

Initial evaluation:

- Assess duration, frequency, characteristics of symptoms
- Assess hydration status
- Evaluate for exposures or comorbidities/risk factors
- Food and recreational water exposure, animal contact, travel to resource-limited settings, occupation (e.g., in daycare centers)

- Recent hospitalization in past 3 months and/or
- Recent antimicrobial therapy

yes

Possible Clostridium difficile Infection¹

- Order Clostridium diff. antigen/toxin test
- Consider ID consult for toxic mega-colon or multiple recurrences
- Evaluate for other risk factors
 - Age
 - Higher risk antibiotic (fluoroquinolones, penicillins, 2nd & 3rd generation cephalosporins, clindamycin)
 - Gastric acid suppression
 - Immunosuppression
 - Gastrointestinal surgery

no

Differentiating Symptoms

Inflammatory Diarrhea vs. Watery Diarrhea vs. Nausea & Vomiting only

Inflammatory Diarrhea²

- Fever
- Severe abdominal pain
- Bloody or mucoid diarrhea
- Presence of inflammatory cells/markers in stool
- See page 2 for common lab tests and pathogens
- See page 4 for risk factors/sources and treatment (empiric vs. targeted vs. supportive treatment only)

Watery Diarrhea²

- Large volume
- Abdominal bloating
- Usually no fever or bloody stools
- See page 2 for common lab tests and pathogens
- See page 3 for risk factors/sources and treatment (empiric vs. targeted vs. supportive treatment only)

Acute Nausea and Vomiting without Diarrhea^{2,4}

(r/o other intra-abdominal or urinary pathology)

Staphylococcus aureus enterotoxin

- S. aureus is ubiquitous in the environment and colonizes the skin and mucous membranes of many mammals and birds
- Associated with consumption of food (e.g. dairy, produce, meats, eggs, and salads) contaminated w/ food handler
- Symptoms manifest rapidly (within 1-6 hours)

Bacillus cereus enterotoxin

- B. cereus is ubiquitous in the environment, being found in decaying organic matter, soil, freshwater and salt water, vegetables, and the intestinal tracts of invertebrates
- Associated with consumptions of contaminated starchy food (e.g. rice)
- Symptoms manifest rapidly (within 1-6 hours)

Enteric viruses (norovirus, sapovirus, rotovirus, astrovirus)

- In addition to causing diarrhea, can also present with vomiting as the predominant feature

Treatment: self-limiting, provide adequate hydration, and monitor & correct electrolytes

Persistent diarrhea \geq 14 days should be worked up by culture and/or culture-independent microbiologic assessment, then treatment with anti-microbial agent directed to cause.³

Common Lab Tests

Watery diarrhea (Most common cause in resource-rich setting: Enteric viruses)^{2, 4, 5}:

Typical Pathogens		Common Lab Tests (Turn-around time)	
Enteric viruses, specifically Norovirus [5,509,597]		Norovirus Ag stool	ARUP 1-5 days
		Rotavirus Ag stool	ARUP 1-2 days
		Viral PCR panel	ARUP 2-5 days
Parasites:	<ul style="list-style-type: none"> • Giardia duodenalis [76,84]★ • Cryptosporidium spp. [57,616] 	Stool Ova and Parasites (O&P) exam	Copley 3-4 days
		Crypto/Giardia rapid Ag stool (optimal)	Copley 1-2 days
Parasites:	Cyclospora spp. [11,407] ★	Stool O&P exam	Copley 3-4 days
		Cyclospora/Isospora stain	Copley 1-2 days
Bacteria:	• Enterotoxigenic E. Coli [17,894]	Routine stool culture	Copley 3 days
	• Aeromonas, Plesiomonas shigelloides	Aeromonas, Plesiomonas shigelloids routine stool culture	Copley 3 days
	• Vibrio cholera [84], noncholeraic Vibrio spp. [52,228] ★	Vibrio culture (stool culture which requires selective media)	Copley reports neg after 3 days
	• Clostridium perfringens enterotoxin [966,958]	Symptoms are relatively mild and testing is NOT routinely performed	Public Health lab referral: Food and stool cultured for outbreak investigations
	• Listeria [1591]	Blood cultures	Copley 5 days for negative

Inflammatory diarrhea (Bacteria are more likely pathogens in this case compared with milder watery diarrhea)^{2, 4, 5}:

Typical Pathogens/Marker	Common Lab Tests (Turn-around time)	
Bacteria: Shiga toxin-producing E. Coli (STEC) [175,905], nontyphoidal Salmonella [1,027,561], Campylobacter [845,024]★, Shigella [131,254]	Routine stool culture	Copley 3 days
	E. coli Shiga-like Toxin by EIA	ARUP 2 days
Bacteria: Yersinia [97,656]	Yersinia culture (stool culture which requires selective media)	Copley Negatives reported after 3 days
Parasites: Entamoeba histolytica ★	Stool O&P exam	Copley 3-4 days
	Entamoeba histolytica Antigen, EIA (optimal)	ARUP 2 days
Inflammatory cells/markers in stool	Fecal leukocyte test (not to be used to establish the cause of acute infectious diarrhea but to differentiate inflammatory diarrhea from secretory diarrhea)	Copley: same day when sample arrives

[.]: CDC estimated number of cases per year in the U.S.

