GUIDELINES FOR TREATMENT OF ACUTE INFECTIOUS DIARRHEA IN ADULTS

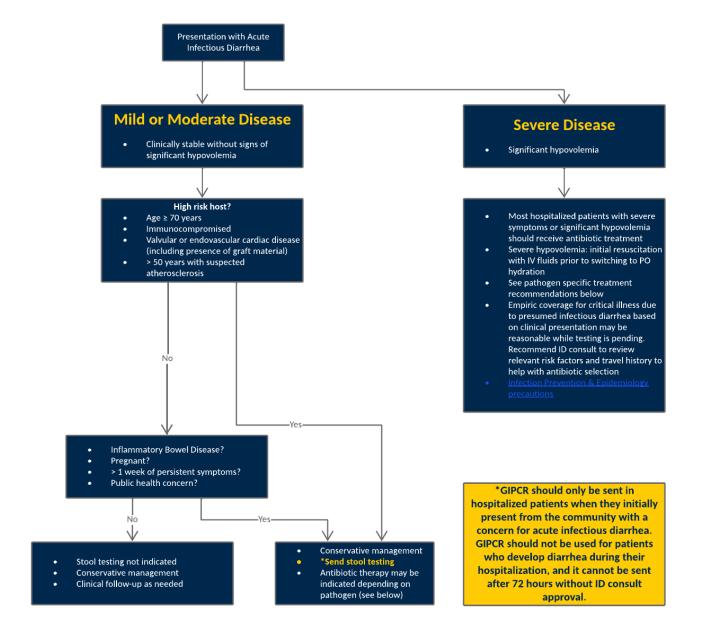


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<u>Campylobacter</u>	<u>Plesiomonas</u>	Nontyphoidal Salmonella (NTS)		
<u>Salmonella enterica, Typhi, or</u> <u>Paratyphi</u>	<u>Shigella</u>	<u>Vibrio</u>		
Yersinia enterocolitica	Shiga toxin producing E. coli (STEC)	Enteropathogenic E. coli (EPEC) & Enterotoxigenic E. coli (ETEC)		
Enteroaggregative E. coli (EAEC)	<u>Giardia</u>	Cryptosporidium		
<u>Cyclospora</u>	Entamoeba histolytica	<u>Viruses</u>		
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Clostridioides (formerly Clostridium difficile) Please refer to Guidelines for Evaluation and Treatment of Clostridium difficile Colitis in Adults



Most types of infectious diarrhea do not warrant therapy with antibiotics, as the course is typically mild and self-limited. Treatment should be considered for patients with severe infections (including those requiring hospitalization), immunocompromised hosts, and those with risk factors for complicated disease (listed below).

General Outpatient Recommendations:

For outpatients who are presenting with mild to moderate symptoms, conservative management is typically appropriate.

- Supportive care:
 - Ensure adequate rehydration:
 - For patients with mild symptoms diluted fruit juice, sports drinks or soup/broth may be adequate
 - For patients with more severe symptoms but still appropriate for outpatient management such as those with more frequent or voluminous diarrhea may require more aggressive rehydration with an oral rehydration solution such as Pedialyte.
 - Please note sports drinks (such as Gatorade[™]) are NOT equivalent to oral rehydration solutions.

- Antibiotic Therapy:

