • Schools and childcare cente • Cruise ships • Military populations
	Clostridioides (formerly *Clostridium*) *difficile**	N/A	N/A	▪ Antibiotic use ▪ Hospitalization ▪ Cancer chemother ▪ Gastric acid suppression ▪ Inflammatory bow disease
	Clostridium perfringens	8 to 16 hours	Meat, poultry, gravy, home-canned goods	
	Enterotoxigenic *Escherichia coli*	1 to 3 days	Fecally contaminated food or water	▪ Travel to resource-limited settings
	Other enteric viruses (rotavirus, enteric adenovirus, astrovirus, sapovirus)	10 to 72 hours	Fecally contaminated food or water	▪ Daycare centers ▪ Gastroenteritis in children ▪ Immunocomprom adults
	Giardia lamblia	7 to 14 days	Fecally contaminated food or water	▪ Daycare centers ▪ Swimming pools ▪ Travel, hiking, cam (particularly when there is contact wi water in which bea reside)

	Cryptosporidium parvum	2 to 28 days	Vegetables, fruit, unpasteurized milk	▪ Daycare centers ▪ Swimming pools a recreational water sources ▪ Animal exposure ▪ Chronic diarrhea i advanced HIV infe
	Listeria monocytogenes	1 day (gastroenteritis)	Processed/delicatessen meats, hot dogs, soft cheese, pâtés, and fruit	▪ Pregnancy ▪ Immunocomprom condition ▪ Extremes of age
	Cyclospora cayetanensis	1 to 11 days	Imported berries, herbs	▪ Chronic diarrhea i advanced HIV infe
Inflammatory diarrhea (fever, mucoid or bloody stools)[¶]	Nontyphoidal *Salmonella*	1 to 3 days	Poultry, eggs, and egg products, fresh produce, meat, fish, unpasteurized milk or juice, nut butters, spices	▪ Animal contact (petting zoos, rept live poultry, other pets) ▪ Travel to resource- limited settings
	Campylobacter spp	1 to 3 days	Poultry, meat, unpasteurized milk	▪ Travel to resource- limited settings ▪ Animal contact (yc puppies or kittens occupational conta
	Shigella spp	1 to 3 days	Raw vegetables	▪ Daycare centers ▪ Crowded living conditions ▪ Men who have sex with men ▪ Travel to resource- limited settings
	Enterohemorrhagic *E. coli*	1 to 8 days	Ground beef and other meat, fresh produce, unpasteurized milk and juice	▪ Daycare centers ▪ Nursing homes ▪ Extremes of age
	Yersinia spp	4 to 6 days	Pork or pork products, untreated water	▪ Abnormalities of i metabolism (eg, cirrhosis, hemochromatosis thalassemia)

				▪ Blood transfusion
	Vibrio parahemolyticus	1 to 3 days	Raw seafood and shellfish	▪ Cirrhosis
	Entamoeba histolytica	1 to 3 weeks	Fecally contaminated food or water	▪ Travel to resource-limited settings ▪ Men who have sex with men

* *Clostridioides* (formerly *Clostridium*) *difficile* can also present with inflammatory diarrhea.

¶ Pathogens that are more classically associated with inflammatory diarrhea can also cause watery diarrhea, particularly early in the course of infection.

Graphic 116097 Version 2.0

Enteric pathogens

Pathogen	Small bowel	Colon
Bacteria	*Salmonella**	*Campylobacter**
	Escherichia coli¶	*Shigella*
	Clostridium perfringens	*Clostridioides difficile*
	Staphylococcus aureus	*Yersinia*
	Aeromonas hydrophila	*Vibrio parahaemolyticus*
	Bacillus cereus	Enteroinvasive *E. coli*
	Vibrio cholerae	*Plesiomonas shigelloides*
		Klebsiella oxytoca (rare)
Virus	Rotavirus	Cytomegalovirus*
	Norovirus	Adenovirus
	Astrovirus	Herpes simplex virus
Protozoa	*Cryptosporidium**	*Entamoeba histolytica*
	*Microsporidium**	
	Cystoisospora	
	Cyclospora	
	Giardia lamblia	

* Can involve both the small and large bowel, but are most likely to occur as listed.