Giardia duodenalis^{2, 6, 9}

- Protozoan parasite
- **Persistent/chronic diarrhea (> 14 days)**
- Mean incubation period: 7-14 days
- Classic food sources: fecal contaminated food or water

Risk Factors/Source ★

- Men who have sex with men
- Child care center attendance/employment
- Hiking, camping (particularly when in contact with water)

Treatment:

- Tinidazole 2g PO x 1 dose (WAC \$14.50)
- Nitazoxanide 500mg PO BID x 3 days (WAC \$625)

Cyclosporidium cayatanensis^{2,11} ★

- Protozoan parasite
- Mean incubation period: 2-28 days
- Classic food sources: imported berries, herbs
- Relatively chlorine insensitive

Risk Factors/Source

- Travel to resource-challenged countries
- Contaminated drinking or swimming water
- Chronic diarrhea in advanced HIV infection

Treatment:

- Bactrim DS tablet PO BID X 7-10 days

Alternative: Nitazoxanide 500 mg PO BID x 7days (WAC \$1458)

Aeromonas and Plesiomonas shigelloides^{4,12,14,15}

- Gram-negative bacilli widely distributed in water environments
- Aeromonas: concentrations peak when water temperatures rise substantially during summer months.
- P. shigelloides: transmission primarily through the consumption of seafood or water that has been contaminated with sewage.

Risk Factors/Source

- Travel to resource-challenged countries ★
- Swimming/drinking in fresh water sources/recreational water sources (swimming pools)

Treatment: (self-limiting, Abx reasonable for severe cases)

- Azithromycin 500mg daily X 3 days or Ciprofloxacin 750 mg daily X 3 days.

WATERY DIARRHEA

- large volume of diarrhea
- abdominal bloating
- usually no fever or bloody stools

Empiric Therapy⁶

- **Not recommended except in:**
 - Immunocompromised pts or young infants who are ill-appearing. **Tx:** Azithromycin po 1g x 1 dose or 500mg daily x 3 days.
 - **Patients with persistent watery diarrhea lasting >=14 days should have therapy targeted to cause:**
- Tests:** O&P, Crypto/giardia rapid Ag, stool culture

Enteric Viruses^{2,3,7,8}

- Begins 12 hours to 5 days after exposure
- Lasts three to seven days
- Most community-acquired diarrhea is viral in origin and is NOT shortened by the use of antibiotics

Norovirus

- Most common viral cause of epidemic gastroenteritis worldwide
- Vomiting is more prominent than in gastroenteritis caused by other viruses

Rotavirus

- Usually in children between 6 months and 2 years
- Vaccine available

Treatment: self-limiting, provide adequate hydration, monitor & correct electrolytes

Vibrio spp. ^{2,6,18}

- Gram-negative rods widely distributed in saltwater environments
- Toxin-producing strains of *V. cholerae* cause Cholera, characterized by passage of profuse “rice-water” stool. Rare in U.S. Mostly from travelers. ★
- Non-choleraic Vibrios are associated w/ shellfish and seafood and present as watery diarrhea w/ or w/o dysenteric characteristics
- Mean incubation period: 1-3 days

Treatment:

- Doxycycline 300 mg x 1 dose (resistance concern) or Azithromycin 500mg daily x 3 days

Cryptosporidium parvum^{2,10}

- Protozoan parasite
- **Persistent/chronic diarrhea (> 14 days)**
- Mean incubation period: 2-28 days
- Classic food sources: vegetables, fruit, unpasteurized milk

Risk Factors/Source

- Child care center attendance/employment
- Recreational water sources (swimming pools)
- Visiting a farm or petting zoo
- Chronic diarrhea in advanced HIV infection

Treatment (for severe acute symptoms or symptoms >= 14 days)

- Nitazoxanide 500mg PO BID x 3 days (WAC \$625)

Enterotoxigenic E. coli (ETEC)^{2,12, 13}

- Most common cause of traveler’s diarrhea
- Undistinguishable from other E. coli strains in routine stool cultures
- Mean incubation period: 1-3 days

Risk Factors/Source

- Travel to resource-challenged countries
- Foodborne outbreaks in hotels, cruise ships, restaurants, catered events

Treatment: (usually self-limiting; Abx is reasonable in severe/persistent diarrhea particularly for children or immunocompromised hosts)

- Azithromycin 1g X 1 dose or 500 mg daily X 3 days

Clostridium Perfringens^{2,16}

- Second most common bacterial cause of foodborne outbreak-associated illnesses; Serotype A is the most common serotype associated w/ food poisoning and diarrhea, with mean incubation period of 8-16 hours.

Risk Factors/Source

- Beef, poultry, gravies, and dried or pre-cooked foods, when kept warm for a long time before serving.

Treatment: Self-limiting; antibiotics are **not** recommended. Hydration and electrolyte support only.

Listeria (13x more common in pregnancy & can cause fetal and newborn harm.) Check blood cultures.