- Generally, antibiotics are not recommended for adults with mild to moderate symptoms who are appropriate for outpatient management.
- Bloody stools alone are not an indication for empiric antibiotics, except in the setting of bacillary dysentery (frequent scant bloody stools, abdominal pain, tenesmus, fever) due to presumptive Shigella
- Situations when antibiotics would be appropriate:
 - Severe disease or signs of sepsis
 - High Risk Hosts (Including those age >70, immunocompromised patients, valvular or endovascular cardiac disease – including presence of prosthetic graft material, and those greater than age 50 with atherosclerosis)
 - These patients should be closely assessed for the need for hospitalization. Stool testing should be performed, and antibiotics may be appropriate as outlined below
- Blood cultures should be obtained:
 - if signs of sepsis or systemic manifestations of infection
 - when there is concern for enteric fever (Typhoid fever) or recent travel to an area with endemic enteric fever
 - immunocompromised hosts
 - certain high-risk conditions which could indicate invasive disease (such as hemolytic anemic)
- o Certain special populations including pregnant women and those with public health implications (such as food service employees) may have specific considerations for treatment depending on the pathogen.
- Symptomatic Therapy:
 - Anti-motility agents such as loperamide can be considered on an individual basis but are not recommended for routine use
 - Should be avoided in patient with features of dysentery (fever, bloody or mucoid stools) or presentations concerning for Clostridium difficile infection.
 - Patients who use anti-motility agents should be advised to rehydrate aggressively as these can mask fluid losses
 - o Bismuth salicylate (Pepto-Bismol) is an acceptable alternative for symptomatic management

Probiotics:

 There is insufficient evidence to recommend the routine use of probiotics for treatment of acute infectious diarrhea.



Pathogen/ Infectious Agent	Outpatient	Hospitalized	Comments
Bacteria			
Exposures: Poultry Unpasteurized milk and dairy Season: Spring/Summer	Uncomplicated: - Supportive care, including oral rehydration, recommended for all patients. - No antibiotics recommended unless indications present Antibiotic Indications: - Prolonged or severe disease - Immunocompromised host First line: - Azithromycin 500 mg daily - Duration: 3 days Second line (if macrolide allergy): - Ciprofloxacina 750 mg BID - Duration: 3 days	Supportive care, including rehydration (oral vs IV), recommended for all patients. Uncomplicated: First line: - Azithromycin 500 mg daily - Duration: 3 days Second line (if macrolide allergy): - Ciprofloxacina 750 mg BID - Duration: 3 days Complicated*: Infectious disease consult recommended. First line: - Azithromycin 500 mg daily - Duration: 7 days** Second line (if macrolide allergy): - Ciprofloxacina 750 mg BID - Duration: 7 days** Critical Illness/ ICU Level of Care: Infectious disease consult strongly recommended. Preferred: - IV Meropenema*** - Duration: 14 days - Step-down therapy to Azithromycin (first line) or ciprofloxacin (if macrolide allergy) may be	 Typically a self-limited illness and only a small reduction of symptom duration observed with treatment (about 1 day), therefore most cases do not require antimicrobial treatment. NARMS data (prelim) from 2022 shows that 30% of isolates are quinolone resistant whereas only 1-2% are resistant to azithromycin. If Campylobacter fetus suspected, send Campylobacter stool culture (not detected on GI panel) *Complicated infection includes those with bacteremia or evidence of invasive infection. **A longer course of up to 14 days may be considered for patients with delayed improvement after starting therapy ***In the setting of severe systemic illness from Campylobacter – meropenem is recommended as Campylobacter is inherently resistant to most other betalactam antibiotics If desired, residual sample from GI panel can be sent to Mayo for susceptibility testing at team's request.
Clostridioides (formerly Clostridium difficile)	Please refer to <u>Guidelines for Evaluat</u>	appropriate pending clinical course tion and Treatment of Clostridium difficile Coli	itis in Adults