¶ EPEC, EAggEC, EHEC, ETEC may all contribute; routine laboratories and cultures will not differentiate these from E. coli which are normal flora.

Graphic 81945 Version 7.0

Major foodborne microbes by the principal presenting gastrointestinal symptom

Major presenting symptom	Likely microbes	Incubation period	Likely food sources
Vomiting	*S. aureus*	1 to 6 hours	Prepared food, eg, salads, dairy, meat
	B. cereus	1 to 6 hours	Rice, meat
	Norwalk-like viruses	24 to 48 hours	Shellfish, prepared foods, salads, sandwiches, fruit
Watery diarrhea	*C. perfringens*	8 to 16 hours	Meat, poultry, gravy
	Enterotoxigenic *E. coli*	1 to 3 days	Fecally contaminated food or water
	Enteric viruses	10 to 72 hours	Fecally contaminated food or water
	C. parvum	2 to 28 days	Vegetables, fruit, unpasteurized milk water
	C. cayetanensis	1 to 11 days	Imported berries, basil
Inflammatory diarrhea	*Campylobacter* spp	2 to 5 days	Poultry, unpasteurized milk, water
	Nontyphoidal S*almonella*	1 to 3 days	Eggs, poultry, meat, unpasteurized milk or juice, fresh produce
	Shiga toxin-producing *E. coli*	1 to 8 days	Ground beef, unpasteurized milk and juice, raw vegetables, water
	Shigella spp	1 to 3 days	Fecal contamination of food and water
	V. parahemolyticus	2 to 48 hours	Raw shellfish

Incubation period and likely food sources are shown for each.

Modified from Centers for Disease Control and Prevention. Diagnosis and management of food borne illness, a primer for physicians. MMWR Recomm Rep 2001; 50:(RR-2):1.

Graphic 56595 Version 2.0

Composition of oral rehydration solutions and commonly used beverages

	Carbohydrate (g/L)	mEq/L			Osmolarity (mOSM/kg H_2O)
		Sodium	Potassium	Base (HCO_3–)	
Oral rehydration solutions					
CeraLyte	40	70	20	10	235
Enfalyte	30	50	25	30	200
Pedialyte	25	45	20	30	250
WHO (2002)	13.5	75	20	30	245
Commonly used beverages (not appropriate for rehydration therapy)					
Apple juice	100 to 150	3	20	0	700
Chicken broth	0	250	5	0	450
Colas	100 to 150	2	0.1	13	550
Gatorade	61	20	3	3	330
Ginger ale	90	3.5	0.1	3.6	565
Tea	0	0	0	0	5

WHO: World Health Organization.

Graphic 67494 Version 7.0

Antibiotic agents for empiric treatment of adults with acute diarrhea in resource-rich settings

Agent	Patients with watery (nonbloody) diarrhea	Patients with dysentery (diarrhea with visible blood or mucus)
Azithromycin	▪ 500 mg orally once daily for three days **or** ▪ 1 g (single dose); may divide in two equal doses to reduce nausea*	▪ 500 mg orally once daily for three days
Ciprofloxacin	▪ 500 mg orally twice daily for three to five days **or** ▪ 750 mg (single dose)*	▪ 500 mg orally twice daily for three to five days
Levofloxacin	▪ 500 mg orally once daily for three to five days **or** ▪ 500 mg (single dose)*	▪ 500 mg orally once daily for three to five days

Refer to UpToDate text for discussion of indications for empiric antibiotic therapy. Antibiotics may be combined with loperamide (first dose 4 mg, and then 2 mg dose after each loose stool; not to exceed 16 mg in a 24-hour period).

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* If symptoms persist 24 hours after single-dose regimen, complete a three-day course using multiple-dose regimen.

Data from:

1. *Lexicomp Online. Copyright © 1978-2024 Lexicomp, Inc. All Rights Reserved.*
2. *Riddle MS, DuPont HL, Connor BA. ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults. Am J Gastroenterol 2016; 111:602.*

Graphic 141493 Version 3.0