Treatment: Ampicillin 2 g IV q 4h x 14 days

Therapy should be accompanied by supportive care: fluid, electrolytes and nutrition. ★ **Travel-related pathogen: Travel-related illnesses > 40% of total number of illnesses.**⁵

Boxes with thicker borders highlight organisms usually requiring antimicrobial treatment, as opposed to organisms that are self-limiting or treatment is not recommended

Higher cost antimicrobials are listed with WAC= wholesale acquisition cost

INFLAMMATORY DIARRHEA

Entamoeba histolytica^{2,23}

- Protozoan parasite
- Mean incubation period: 1-3 weeks
- Classic food source: fecal contaminated food or water

Risk Factors/Source ★

- Men who have sex with men
 - Generally seen in migrants from and travelers to endemic areas, including Africa, Mexico, parts of Central and South America

Treatment:

- All E. histolytica infections should be treated, even in the absence of symptoms, given the potential risk of developing invasive disease and the risk of spread to family members.
- Metronidazole 500-750mg PO TID x 7-10 days plus or followed by luminal agent

Luminal agent:

- Paromomycin 25-30mg/kg PO divided in 3 doses x 7 days (WAC \$4/250 mg tab, ~\$224/7-day course)

Yersinia enterocolitica^{2,6,24}

- Gram-negative coccobacilli
- Mean incubation period: 4-6 days

Risk Factors/Source

- **Contaminated pork or pork products** but also may be found in unpasteurized milk/dairy products or undercooked/raw meat
- Pets with diarrhea
- Abnormalities of iron metabolism (e.g. cirrhosis hemochromatosis, thalassemia)
- Blood transfusion

Treatment:

- Bactrim DS tablet PO BID X 5 days
- IV Ceftriaxone 2g daily + gentamicin 5 mg/kg per day in 1 to 3 divided doses for hospitalized pts with severe disease

Alternative: Cipro 500mg PO BID x 5 days

- Fever
- Severe abdominal pain
- Bloody or mucoid diarrhea
- Presence of inflammatory cells/markers in stool

Empiric Therapy^o

Not recommended except:

1. Patients who have recently traveled internationally w/ T $\geq 38.5^{\circ}\text{C}$ and/or signs of sepsis
2. Infants <3 months of age with suspicion of bacterial etiology.
3. Immunocompromised patients with severe illness and bloody diarrhea.
4. Immunocompetent patients with symptoms presumptively due to Shigella, e.g. abdominal pain, bacillary dysentery (frequent scant bloody stools, fever, abdominal cramps, tenesmus).

Tests: Stool culture, Fecal leukocytes, E.coli Shiga-like toxin EIA, Yersinia and for parasites: O&P, Entamoeba ag

Drug choices:

-Azithromycin PO 1g x 1 dose or 500mg daily x 3 days

Campylobacter, Nontyphoidal Salmonella, Shigella^{2,12,19,20,21}

- Most common causes of bacterial gastroenteritis
- Mean incubation period: 1-3 days
- Classic food source: undercooked contaminated meat and meat products or unpasteurized milk/dairy products

Risk Factors/Source

- Men who have sex with men (Shigella)
- Travel to resource-challenged countries (Campylobacter) ★
- Child care center attendance or employment (Shigella)
- Animal contact (petting zoo, farm, reptiles, house pets w/ diarrhea)
- Swimming in or drinking untreated fresh water
- Immunocompromised patients (longer course of therapy recommended x 7-14days)

Treatment (usually self-limiting):

- Azithromycin PO 500 mg daily X 3 days
- Shigella: for individuals at high resistance risk, e.g. infection acquired in Asia or Africa, HIV, men who have sex with men, suggest Ceftriaxone iv 1-2 g daily X 5 days.

Shiga toxin-producing E.coli (STEC)^{2,6,22}

- Clinical manifestations: **a visibly blood stool, no reported fever, a WBC >10,000/ μL , and abdominal tenderness.**
- Mean incubation period: 1-8 days.
- Classic food source: ground beef and other meat, fresh produce, unpasteurized milk/juice.
- Other risk factors: daycare centers, nursing homes, extremes of age.

Major complication

- Hemolytic-uremic syndrome (HUS): characterized by triad of acute renal failure, microangiopathic hemolytic anemia, and non-immune thrombocytopenia.
- HUS complicated 6-9% of STEC infections overall and about 15% of STEC infections in children < 10 years old.
- Risk factors of HUS: serotype O157, shiga toxin type 2, host age, immune status, use of drugs (e.g. antibiotics, PPI, and antimotility drugs)

Treatment:

- Supportive care and monitoring for complications (HUS)
- **Avoid anti-peristaltic agents and antibiotics** given their potential to increase toxin production and the risk of HUS

Therapy should be accompanied by supportive care: fluid, electrolytes and nutrition. ★ Travel-related pathogen: Travel-related illnesses > 40% of total number of illnesses.⁵

Boxes with thicker borders highlight organisms usually requiring antimicrobial treatment, as opposed to organisms that are self-limiting or treatment is not recommended

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