Pathogen/ Infectious Agent	Outpatient	Hospitalized	Comments
Non-Typhoidal Salmonella	Uncomplicated: - Supportive care, including oral rehydration,	Supportive care, including rehydration (oral vs IV), recommended for all patients.	*Treatment may prolong shedding in the stool.
Exposures: Contaminated food Live poultry Reptile contact	recommended for all patients Antibiotics not recommended unless indication present*	Mild-Moderate Disease: Preferred: - Azithromycin 1 g once followed by 500 mg daily - Duration: 5 days‡	**Treatment indicated in these groups due to the increased risk for invasive disease. ‡Could extend duration up to 7 days for patients with bacteremia or significant immunosuppression. Consider infectious
Season: Summer/Fall	Antibiotic Indications: - Severe disease – severe diarrhea (>9 stools daily), fever >102°F, persistent fever, need for hospitalization - Sickle cell disease or other hemoglobinopathy - >50 years old** - Immunocompromised** - Valvular or Endovascular Cardiac Disease including presence of prosthetic graft material**	Alternative†: - TMP-SMX ^a 1 DS tablet BID - Duration: 5 days‡ OR - Ciprofloxacin ^a 500 mg BID - Duration: 5 days‡ Severe Disease: Infectious disease consult recommended. Preferred: - Ceftriaxone 2 g IV q24h - Duration: 7 days	disease consult. †Alternative choices with comparable expected efficacy therefore choice should be based on allergies and comorbid diseases. If hardware or graft material present consider imaging. A positive GI panel result for Salmonella will reflex to stool culture with susceptibilities.
	Preferred: - Azithromycin 1 g once followed by 500 mg daily - Duration: 5 days Alternative†: - Ciprofloxacina 500 mg BID - Duration: 5 days OR - TMP-SMXa 1 DS tablet BID - Duration: 5 days OR - Cefiximea 400 mg daily - Duration: 5 days	Alternative: - Ciprofloxacina 750 mg BID - Duration: 7 days	



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Pathogen/ Infectious Agent	Outpatient	Hospitalized	Comments
Salmonella enterica, Typhi or Paratyphi Exposures: Travel to Southern Asia (India, Pakistan, Bangladesh), Africa, SE Asia Season: Travel during monsoon season in endemic areas increases risk, but present year-round	Infectious Disease consult recommended Antimicrobial treatment is recommended for all patients Preferred: - Azithromycin 1 g daily (or 1 g once then 500 mg daily) - Duration: 5 days Alternative: - Ciprofloxacina 500 mg BID - Duration: 7 days OR - Cefixime 200 mg BID - Duration: 7 days*	Infectious Disease consult recommended Antimicrobial treatment is recommended for all patients Preferred: - Ceftriaxone 2 g IV q24h - Duration: 10-14 days** Alternative: - Ciprofloxacin³ 500 mg BID - Duration: 7-10 days	Region-specific recommendations: If patient acquired severe infection after travel to Pakistan, recommended first line agent is meropenem given ongoing outbreak of XDR Salmonella typhi in the area. Infection acquired in South Asia has risk of fluoroquinolone non-susceptibility, making preferred oral treatment azithromycin. Preliminary NARMS data from the 2020-2023 has ceftriaxone resistance across all typhoidal Salmonella spp to be 4-12% (an increase from essentially no resistance previously). Similarly, cipro resistance in preliminary data is 10-20%, an increase from previously. Blood cultures and stool testing (GI panel, which will reflex to cx if + for Salmonella) should always be obtained prior to initiation of antibiotics. Stool culture has low sensitivity for the diagnosis of Typhoid/Enteric Fever. In a patient with appropriate exposures and a compatible clinical syndrome negative stool testing would not exclude the disease. *Cefixime may have a higher risk of treatment failure than fluoroquinolone or azithromycin ** If rapid clinical improvement, 10-day course is appropriate; however, if slower improvement course should be extended to 14 days Can cause bacteremic illness (enteric fever) — headache, lethargy, malaise, abdominal pain, diarrhea (uncommon) In older patients with sustained fever or bacteremia, or in patients with underlying atherosclerosis or new onset chest back abdominal pain consider imaging to detect aortitis, mycotic aneurysm, signs/symptoms of peritonitis, intra-abdominal free air, toxic megacolon, or other extravascular foci of infection Resistance varies globally Step-Down Therapy: For hospitalized patients, can consider step down therapy (once clinically improved) with azithromycin, ciprofloxacin, or cefixime as above. Alternatively, Amoxicillina 1 g TID x10-14 days can be considered if the isolate is susceptible. A positive GI panel result for Salmonella will reflex to stool culture with susceptibilities.





