INTRODUCTION — Diarrheal diseases represent one of the five leading causes of death worldwide [1,2]. Morbidity and mortality are significant even in the United States, where diarrhea is more often than not a "nuisance disease" in the normally healthy individual [3,4].

The following definitions have been suggested according to the duration of diarrhea [5]:

- **Acute** — ≤14 days in duration
- **Persistent diarrhea** — more than 14 days in duration
- **Chronic** — more than 30 days in duration

Most cases of acute diarrhea are due to infections with viruses and bacteria and are self-limited. Noninfectious etiologies become more common as the course of the diarrhea persists and becomes chronic. The evaluation of patients for a noninfectious etiology should be considered in those patients in whom evaluation fails to identify a pathogen (eg, bacterial, viral, or protozoal) and the diarrhea worsens or becomes chronic. (See "Approach to the adult with chronic diarrhea in developed countries".)

One of the dilemmas in assessing patients with acute diarrhea is deciding when to test and to initiate therapy. The approach to such patients will be reviewed here and generally focuses on distinguishing acute infectious etiologies, for which treatment is beneficial, from other causes (algorithm 1). The evaluation of persistent and chronic diarrhea, most commonly noninfectious etiologies, and specific causes of acute diarrhea and chronic diarrhea are discussed separately. (See "Epidemiology and causes of acute diarrhea in developed countries", section on 'Frequency of isolating an organism'.)

ETIOLOGY — The major causes of acute infectious diarrhea include viruses (norovirus, rotavirus, adenoviruses, astrovirus, and others), bacteria (salmonella, campylobacter, shigella, enterotoxigenic E. coli, C. difficile, and others), and protozoa (cryptosporidium, giardia, cyclospora, entamoeba, and others) [6]. Exact data on the frequency of different causes of acute diarrhea vary according to the definition used 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 [7]. (See "Epidemiology and causes of acute diarrhea in developed countries", section on 'Frequency of isolating an organism'.)

Most cases of acute infectious gastroenteritis are probably viral, as indicated by the observation that stool cultures in patients with acute diarrhea have, in most studies, been positive in 1.5 to 5.6 percent of cases (table 1) [5]. Support for viral infection causing most cases comes from a pilot study of foodborne outbreaks in which stool collection kits were delivered to and from the patients' homes [8]. A pathogen was identified in 71 percent of patients, three-quarters of which were norovirus.

In contrast, bacterial causes are responsible for most cases of severe diarrhea. This was illustrated in a study of 173
healthy adults with severe (defined as ≥4 fluid stools per day for more than three days) acute community-acquired diarrhea; a bacterial pathogen was identified in 87 percent of cases [9].

Protozoa are less commonly identified as the etiologic agents of acute gastrointestinal illness. Indications for testing for protozoa are discussed below. (See 'When to obtain stool for ova and parasites' below.)

**DIAGNOSTIC APPROACH** — The initial evaluation of patients with acute diarrhea should include a careful history to determine the duration of symptoms and the frequency and characteristics of the stool. There should be an attempt to elicit evidence of extracellular volume depletion (eg, decreased skin turgor, orthostatic hypotension). Fever and peritoneal signs may be clues to infection with an invasive enteric pathogen.

**Indications for diagnostic evaluation** — A diagnostic evaluation is indicated in patients with relatively severe illness, as suggested by one or more of the following (algorithm 1) [5,10,11]:

- Profuse watery diarrhea with signs of hypovolemia
- Passage of many small volume stools containing blood and mucus
- Bloody diarrhea
- Temperature ≥38.5°C (101.3°F)
- Passage of ≥6 unformed stools per 24 hours or a duration of illness >48 hours
- Severe abdominal pain
- Hospitalized patients or recent use of antibiotics
- Diarrhea in the elderly (≥70 years of age) or the immunocompromised
- Systemic illness with diarrhea, especially in pregnant women (in which case listeriosis should be suspected)

**Historical clues** — The patient's history can be useful in identifying the pathogens associated with an episode of acute diarrhea and may help to guide empiric therapy when it is indicated. In addition to identifying the diarrhea as originating in the small or large bowel (table 2), further diagnostic clues may be provided by questioning about factors that might expose a patient to potential pathogens, such as residence, occupational exposure, recent and remote travel, pets, and hobbies. (See "Travelers' diarrhea".)

A diagnostically important finding is fever, which suggests infection with invasive bacteria (eg, Salmonella, Shigella, or Campylobacter), enteric viruses, or a cytotoxic organism such as Clostridium difficile or Entamoeba histolytica [10]. (See "Microbiology and epidemiology of salmonellosis" and "Shigella infection: Epidemiology, microbiology, and pathogenesis" and "Microbiology, pathogenesis, and epidemiology of Campylobacter infection" and "Epidemiology and pathogenesis of viral gastroenteritis in adults" and "Clostridium difficile in adults: Epidemiology, microbiology, and pathophysiology" and "Intestinal Entamoeba histolytica amebiasis".)

A food history may also provide clues to a diagnosis. Consumption of unpasteurized dairy products, raw or undercooked meat or fish, or organic vitamin preparations may suggest certain pathogens (table 3A-B). In addition, the timing of symptoms with regard to exposure to suspected offending food can be important clues to the diagnosis (table 4) [10]. Women who are pregnant have a 20-fold increased risk of developing listeriosis from meat products or unpasteurized dairy products (such as soft cheeses). (See "Differential diagnosis of microbial foodborne disease".)

- Symptoms that begin within six hours suggest ingestion of a preformed toxin of Staphylococcus aureus or Bacillus cereus
- Symptoms that begin at 8 to 16 hours suggest infection with Clostridium perfringens
- Symptoms that begin at more than 16 hours can result from viral or bacterial infection (eg, contamination of food with enterotoxigenic or enterohemorrhagic E. coli).
 Syndromes that may begin with diarrhea but progress to fever and more systemic complaints such as head ache, muscle aches, stiff neck may suggest infection with Listeria monocytogenes, particularly in pregnant woman.

It is also important to ask about recent antibiotic use (as a clue to the presence of C. difficile infection, although it is possible for community-associated C. difficile infection to occur in patients without antibiotic exposure), other medications, and to obtain a complete past medical history (eg, to identify an immunocompromised host or the possibility of nosocomial infection). (See "Clostridium difficile in adults: Epidemiology, microbiology, and pathophysiology" and "Epidemiology and causes of acute diarrhea in developed countries" and "Clostridium difficile in adults: Clinical manifestations and diagnosis" and "Evaluation of the HIV-infected patient with diarrhea".)

**Bloody diarrhea** — Acute bloody diarrhea is an uncommon disorder, being present in 3 percent of more than 30,000 stool cultures in a review from the United States [12]. A pathogen was identified in 20 percent. E. coli O157:H7 was present in 7.8 percent of visibly bloody specimens (compared to 0.1 percent of specimens that were not visibly bloody) and accounted for 39 percent of cultured pathogens in visibly bloody specimens compared to only 7 percent of cultured pathogens in all stools (bloody and nonbloody). Less common bacterial causes of visibly bloody diarrhea were Shigella, Campylobacter, and Salmonella species. (See "Epidemiology and causes of acute diarrhea in developed countries", section on ‘Bloody diarrhea’.)

**Fecal leukocytes and occult blood** — Several studies have evaluated the accuracy of fecal leukocytes alone or in combination with occult blood testing. The ability of these tests to predict the presence of an inflammatory diarrhea has varied greatly, with reports of sensitivity and specificity ranging from 20 to 90 percent [13-16].

- A meta-analysis of diagnostic test accuracy estimated that, at a peak sensitivity of 70 percent, the specificity of fecal leukocytes was only 50 percent [16].
- A 2004 review estimated that, in developed countries, the sensitivity and specificity of fecal leukocytes for inflammatory diarrhea were 73 and 84 percent, respectively [11].
- In other studies, fecal leukocytes were not accurate predictors of the response to antibiotic therapy [9,17].

The variable estimates across studies may be partially due to differences in specimen processing and in operator experience. Because of these concerns about test performance, the role of testing for fecal leukocytes has been questioned [18]. However, the presence of occult blood and fecal leukocytes supports the diagnosis of a bacterial cause of diarrhea in the context of the medical history and other diagnostic evaluation [19]; we perform this examination in addition to obtaining a bacterial culture in high risk patients. (See ‘When to obtain stool cultures’ below.)

Fecal leukocyte determination is probably not of value in patients who develop diarrhea while hospitalized, in whom testing for Clostridium difficile is much more likely to be helpful [20]. (See "Clostridium difficile in adults: Clinical manifestations and diagnosis".)