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Pathogen/ Infectious Agent	Outpatient	Hospitalized	Comments
Shigella Exposures: Egg salad Lettuce Day care MSM Season: No specific season	Uncomplicated: - Supportive care, including oral rehydration, recommended for all patients - Antibiotics not recommended unless indication present Antibiotic Indications: - Immunocompromised - Severe Disease - Food Handlers, Childcare Providers, Residents of Nursing Homes - Consider treatment for other patients who pose a public health risk due to an increased risk of exposing others Preferred: - Ciprofloxacina* 500 mg BID - Duration: 3 days Second line (if FQ allergy): - Cefiximea 200 mg BID - Duration: 5 days	 Supportive care, including oral or IV rehydration, recommended for all patients. Antibiotics recommended for all patients requiring admission for Shigella Preferred: Ceftriaxone 2 g IV q24h Duration: 5-7 days Alternative: Ciprofloxacina* 500 mg BID Duration: 5-7 days If susceptibility data available, could consider azithromycin 500 mg daily for 5 days or TMP-SMX DS BID for 5 days if susceptible 	*Fluoroquinolones should be avoided if ciprofloxacin MIC is 0.12 ug/mL or higher, even if labeled as susceptible. From preliminary NARMS data for 2018-2023, Azithromycin has about 25% resistance, TMP-SMX has about 60% resistance, Ciprofloxacin with 20%, and Ceftriaxone with 12%. Shigella dysenteriae type 1 may produce Shiga toxin and can cause HUS Oral step-down recommendations: With rapid clinical improvement with ciprofloxacin therapy, would recommend 5-day total course With immunocompromised host or slower clinical improvement with ciprofloxacin therapy, would recommend 7-day total course With improvement on ceftriaxone therapy, could transition to cefixime therapy to complete treatment as an outpatient A positive GI panel result for Shigella will reflex to stool culture with susceptibilities.
Vibrio vulnificus or Vibrio parahaemolyticus Exposures: Shellfish Brackish Water Season: No specific season	For patients with mild disease who are appropriate for outpatient management antibiotic therapy is usually not indicated unless risk factors for invasive disease present. Risk Factors for Invasive Disease: - Chronic Liver Disease (including cirrhosis, alcoholic liver disease and hepatitis) - Iron Overload states (hemochromatosis, hemolytic anemia or chronic renal failure) - Immunocompromised Mild/Non-Invasive Disease With Risk For Invasive Disease: Preferred: - Doxycycline 100 mg BID - Duration: 5 days Second line: - Ciprofloxacina 500 mg BID - Duration: 5 days	Infectious Disease Consult is recommended If wound present, recommend surgical consultation for consideration of debridement Mild/Non-Invasive Disease: Preferred: - Doxycycline 100 mg BID - Duration: 5 days Second line: - Ciprofloxacina 500 mg BID - Duration: 5 days Severe/Invasive Disease: Preferred: - Ceftriaxone 2 g IV q24h + doxycycline 100 mg BID - Treatment duration pending clinical improvement	 Can cause a diarrheal illness. Also associated with wound infections if exposure to brackish water and primary septicemia without a wound. If Vibrio wound infection present, surgical debridement of necrotic tissue is indicated. If any concern for a vibrio septicemia or wound infection patient should be admitted for further assessment and management as there is a high rate of mortality and progression in these patients. ID consult is recommended. If desired, residual sample from GI panel can be sent to Mayo for susceptibility testing at team's request.