**Fecal lactoferrin** — The limitations of fecal leukocyte testing described above, provided the rationale for the development of a fecal lactoferrin latex agglutination assay (LFLA). Lactoferrin is a marker for fecal leukocytes, but its measurement is more precise and less vulnerable to variation in specimen processing [21,22].

Initial reports described sensitivity and specificity ranging from 90 to 100 percent in distinguishing inflammatory diarrhea (eg, bacterial colitis or inflammatory bowel disease) from noninflammatory causes (eg, viral colitis, irritable bowel syndrome) [21,23]. However, the test is not widely available.

**When to obtain stool cultures** — Consensus has not been achieved on the optimal strategies for obtaining stool cultures. The preceding discussion underscores the difficulty in predicting the presence of bacterial causes of acute
diarrhea, which is illustrated by the low rate of positive stool cultures in most reports (1.5 to 5.6 percent) (table 1) [5], with the exception of patients with severe disease [9]. (See ‘Etiology’ above.) Furthermore, the necessity of documenting a pathogen is not always clear since most infectious causes of acute diarrhea are self-limited.

For these reasons, it is reasonable to continue symptomatic therapy for several days before considering further evaluation in patients who do not have severe illness, particularly if occult blood and fecal leukocytes are absent [24]. Routine cultures are of little value in patients who develop diarrhea after being hospitalized for 72 hours or more [25]. Despite these limitations, we recommend obtaining stool cultures on initial presentation in the following groups of patients:

- Immunocompromised patients, including those infected with the human immunodeficiency virus (HIV) (see "Evaluation of the HIV-infected patient with diarrhea")
- Patients with comorbidities that increase the risk for complications
- Patients with more severe, inflammatory diarrhea (including bloody diarrhea)
- Patients with underlying inflammatory bowel disease in whom the distinction between a flare and superimposed infection is critical
- Some employees, such as food handlers, occasionally require negative stool cultures to return to work

The culture results on intraluminal fluid obtained at endoscopy appear to add little to the findings on stool culture [26].

**Processing stool cultures** — The clinician may need to specify the pathogens 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 [19,27,28]. The specimen 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. 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. (See "Aeromonas infections" and "Microbiology and pathogenesis of Yersinia infections", section on 'Laboratory isolation'.)

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. Gastroenteritis due to Listeria should be considered in outbreaks of febrile gastroenteritis with non-bloody diarrhea if routine cultures are negative. (See "Clinical manifestations and diagnosis of Listeria monocytogenes infection", section on 'Febrile gastroenteritis'.)

Unlike ova and parasites, which are often shed intermittently, these pathogens generally are excreted continuously. Thus, a negative culture is usually not a false negative, and repeat specimens are rarely required. Other organisms that should be considered in selected situations include Enterohemorrhagic Escherichia coli (EHEC), viruses, and vibrios.

**When to obtain stool for ova and parasites** — Sending stool samples for ova and parasites is not cost effective for the majority of patients with acute diarrhea [29]. There are, however, several possible indications for ova and parasite study [10]:

- Persistent diarrhea (associated with Giardia, Cryptosporidium, and Entamoeba histolytica)
- Persistent diarrhea following travel to Russia, Nepal, or mountainous regions (associated with Giardia,
Cryptosporidium, and Cyclospora)

- Persistent diarrhea with exposure to infants in daycare centers (associated with Giardia and Cryptosporidium)
- Diarrhea in a man who has sex with men (MSM) or a patient with AIDS (associated with Giardia and Entamoeba histolytica in the former, and a variety of parasites in the latter). (See "Evaluation of the HIV-infected patient with diarrhea").
- A community waterborne outbreak (associated with Giardia and Cryptosporidium)
- Bloody diarrhea with few or no fecal leukocytes (associated with intestinal amebiasis)

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 in contrast to bacterial pathogens.

Endoscopy — Endoscopy is uncommonly needed in the diagnosis of acute diarrhea [30]. It may be helpful in the following settings:

- Distinguishing inflammatory bowel disease from infectious diarrhea (see "Endoscopic diagnosis of inflammatory bowel disease").
- Diagnosing C. difficile infection and looking for pseudomembranes in patients who are toxic while results of tissue culture assays are pending. The widespread adoption of enzyme linked immunosorbent assays (ELISA) for C. difficile toxins A and B has reduced the need for endoscopy in these patients. (See "Clostridium difficile in adults: Clinical manifestations and diagnosis").
- In immunocompromised patients who are at risk for opportunistic infections with agents such as cytomegalovirus.
- In patients in whom ischemic colitis is suspected but the diagnosis remains unclear after clinical and radiologic assessment. (See "Colonic ischemia").

TREATMENT — The management of patients with acute diarrhea begins with general measures such as hydration and alteration of diet. Antibiotic therapy is not required in most cases since the illness is usually self-limited. Nevertheless, empiric and specific antibiotic therapy can be considered in certain situations. The treatment of specific infections is discussed in detail on the appropriate topic reviews.

Oral rehydration solutions — The most critical therapy in diarrheal illness is hydration, preferably by the oral route with solutions that contain water, salt, and sugar [31-35]. Oral rehydration therapy is grossly underutilized in the United States where health care providers tend to overuse intravenous hydration. It is estimated that proper use of oral rehydration could reduce hospitalizations of children by 100,000 per year [36].

Oral rehydration solutions 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.

The composition of the oral rehydration solution (per liter of water) recommended by the World Health Organization consists of:

- 3.5 g sodium chloride
- 2.9 g trisodium citrate or 2.5 g sodium bicarbonate
- 1.5 g potassium chloride
20 g glucose or 40 g sucrose

WHO-ORS is available from the manufacturer (Jinas Brothers, St. Louis, Mo). Rehydralyte (Ross Laboratories, Columbus, Ohio) is available over the counter, but contains 20 percent less sodium, so larger volumes are needed for rehydration. A similar solution can be made by adding one-half teaspoon of salt, one-half teaspoon of baking soda, and four tablespoons of sugar to one liter of water [35]. Cera-lyte is also available over the counter and is a rice based oral rehydration solution.

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 dehydrated. Diluted fruit juices and flavored soft drinks along with saltine crackers and broths or soups may also meet the fluid and salt needs in these less severely ill individuals [10].

If available, racecadotril, an enkephalinase inhibitor, may be an effective adjunct to oral rehydration solutions in children. In one study, it reduced the output and duration of watery diarrhea in a study of 135 Peruvian boys, ages three to 35 months [37].

**Empiric antibiotic therapy** — The lack of rapid diagnostic testing methods for enteric pathogens requires that decisions about therapy are often made empirically at the time of presentation. In general, empiric therapy for community-acquired acute diarrhea may be beneficial but does not appear to dramatically alter the course of illness in unselected populations. A large Swedish trial, for example, randomly assigned 598 adults with acute diarrhea of less than five days' duration to therapy with a five-day course of either norfloxacin 400 mg PO twice daily or placebo [38]. Enteric pathogens were isolated in 51 percent of evaluable cases; Campylobacter (29 percent) and Salmonella (16 percent) were the most frequent pathogens. The following findings were noted:

- Examining all culture-positive patients, there was a modest reduction in time to cure with norfloxacin (1.7 versus 2.8 days). The benefit was somewhat more pronounced in patients classified as being severely ill (1.5 versus 3.4 days) but there was no difference in the mean time until clinical cure in the subset of patients with Salmonella infection (6.5 versus 6.4 days).

- Norfloxacin was less likely than placebo to result in elimination of Salmonella from the stool on day 12 to 17 (18 versus 49 percent), and the median time to negative cultures was prolonged in the norfloxacin group.

This study was unusual in that enteric pathogens were identified in 51 percent of evaluable cases compared with the usual rate of pathogen isolation (eg, 1.5 to 5.6 percent, (table 1)), due to the fact that the majority of the patients had traveler's diarrhea, as 70 percent had traveled abroad within the previous six weeks.

The lack of benefit in otherwise healthy patients with nontyphoidal salmonella gastroenteritis noted in this trial was confirmed in a meta-analysis of 12 trials with 778 participants, including 258 infants and children [39].

**Enterohemorrhagic E. coli** — Antibiotics should be avoided in patients with suspected or proven infection with enterohemorrhagic E. coli (EHEC). There is no evidence of benefit from antibiotic therapy for EHEC infection and there is concern about an increase in the risk of hemolytic-uremic syndrome that might be mediated by an increase in the production or release of Shiga toxin when antibiotics are administered [40]. EHEC infection should be suspected in patients with bloody diarrhea, abdominal pain and tenderness, but little or no fever. (See "Clinical manifestations, diagnosis and treatment of enterohemorrhagic Escherichia coli (EHEC) infection".)