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Pathogen/ Infectious Agent	Outpatient	Hospitalized	Comments	
Yersinia enterocolitica Exposures: Unpasteurized milk Undercooked Pork Chitterlings Season: Winter	Uncomplicated: - Supportive care, including oral rehydration, recommended for all patients Insufficient evidence to recommend outpatient antibiotics.**	Complicated Infection*: Preferred: - Ceftriaxone 2 g IV q24h - Duration: 21 days† Critical Illness: - Consider addition of gentamicin, extended interval dosing	Biofire assay (GI panel) can have false positive results as the media can be contaminated with yersinia nucleic acid, so correlate with the clinical picture. If desired, residual sample from GI panel can be sent to Mayo for susceptibility testing at team's request. Antimicrobial therapy decreases the duration of fecal shedding of Yersinia *Defined as presentation with sepsis or bacteremia **There are no controlled trials that indicate antimicrobial treatment for uncomplicated disease is beneficial. Antibiotics are indicated for complicated illness, including sepsis. If planning to treat uncomplicated disease, duration should not be longer than 5 days. †There are no clear recommendations for duration of antimicrobials, as the literature is primarily from case series. Oral step-down therapy: Can complete therapy with TMP-SMX 1 DS tablet BID, doxycycline 100 mg BID, or ciprofloxacin 500 mg BID to complete 21	
Shiga Toxin Producing E coli (STEC) Exposures: Unpasteurized milk Fresh produce Ground beef Petting zoos Season: No specific season	Supportive care, including oral rehydration, recommended for all patients. Antimicrobials should be avoided.	Supportive care, including oral or IV rehydration, recommended for all patients. Antimicrobials should be avoided.	Treatment with antibiotics should be avoided given the risk of inducing hemolytic uremic syndrome.	
Enteropathogenic E coli (EPEC) & Enterotoxigenic E coli (ETEC) Exposures: International Travel Season: No specific season	Consider alternate etiologies of diarrhea	Consider alternate etiologies of diarrhea Severe illness or significant immunocompromise: - Can be a cause of traveler's diarrhea - Typically occurs at time of international travel - If compatible clinical history could treat with azithromycin 1 g as single dose	Biofire assay (GI panel) has potential for cross reactivity with normal GI flora. In addition, asymptomatic carriage may occur. Other etiologies for diarrhea, including non-infectious etiologies, should be investigated before pursuing treatment.	



Pathogen/ Infectious Agent	Outpatient	Hospitalized	Comments
Enteroaggregative E coli (EAEC) Exposures: International Travel Season: No specific season Plesiomonas shigelloides Exposures: Tropical travel Undercooked seafood Reptiles Contaminated water Season: No specific season	Supportive care, including oral rehydration, recommended for all patients. Preferred: - Azithromycin 1 g - Duration: Single dose Second line (if allergy): - Ciprofloxacin³ 500 mg - Duration: Single dose Uncomplicated: - Supportive care, including oral rehydration, recommended for all patients Antibiotics not recommended unless indication present* *Antibiotic Indications: - Immunocompromised - Elderly Preferred: - Ciprofloxacin³ 500 mg PO BID - Duration: 3-5 days, pending clinical improvement	Supportive care, including oral or IV rehydration, recommended for all patients. Preferred: - Azithromycin 1 g - Duration: Single dose Second line (if allergy): - Ciprofloxacina 500 mg - Duration: Single dose Mild/moderate with antibiotic indications: Preferred: - Ciprofloxacina 500 mg PO BID Severe (Requiring IV rehydration): Preferred: - Meropenema 1 g IV q8h - Duration: 3-5 days, pending clinical improvement	 Associated with both traveler's and nontraveler's diarrhea. Supportive care is the mainstay of treatment. Susceptibility testing is recommended. Step down to narrower agents once susceptibilities have returned There are case reports of patients with extraintestinal infections (bacteremia, skin infections, eye infections, etc), typically immunocompromised, neonates, or hepatobiliary disorders For bacteremia or extra-intestinal infections, consult ID to help with selection and duration.
Parasites			
Giardia lamblia Exposures: Contaminated recreational water Daycare International Travel Season: No specific season	Preferred: - Tinidazole 2 g - Duration: Single Dose Alternative: - Nitazoxanide 500 mg BID - Duration: 3 days	Preferred: - Tinidazole 2 g - Duration: Single Dose Alternative: - Nitazoxanide 500 mg BID - Duration: 3 days OR - Metronidazole 500 mg PO BID - Duration: 5 days	 Acquired lactose intolerance occurs in up to 40% of patients Rarely giardia can cause prolonged infection with chronic malabsorption and weight loss About 10-20% of Giardia infections are refractory, so if persistent diarrhea and positive test results recommend ID referral.