**Clostridium difficile** — Patients with acute diarrhea should be questioned carefully about prior antibiotic therapy and other risk factors for C. difficile infection. The appropriate therapy for this infection is discontinuation of antibiotics, if possible, and consideration of metronidazole or vancomycin if the symptoms are more than mild or worsen or persist. (See "Clostridium difficile in adults: Treatment".)
**Listeria monocytogenes** — Listeria may present with diarrhea and/or systemic illness. If cultured, treatment should be administered with *ampicillin* and *gentamicin* or *trimethoprim-sulfamethoxazole*. Although the latter may be more effective for treatment of listeriosis, it interferes with metabolism of *folic acid* and therefore should be used with caution in pregnant women.

**When to treat** — The 2001 IDSA practice guidelines concluded that any consideration of antimicrobial therapy must be carefully weighed against unintended and potentially harmful consequences [5].

The decision to treat with empiric antibiotic therapy in the following groups is based on randomized controlled trials showing benefit with a significant reduction in duration of diarrhea and other symptoms, practice guidelines, and overwhelming clinical experience [5,9,38,41-44]. The following findings were noted:

- Those with moderate to severe travelers' diarrhea as characterized by more than four unformed stools daily, fever, blood, pus, or mucus in the stool. (See "Travelers’ diarrhea").
- Those with more than eight stools per day, volume depletion, symptoms for more than one week, those in whom hospitalization is being considered, and immunocompromised hosts [9].

Empiric antibiotics can also be considered in patients who present with signs and symptoms of bacterial diarrhea such as fever, bloody diarrhea (except, as noted above, for suspected EHEC or *C. difficile* infection), and the presence of occult blood or fecal leukocytes in the stool.

We recommend empiric therapy with an oral fluoroquinolone (*ciprofloxacin* 500 mg twice daily, *norfloxacin* 400 mg twice daily, or *levofloxacin* 500 mg once daily) for three to five days in the absence of suspected EHEC or fluoroquinolone-resistant campylobacter infection [5,9,11,38,44]. *Azithromycin* (500 mg PO once daily for three days) or *erythromycin* (500 mg PO twice daily for five days) are alternative agents [44], particularly if fluoroquinolone resistance is suspected [45]. (See "Clinical manifestations, diagnosis, and treatment of Campylobacter infection").

**Specific antibiotic therapy** — The treatment of specific intestinal pathogens is discussed in detail on the appropriate topic reviews.

**Symptomatic therapy** — The antimitotility agent *loperamide* (Imodium) may be used for the symptomatic treatment of patients with acute diarrhea in whom fever is absent or low grade and the stools are not bloody. In two randomized controlled studies, loperamide compared with placebo significantly decreased the number of liquid bowel movements or diarrhea when given with *ciprofloxacin* [46,47]. The dose of loperamide is two tablets (4 mg) initially, then 2 mg after each unformed stool, not to exceed 16 mg/day for ≤2 days. Diphenoxylate (Lomotil) is an alternative agent, but it has not been studied in randomized controlled studies. The dose of diphenoxylate is two tablets (4 mg) four times daily for ≤2 days.

Diphenoxylate has central opiate effects and may cause cholinergic side effects. In addition, patients should be cautioned that treatment with these agents may mask the amount of fluid lost, since fluid may pool in the intestine. Thus, fluids should be used aggressively when antimitotility agents are employed.

Another potential problem is that both drugs may facilitate the development of the hemolytic-uremic syndrome (HUS) in patients infected with EHEC [48]. (See "Clinical manifestations, diagnosis and treatment of enterohemorrhagic Escherichia coli (EHEC) infection").

**Bismuth** subsalicylate (Pepto-Bismol) has also been used for symptomatic treatment of acute diarrhea. 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 [49-51]. However, in studies that compared bismuth subsalicylate with *loperamide*, loperamide brought significantly faster relief [49,52,53]. A role for bismuth subsalicylate may be in
patients with significant fever and dysentery, conditions in which loperamide should be avoided. The dose of bismuth subsalicylate is 30 mL or two tablets every 30 minutes for eight doses.

**Probiotics** — Probiotics, including bacteria that assist in recolonizing the intestine with non-pathogenic flora, can also be used as alternative therapy. Probiotics have been shown to be useful in treating traveler's diarrhea and acute non-specific diarrhea in children. (See "Travelers' diarrhea" and "Probiotics for gastrointestinal diseases".)

**Dietary recommendations** — The benefit of specific dietary recommendations other than oral hydration discussed above has not been well-established in controlled trials. However, adequate nutrition during an episode of acute diarrhea is important to facilitate enterocyte renewal [34]; if patients are anorectic, 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 [10]. Foods with high fat content should also be avoided until the gut function returns to normal after a severe bout of diarrhea.

In addition, secondary lactose malabsorption is common following infectious enteritis and may last for several weeks to months. Thus, temporary avoidance of lactose-containing foods may be reasonable. (See "Lactose intolerance".) The benefit of attempting to repopulate the bowel flora with yogurt containing live cultures or other probiotics is unproven 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 information: Diarrhea in adults (The Basics)" and "Patient information: E. coli (The Basics)")
- Beyond the Basics topics (see "Patient information: Acute diarrhea in adults (Beyond the Basics)"

**SUMMARY AND RECOMMENDATIONS**

- The initial evaluation of patients with acute diarrhea should include looking for evidence of extracellular volume depletion (eg, decreased skin turgor, orthostatic hypotension), a careful history to determine the duration of symptoms, and presence of fever and peritoneal signs, which may be clues to infection with an invasive enteric pathogen. (See 'Diagnostic approach' above.)

- A diagnostic evaluation is indicated in patients with relatively severe illness, bloody diarrhea, or high risk patients (eg, elderly or immunocompromised). (See 'Indications for diagnostic evaluation' above.)

- The patient's history can be useful in identifying the pathogens associated with an episode of acute diarrhea and may help to guide empiric therapy when it is indicated. A food history including consumption of unpasteurized dairy products, raw or undercooked meat or fish, or organic vitamin preparations may suggest certain pathogens (table 3A-B). In addition, the timing of symptoms with regard to exposure to suspected offending food can be important clues to the diagnosis (table 4). (See 'Historical clues' above.)
Several studies have evaluated the accuracy of fecal leukocytes alone or in combination with occult blood testing. The ability of these tests to predict the presence of an inflammatory diarrhea has varied greatly. (See 'Fecal leukocytes and occult blood' above.)

We recommend obtaining stool cultures on initial presentation in immunocompromised patients (HIV-infected, elderly, patients with comorbidities or with underlying inflammatory bowel disease), those with severe or bloody diarrhea, and in food handlers. (See 'When to obtain stool cultures' above.)

Sending stool samples for ova and parasites is not cost effective for the majority of patients with acute diarrhea. However, we recommend ova and parasite study in patients with persistent diarrhea, in men who have sex with men, during a community waterborne outbreak (associated with Giardia and Cryptosporidium), or with bloody diarrhea with few or no fecal leukocytes (associated with intestinal amebiasis). (See 'When to obtain stool for ova and parasites' above.)

The management of patients with acute diarrhea begins with general measures such as hydration and alteration of diet. We recommend no antibiotic therapy in most cases. (Grade 1A). (See 'Treatment' above.)

We recommend empiric antibiotic therapy for patients with moderate to severe travelers' diarrhea, those with signs and symptoms of invasive bacterial diarrhea such as fever and bloody diarrhea, the elderly, and immunocompromised hosts. (Grade 1A). We recommend no antibiotic treatment for patients with suspected or proven infection with enterohemorrhagic E. coli (EHEC). (Grade 1B). (See 'Empiric antibiotic therapy' above.)

If empiric therapy is warranted, we recommend treatment with a fluoroquinolone for three to five days in the absence of suspected EHEC or campylobacter infection. (Grade 1A). If campylobacter is suspected we recommend azithromycin or erythromycin as alternative agents, given high rates of fluoroquinolone resistance (Grade 1B). Directed antibiotic therapy should be administered when an intestinal pathogen is identified. (See 'When to treat' above and 'Specific antibiotic therapy' above.)

We suggest the antimotility agent loperamide (Imodium) be used for the symptomatic treatment of patients with acute diarrhea in whom fever is absent or low grade and the stools are not bloody. (Grade 2A). (See 'Symptomatic therapy' above.)

Use of UpToDate is subject to the Subscription and License Agreement.

REFERENCES


Evaluation of acute diarrhea

Initial assessment
Evaluate for: dehydration, duration, and inflammation (fever, blood in stool)

Symptomatic therapy
(hydration, alteration of diet)

Severe illness - hypovolemia, bloody stools, fever, ≥6 unformed stools per 24 hours, duration >1 week, severe abdominal pain, elderly (age ≥65 years), or immunocompromised

Yes

No

Illness continues

Illness resolves

Test for fecal leukocytes
Routine stool culture
Consider nonroutine stool culture or ova and parasites in select situations (see text)
Consider C. difficile if recent antibiotic therapy

Inflammatory
(eg, Campylobacter, Shigella, Salmonella, Entero-hemorrhagic E. coli, C. difficile)

Consider empiric antibiotic therapy while awaiting culture results in the following groups: patients with fever or bloody diarrhea; patients with >8 stools per day, dehydration, symptoms >one week, immunocompromised, if hospitalization considered.