Pathogen/	Outrations	Hamitalian d	Comments
Infectious Agent	Outpatient	Hospitalized	Comments
Cryptosporidium Exposures: Contaminated water Unpasteurized Apple Cider Season: No specific season	Immunocompetent hosts: - Supportive Care Immunocompetent hosts with severe or persistent symptoms (> 2 weeks): Preferred: - Nitazoxanide 500 mg BID - Duration: 3 days Alternative (If allergy): - Paromomycin 500 mg TID - Duration: 7 days Immunocompromised hosts: - Reduction of immunosuppression as possible, or initiation of ART if patient is HIV positive Preferred: - Nitazoxanide 500 mg BID - Duration: 14 days	Immunocompetent hosts: - Supportive Care Immunocompetent hosts with severe or persistent symptoms (> 2 weeks): Preferred: - Nitazoxanide 500 mg BID - Duration: 3 days Alternative (If allergy): - Paromomycin 500 mg TID - Duration: 7 days Immunocompromised hosts: - Reduction of immunosuppression as possible, or initiation of ART if patient is HIV positive Preferred: - Nitazoxanide 500 mg BID - Duration: 14 days	Consider screening for HIV with diagnosis Treatment failures can occur necessitating prolonged or combined therapy. For persistent or refractory cases, recommend referral to ID.
Cyclospora Exposures: Imported fresh	All cases of <i>Cyclospora</i> warrant treatment.	All cases of <i>Cyclospora</i> warrant treatment. Preferred:	Immunocompromised hosts may need extended duration of therapy pending resolution of symptoms
produce	Preferred: - TMP-SMX 1 DS tablet BID - Duration: 7 days	- TMP-SMX 1 DS tablet BID - Duration: 7-10 days	
<u>Season:</u>	, ,	Alternative (if allergy):	
No specific season	Alternative (if allergy):	- Nitazoxanide 500 mg BID	
	Nitazoxanide 500 mg BIDDuration: 7 days	- Duration: 7 days	



Pathogen/	Outpatient	Hospitalized	Comments
Entamoeba histolytica Exposures: International Travel Season: No specific season	All E histolytica should be treated given the risk of invasive disease. ID Referral recommended Asymptomatic: - Can be treated with a luminal agent alone. Preferred: - Paromomycin 25-30 mg/kg daily in 3 divided doses for 7 days Symptomatic Patients: Refer to next column	ID Consult recommended Symptomatic: - Patients with any symptoms requires metronidazole or tinidazole followed by a luminal agent Intestinal E histolytica Preferred: - Metronidazole 500 mg TID for 7-10 days Alternative: - Tinidazole 2 g daily for 3 days FOLLOWED BY: - Paromomycin 25-30 mg/kg/day divided TID for 7 days Any Extra-Intestinal E histolytica Preferred: - Metronidazole 500 - 750 mg TID for 7-10 days Alternative: - Tinidazole 2 g daily for 5 days FOLLOWED BY: - Paromomycin 25-30 mg/kg/day divided TID for 7 days	 E histolytica has a broad spectrum of illness including asymptomatic carriage, subacute or chronic diarrhea, dysentery, or fulminant colitis, as well as having numerous extra-intestinal manifestations including liver abscesses. Amoebic Liver abscesses require longer duration of Tinidazole or metronidazole for same duration but at a higher dose. ID consult required. If slow response to initial treatment, may require needle aspiration or increased duration of therapy.
Viruses			
Adenovirus, Rotavirus, Norovirus, Astrovirus, Sapovirus, etc.	Supportive care is recommended. An infections. Consider Transplant ID consult for to prolonged norovirus in immunocom	If concern for viruses other than those on GI panel, or for persistent disease in an immunocompromised host- CMV, for instance - consider Infectious Diseases consult	

^aDose may need to be <u>adjusted for renal dysfunction</u>

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Revision History:			

The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider's professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.