Noninflammatory
(eg, Norwalk, Rotavirus, C. perfringens, S. aureus, B. cereus, Giardia, drugs, occasionally IBD)

Continue symptomatic therapy

Further evaluation if symptoms persist

Consider specific therapy once pathogen identified (see text for indications, type of treatment)

Graphic 68348 Version 3.0
## Isolates recovered from stool cultures performed in the United States, 1980-1997

<table>
<thead>
<tr>
<th>Reference, study</th>
<th>Number of cultures performed</th>
<th>Isolates recovered, percent of cultures</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>Salmonella; Shigella; Campylobacter jejuni</td>
<td>STEC</td>
</tr>
<tr>
<td>Koplan, JP, et al. Lancet 1980; 2:413</td>
<td>2468</td>
<td>2.4</td>
<td>2.4*</td>
<td>-</td>
</tr>
<tr>
<td>Guerrant, RL, et al. Bull NY Acad Med 1987; 63:484</td>
<td>2020</td>
<td>1.5</td>
<td>1.5*</td>
<td>-</td>
</tr>
<tr>
<td>Siegel, DL, et al. JAMA 1990; 263:979</td>
<td>1964</td>
<td>2</td>
<td>0.6; .2; 1.2</td>
<td>-</td>
</tr>
<tr>
<td>Ova and parasites</td>
<td>1423</td>
<td>3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>2668</td>
<td>21</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Choi, SW, et al. J Clin Microbiol 1996; 34:928</td>
<td>1800</td>
<td>2.9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Slutsker, L, et al. Ann Intern Med 1997; 126:505</td>
<td>30,463</td>
<td>5.6</td>
<td>1.8; 1.1; 2.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Voetsch, AC, et al. Clin Infect Dis 2004; 38:S190</td>
<td>339,000</td>
<td>2.9</td>
<td>0.9; 0.4; 1.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Ova and parasites</td>
<td>217,886</td>
<td>2.1•</td>
<td>0.9; 0.4; 1.3</td>
<td>-</td>
</tr>
</tbody>
</table>

STEC: Shiga toxin producing Escherichia coli.
* Cumulative percentages for isolates of all 3 organisms.
• Cryptosporidium, 1.7 percent; Cyclospora, 0.4 percent.

### Enteric pathogens

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Small bowel</th>
<th>Colon</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacteria</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmonella*</td>
<td></td>
<td>Campylobacter*</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td></td>
<td>Shigella</td>
</tr>
<tr>
<td>Clostridium perfringens</td>
<td></td>
<td>Clostridium difficile</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td></td>
<td>Yersinia</td>
</tr>
<tr>
<td><em>Aeromonas hydrophila</em></td>
<td></td>
<td>Vibrio parahaemolyticus</td>
</tr>
<tr>
<td><em>Bacillus cereus</em></td>
<td></td>
<td>Enteroinvasive E. coli</td>
</tr>
<tr>
<td><em>Vibrio cholerae</em></td>
<td></td>
<td>Plesiomonas shigelloides</td>
</tr>
<tr>
<td><strong>Virus</strong></td>
<td>Rotovirus</td>
<td>Cytomegalovirus*</td>
</tr>
<tr>
<td></td>
<td>Norovirus</td>
<td>Adenovirus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Herpes simplex virus</td>
</tr>
<tr>
<td><strong>Protozoa</strong></td>
<td>Cryptosporidium*</td>
<td>Entamoeba histolytica</td>
</tr>
<tr>
<td></td>
<td>Microsporidium*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Isospora</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cyclospora</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Giardia lamblia</em></td>
<td></td>
</tr>
</tbody>
</table>

* 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 2.0
### Exposures associated with specific intestinal pathogens

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Epidemiologic clue(s) to diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacteria</strong></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Beef, pork, poultry, eggs</td>
</tr>
<tr>
<td>Clostridium perfringens</td>
<td>Beef, pork, poultry, home-canned foods</td>
</tr>
<tr>
<td>Bacillus cereus</td>
<td>Beef, pork, fried rice (Chinese), vegetables</td>
</tr>
<tr>
<td>Enterhemorrhagic E. coli</td>
<td>Beef, pork, fast food restaurants (undercooked hamburger), apple cider, leaf lettuce, milk, cheese, extremes of age</td>
</tr>
<tr>
<td>Enteroinvasive E. coli</td>
<td>Milk, cheese</td>
</tr>
<tr>
<td>Enterotoxigenic E. coli</td>
<td>Travelers to developing world</td>
</tr>
<tr>
<td>Salmonella</td>
<td>Beef, pork, poultry, eggs, (eg, Caesar salad), raw milk, ice cream, vegetables (eg, alfalfa sprouts), unpasteurized orange juice, pet ducklings, lizards, rattlesnake meat</td>
</tr>
<tr>
<td>Campylobacter</td>
<td>Poultry (undercooked at barbecues), raw milk and cheeses</td>
</tr>
<tr>
<td>Shigella</td>
<td>Daycare centers, vegetables (eg, green onions)</td>
</tr>
<tr>
<td>Yersinia</td>
<td>Pork (not common), beef, milk, cheeses, hemochromatosis</td>
</tr>
<tr>
<td>Vibrio cholerae</td>
<td>Shellfish from the Gulf of Mexico, inadequately cooked seafood from South America, coconut milk from Thailand, airline outbreaks</td>
</tr>
<tr>
<td>Vibrio parahaemolyticus</td>
<td>Ingestion of raw seafood, particularly in East Asia, shellfish, cirrhosis</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>Hospitalization, inpatient or outpatient antibiotic(s) or chemotherapy within the last several weeks, daycare centers</td>
</tr>
<tr>
<td>Listeria</td>
<td>Beef, pork, poultry, milk cheese, coleslaw, hot dogs, potato salad, pregnancy, neonates, immunocompromised patients</td>
</tr>
</tbody>
</table>

Graphic 75543 Version 1.0
### Exposures associated with specific intestinal pathogens

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Epidemiologic clue(s) to diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Viruses</strong></td>
<td></td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Daycare centers, nurseries, Australia</td>
</tr>
<tr>
<td>Noroviruses</td>
<td>Schools, nursing homes, cruise ships, camps, military barracks, vegetables, waterborne, foodborne, and shellfish-associated outbreaks</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Overcrowding, lack of clean water, patients and staff of institutions, day care centers, men who have sex with men, IV drug users, travelers, military barracks, shellfish (clams, oysters, mussels)</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>Infantile diarrhea, ?AIDS</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>HIV-infected homosexual men with AIDS, organ transplantation</td>
</tr>
<tr>
<td><strong>Protozoa</strong></td>
<td></td>
</tr>
<tr>
<td>Giardia lamblia</td>
<td>Daycare centers, swimming pools, travel (eg, St. Petersburg, mountainous areas with ingestion of stream water), fruit salad</td>
</tr>
<tr>
<td>Entamoeba histolytica</td>
<td>Travelers to endemic areas (eg, Mexico), for more than one month, men who have sex with men, institutions</td>
</tr>
<tr>
<td>Cryptosporidium</td>
<td>Daycare centers, swimming pools, AIDS, farm animal exposure, city water supply contamination</td>
</tr>
<tr>
<td>Cyclospora</td>
<td>Raspberries (from Guatemala)</td>
</tr>
<tr>
<td>Isospora</td>
<td>Haiti, HIV infection</td>
</tr>
<tr>
<td>Microsporidium</td>
<td>AIDS ( ? travelers, ? fresh water)</td>
</tr>
</tbody>
</table>
### Major foodborne microbes by the principal presenting gastrointestinal symptom

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

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 1.0
Disclosures

Disclosures: Christine A Wanke, MD Grant/Research/Clinical Trial Support: GSK [Provision of drug and placebo for NIH-funded clinical trial (Lovaza)]. Consultant/Advisory Boards: Pfizer [Clinical event adjudication (Maraviroc)]; Cubist [DSMB]; Par [Patent case]. Other Financial Interest: Vindico [CME program]. Stephen B Calderwood, MD Consultant/Advisory Boards: Pulmatrix [Inhaled antimicrobial products (Not currently released)]. Patent Holder: Vaccine Technologies [Cholera (Cholera vaccines)]. Equity Ownership/Stock Options: PharmAthene [Biodefense (Anthrax)]. Allyson Bloom, MD Employee of UpToDate, Inc.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy