

ACG guideline: Acute Diarrheal infections in Adults

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ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults

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Acute diarrheal infections are a common health problem globally and among both individuals in the United States and traveling to developing world countries. Multiple modalities including antibiotic and non-antibiotic therapies have been used to address these common infections. Information on treatment, prevention, diagnostics, and the consequences of acute diarrhea infection has emerged and helps to inform clinical management. In this ACG Clinical Guideline, the authors present an evidence-based approach to diagnosis, prevention, and treatment of acute diarrhea infection in both US-based and travel settings.

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Acute diarrheal infection is a leading cause of out patient visits , hospitalizations, and lost quality of life occurring in both domestic settings and among those traveling abroad.

Acute diarrhea can be defined as the passage of a greater number of stools of decreased form from the normal lasting <14 days.

Some definitions require an individual to present with an abrupt onset 3 or more loose or liquid stools above baseline in a 24-h period to meet the criteria of acute diarrhea.

Persistent diarrhea is typically defined as diarrhea lasting between 14 and 30 days, with chronic diarrhea generally considered as diarrheal symptoms lasting for greater than a month.

This guideline provides recommendations for the diagnosis, management, and prevention of acute gastrointestinal infection focusing primarily on immune-competent adult individuals and does not consider *Clostridium difficile*-associated infections.

This guideline is structured into five sections of clinical focus to include epidemiology and population health, diagnosis, treatment of acute disease, evaluation of persisting symptoms, and prevention.

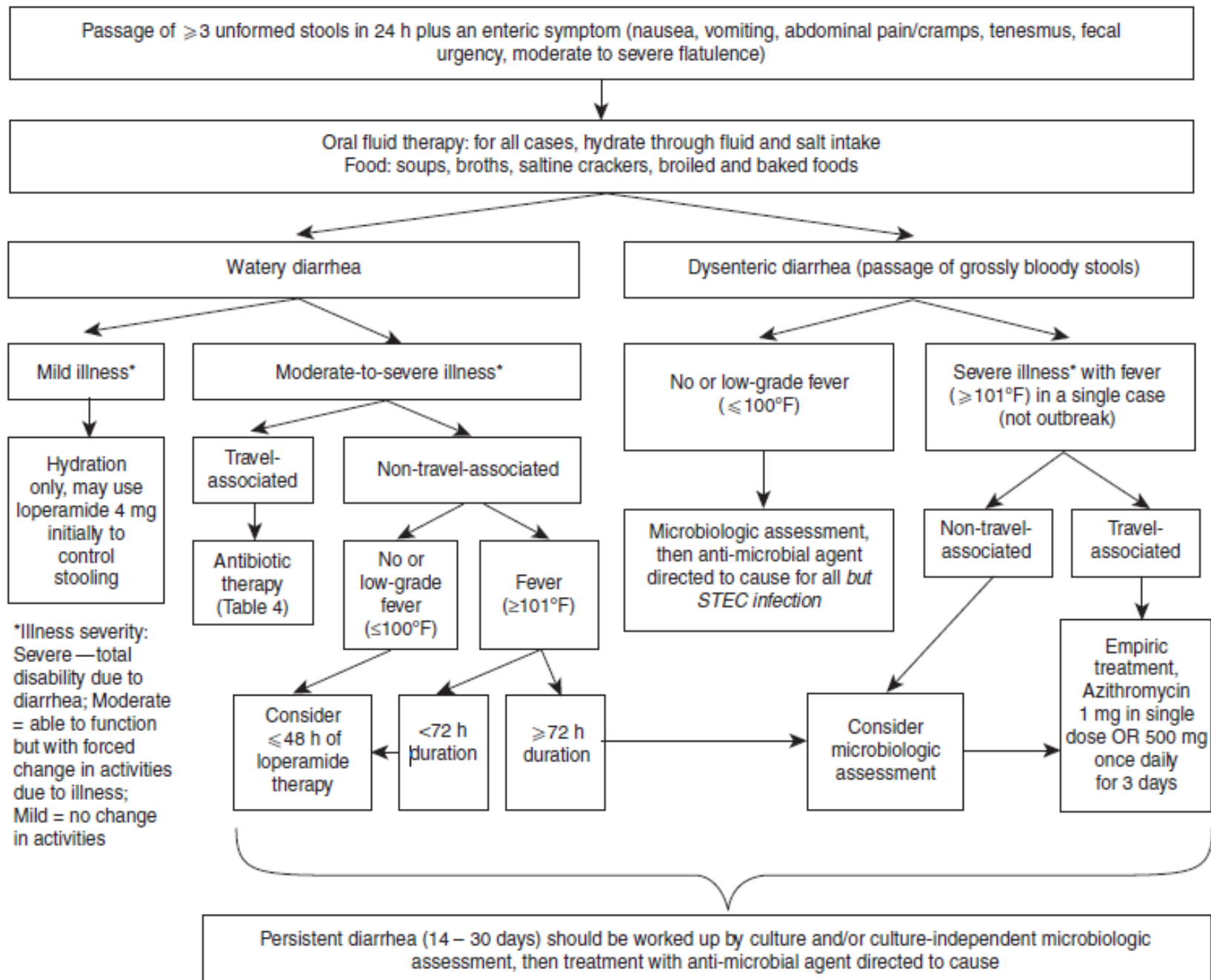


Figure 1. Approach to empiric therapy and diagnostic-directed management of the adult patient with acute diarrhea (suspect infectious etiology).

EPIDEMIOLOGY AND PUBLIC HEALTH

CONSIDERATIONS:

Recommendation

1 . Diagnostic evaluation using stool culture and culture independent methods if available should be used in situations where the individual patient is at high risk of spreading disease to others, and during known or suspected outbreaks.

Specifically focusing on infectious causes of acute diarrheal illness, in 2011 the Centers for Disease Control and Prevention updated the estimates of infectious gastroenteritis caused by a myriad of viruses, bacteria, and parasites. Based on empirical modeling of active, passive, and outbreak surveillance data ~47.8 million foodborne-related illnesses occur annually (one out of every six persons) in the United States.

In addition to domestically acquired infections, over 44 million US residents traveled abroad to non-Canadian and non-European destinations in 2014, resulting in roughly 4 to 17 million cases of traveler's diarrhea (TD) based on 10–40% attack rates.

In addition to the significant burden of the acute illness associated with these infections, recent evidence suggests that these pathogens are linked with chronic health sequelae, including functional gastrointestinal disorders, reactive arthritis, hemolytic uremic syndrome, and Guilliane Barré syndrome.

Table 1. Summary and strength of recommendations

Epidemiology and public health

1. Diagnostic evaluation using stool culture and culture-independent methods if available should be used in situations where the individual patient is at high risk of spreading disease to others, and during known or suspected outbreaks. (Strong recommendation, low level of evidence)

Diagnosis

2. Stool diagnostic studies may be used if available in cases of dysentery, moderate–severe disease, and symptoms lasting >7 days to clarify the etiology of the patient’s illness and enable specific directed therapy. (Strong recommendation, very low level of evidence)

3. Traditional methods of diagnosis (bacterial culture, microscopy with and without special stains and immunofluorescence, and antigen testing) fail to reveal the etiology of the majority of cases of acute diarrheal infection. If available, the use of FDA-approved culture-independent methods of diagnosis can be recommended at least as an adjunct to traditional methods. (Strong recommendation, low level of evidence)

4. Antibiotic sensitivity testing for management of the individual with acute diarrheal infection is currently not recommended. (Strong recommendation, very low level of evidence)

Treatment of acute disease

5. The usage of balanced electrolyte rehydration over other oral rehydration options in the elderly with severe diarrhea or any traveler with cholera-like watery diarrhea is recommended. Most individuals with acute diarrhea or gastroenteritis can keep up with fluids and salt by consumption of water, juices, sports drinks, soups, and saltine crackers. (Strong recommendation, moderate level of evidence)

6. The use of probiotics or prebiotics for the treatment of acute diarrhea in adults is not recommended, except in cases of postantibiotic-associated illness. (Strong recommendation, moderate level of evidence)

7. Bismuth subsalicylates can be administered to control rates of passage of stool and may help travelers function better during bouts of mild-to-moderate illness. (Strong recommendation, high level of evidence)

8. In patients receiving antibiotics for traveler’s diarrhea, adjunctive loperamide therapy should be administered to decrease duration of diarrhea and increase chance for a cure. (Strong recommendation, moderate level of evidence)

9. The evidence does not support empiric anti-microbial therapy for routine acute diarrheal infection, except in cases of TD where the likelihood of bacterial pathogens is high enough to justify the potential side effects of antibiotics. (Strong recommendation, high level of evidence)

10. Use of antibiotics for community-acquired diarrhea should be discouraged as epidemiological studies suggest that most community-acquired diarrhea is viral in origin (norovirus, rotavirus, and adenovirus) and is not shortened by the use of antibiotics. (Strong recommendation, very low-level evidence)

Evaluation of persisting symptoms

11. Serological and clinical lab testing in individuals with persistent diarrheal symptoms (between 14 and 30 days) are not recommended. (Strong recommendation, very low level of evidence)
12. Endoscopic evaluation is not recommended in individuals with persisting symptoms (between 14 and 30 days) and negative stool work-up. (Strong recommendation, very low level of evidence)

Prevention

13. Patient level counseling on prevention of acute enteric infection is not routinely recommended but may be considered in the individual or close contacts of the individual who is at high risk for complications. (Conditional, very low level of evidence)
14. Individuals should undergo pretravel counseling regarding high-risk food/beverage avoidance to prevent traveler's diarrhea. (Conditional, very low level of evidence)
15. Frequent and effective hand washing and alcohol-based hand sanitizers are of limited value in preventing most forms of traveler's diarrhea but may be useful where low-dose pathogens are responsible for the illness as for an example during a cruise ship outbreak of norovirus infection, institutional outbreak, or in endemic diarrhea prevention. (Conditional recommendation, low level of evidence)

Prophylaxis

16. Bismuth subsalicylates have moderate effectiveness and may be considered for travelers who do not have any contraindications to use and can adhere to the frequent dosing requirements. (Strong recommendation, high level of evidence)
17. Probiotics, prebiotics, and synbiotics for prevention of TD are not recommended. (Conditional recommendation, low level of evidence)
18. Antibiotic chemoprophylaxis has moderate to good effectiveness and may be considered in high-risk groups for short-term use. (Strong recommendation, high level of evidence)

TD, traveler's diarrhea.

The cost of acute and chronic illness attributable to these infections is estimated to be upwards of US \$145 billion to the US economy .

In light of these data, acute diarrheal illness is considered a major public health issue against which control efforts are needed.

Public health surveillance and response in the field of acute diarrhea include strategies of infection control, anti-microbial stewardship, outbreak investigation, as well as food and water safety interventions and regulatory policy.

However, a comprehensive laboratory evaluation and advanced characterization work-up is neither practicable nor cost-effective for every patient presenting with an acute diarrheal infection.

No formal cost-effectiveness studies on the optimization of testing and reporting has been reported and these would be challenging to conduct.

Public health fundamentals would strongly support individual patient testing and reporting in a number of situations:

Include diarrhea outbreaks among workers who prepare and handle food, health-care workers, daycare (adult and child) attendees/employees, and residents of institutional facilities

Although culture-independent methods provide a promise for more sensitivity of pathogen identification (leading to more accurate disease burden estimates), they do so with a detrimental impact on the advanced characterization and typing, which is needed in outbreak investigation and resistance monitoring efforts.

Until new methods have evolved in which genotypic advanced characterization platforms are widely available, it is recommended that culture-based and culture-independent testing be used in parallel when practicable to support public health purposes.

DIAGNOSIS

Recommendations

2. Stool diagnostic studies may be used if available in cases of dysentery, moderate-to-severe disease, and symptoms lasting >7 days to clarify the etiology of the patient's illness and enable specific directed therapy.
3. Traditional methods of diagnosis (bacterial culture, microscopy with and without special stains and immunofluorescence, and antigen testing) fail to reveal the etiology of the majority of cases of acute diarrheal infection.

If available, the use of Food and Drug Administration-approved culture independent methods of diagnosis can be recommended at least as an adjunct to traditional methods.

4. Antibiotic sensitivity testing for management of the individual with acute diarrheal infection is currently not recommended.

Summary of the evidence .

The commonly accepted statement that specific investigation is not normally required in the majority of cases of acute watery diarrhea because it is usually self-limiting and resolves without specific treatment may under inform the ability to provide a more rapid resolution of symptoms with appropriate directed therapy and potentially prevent post infectious sequelae.

As symptoms of acute diarrhea are protean, attempts to diagnose etiologic agents or classes are subjective at best and fraught with imprecision due to overlap in symptoms.

Conventional diagnostic approaches to diarrheal disease require multiple procedures.

Culture methods are laborious and time consuming, with results often not available for 48 to 72 h.

Decision to obtain a stool culture in an individual with diarrhea has often been guided by the finding of fecal leukocytes or the presence of stool lactoferrin.

The latter is a more sensitive predictor of a positive stool culture, using these markers to guide further diagnostic studies has been proven to be imprecise and probably unnecessary.

Diarrheal disease by definition has a broad range of potential pathogens particularly well suited for multiplex molecular testing.

Several well-designed studies show that molecular testing now surpasses all other approaches for the routine diagnosis of diarrhea.

They are also faster, providing results in hours rather than days, As a result they can detect microbes at nonpathogenic levels. Given the high rates of asymptomatic carriage of enteropathogens, this can be a considerable problem.

Specimens collected for culture-independent testing may, in some cases, be incompatible with culture because of the collection methods or media that are used for collection.

The future may hold a combination approach where culture specimens that have yielded a positive result by culture-independent testing are then submitted to public health laboratories for subtyping and sensitivity analysis.

In general, there appears to be a low failure rate with the use of empiric anti-microbial therapy, especially with the fluoroquinolones and macrolides.

Anti-microbial susceptibility testing will continue to have a role in the outbreak setting and for ongoing surveillance of local trends in resistance patterns and mechanisms.

TREATMENT OF ACUTE DISEASE:

Oral rehydration

Recommendation:

5. The usage of balanced electrolyte rehydration over other oral rehydration options in the elderly with severe diarrhea or any traveler with cholera-like watery diarrhea is recommended.

Most individuals with acute diarrhea or gastroenteritis can keep up with fluids and salt by consumption of water, juices, sports drinks, soups, and saltine crackers.

Summary of the evidence

One of the most significant advances in the past century was development of a balanced sodium-glucose solution that allows optimal absorption of electrolytes and water.

Availability of oral rehydration solution (ORS) has reduced infant mortality in developing countries by at least 50%.

In TD dehydration is not common and mortality occurs only very rarely, More than 80% of deaths in the United States associated with diarrhea occur in the elderly.

For most otherwise healthy adults with TD, formal ORS is not needed as they can keep up with fluid losses by taking in salty soups, fruit juices, and carbohydrates to provide the glucose-sodium co transport.

In severe diarrhea, a balanced ORS can usually be purchased at a local pharmacy with sodium of 60–75 mEq/l and glucose of 75–90 mmol/l with value in replacing fluids and salt in dehydrating forms of diarrhea as studied in infants and children.

Probiotics and prebiotics

Recommendation

6. The use of probiotics or prebiotics for treatment of acute diarrhea in adults is not recommended, except in cases of post antibiotic-associated illness.

Summary of the evidence

As our understanding of the importance of the human microbiome in health and disease has advanced, interest in the use of nonpathogenic bacteria and yeast, as well as nutrients that enhance the growth of favorable microbes in our bodies producing enhanced colonization resistance has also expanded

Probiotics supposedly act by prohibiting pathogen attachment, enhancing the immune response and by assisting in re-establishing the microflora.

Prebiotics are non-digestible food ingredients that are fermentable in the colon and stimulate potentially health-promoting bacteria, chiefly bifidobacteria and/or lactobacilli, conferring a beneficial shift in the microbial equilibrium of the host gut flora.

These organisms have been associated with an increased resistance to infection and diarrheal disease.

Prebiotics when combined with probiotics form synbiotics.

Synbiotic formulations have been tested in animal models with beneficial effects on reducing adherence of pathogenic bacteria to the jejunum and colonic mucosa.

With respect to treatment of infectious diarrhea, it is theorized that by enhancing intestinal colonization by specific organisms there would be a reduction in the environmental niche for the offending pathogen.

In 2010, a Cochrane systematic review was published on the topic of probiotics and treatment of intestinal infection.

In this review, they identified 63 randomized and quasi-randomized controlled trials comparing specific probiotic agent(s) compared with a placebo or no-treatment with acute diarrhea of presumed infectious etiology.

The pediatric studies, mostly of which were conducted among developing world populations and varied greatly with respect to settings, organisms tested and dosage, probiotics significantly reduced the duration of diarrhea.

Based on the current evidence, there are not enough studies, which would support the recommended use of any particular probiotic product for treatment in acute adult diarrhea infection.

Although a statistically significant summary treatment effect was observed for Enterococcus LAB SF68, heterogeneity in results does not allow for generalization, theoretical safety concerns, and no recent studies with this product have been reported.

Recommendations on use of probiotics in pediatric populations have recently been published.

A single study of polyphenol-based prebiotic has been described in the treatment of acute diarrhea in children and adults seeking treatment at community health centers in Managua, Nicaragua.

No diarrhea case definition (e.g., frequency or duration) for inclusion was reported; however, exclusion criteria included those with high fever, vomiting, severe dehydration, and bloody stools.

A remarkable treatment effect on mean time to last unformed stools among the treatment group compared with placebo was reported

While evidence supporting therapy of probiotics in treatment of acute diarrheal infection is lacking, there is supporting evidence for the role of probiotics in prevention of acute diarrhea associated with antibiotic use.

Future research is needed to support directed therapy and effectiveness among various patient populations, clinical indications, antibiotics, and probiotic strains, as well as further understanding the risk of adverse events associated with probiotic use for these indications.

Non-antibiotic therapies

Recommendation

7. Bismuth subsalicylates (BSSs) can be administered to control rates of passage of stool and may help travelers function better during bouts of mild to moderate illness.
8. In patients receiving antibiotics for TD, adjunctive loperamide therapy can be administered to decrease duration of diarrhea and increase chance for a cure.

Summary of the evidence .

Medical treatment is not required in patients with non-severe, non-cholera-like diarrhea.

Non-antibiotic anti-diarrheal drugs have been shown to reduce the number of stools passed in cases of diarrhea allowing the ill people to continue their planned schedule.

The drugs with value in controlling symptoms with reduced rate of stooling are the anti secretory and antimotility drugs.

Intestinal secretion is the major pathophysiologic mechanism leading to watery diarrhea in some forms of acute diarrheal infection including TD.

The antisecretory drugs that have been evaluated and shown to have value for therapy in secretory forms of diarrhea are BSS, zaldaridemaleate and crofelemer.

It is the salicylate part of BSS that has antisecretory anti-diarrheal properties. BSS will reduce the stools passed by ~40%.

Crofelemer is a cystic fibrosis transmembrane regulator chloride-channel blocker and is effective in some forms of diarrhea including TD and AIDS-associated diarrhea.

Zaldaride is a calmodulin-inhibiting drug that has antisecretory properties related to intracellular concentrations of calcium . The drug significantly shortened the stools passed in subjects studied with TD compared with placebo therapy

Racecadotril, a specific enkephalinase inhibitor that prevents degradation of the endogenous antisecretory peptide neurotransmitter enkephalins that inhibit cyclic nucleotide secretory pathways without effect on gut motility and has been used successfully in pediatric diarrhea.

Although this anti diarrheal drug needs to be studied further in diverse forms of diarrhea.

Of the strictly antisecretory, only two agents are approved for use by the Food and Drug Administration in the United States, BSS for treatment of acute diarrhea and crofelemer for HIV-associated diarrhea.

The recommended dose of BSS for therapy of acute diarrhea is 30 ml (525 mg) of liquid formulation or two tablets (263 mg per tablet) chewed well each 30–60 min not to exceed eight doses in 24 h.

The major antimotility drugs used for therapy of acute diarrhea are loperamide and diphenoxylate, Of these, the most useful drug is loperamide, which has less central opiate effects.

Another limitation of diphenoxylate is that it contains atropine, which has no antidiarrheal effectiveness and may produce objectionable side effects.

Loperamide works through two mechanisms:

1:The most important being the production of segmental contraction of the gut, which slows the intraluminal movement of fluids and allows greater absorption.

2:A secondary effect appears to be inhibition of calmodulin leading to Reduced mucosal secretion.

In a comparative randomized trial in patients with TD, loperamide reduced the number of diarrheal stools passed when compared with BSS and loperamide was shown to shorten diarrhea in both children and adults with acute diarrhea.

The recommended dose of loperamide for therapy for adults with diarrhea is 4 mg initially followed by 2 mg after subsequently passed watery stools not to exceed 8 mg per day.

The most valuable use of loperamide in the self-treatment of TD is as a combination drug with antibacterial drugs where the antimotility drug quickly reduces the number of diarrhea stools passed while the antibiotic cures the enteric infection.

It is important to use the lowest dose of loperamide to provide antidiarrheal effects without the post-treatment constipation effects of the drug.

Antimotility drugs have been associated with intestinal complications such as toxic dilatation of the colon or prolonged illness when used in bacterial inflammatory, although the association is rare and if it occurs it is seen with otherwise untreated diarrhea caused by the highly inflammatory bacterial pathogens.

When inflammatory forms of colitis are also treated with anti-microbial drugs, this potentiation is very unlikely to occur

Adsorbent drugs such as kaolin, pectin, charcoal, and attapulgite do have an effect on form of stools passed, but the number of stools passed and duration of post-treatment diarrhea are not shortened and are not recommended

Antibiotic therapy

Recommendation

9. The evidence does not support empiric anti-microbial therapy for routine acute diarrheal infection, except in cases of TD where the likelihood of bacterial pathogens is high enough to justify the potential side effects of antibiotics.
10. Use of antibiotics for community-acquired diarrhea should be discouraged as epidemiological studies suggest that most community-acquired diarrhea is viral in origin (norovirus, rotavirus, and adenovirus) and is not shortened by the use of antibiotics.

Summary of evidence

The evidence for the use of anti-microbial therapy is strongly supported for cases of TD

Numerous studies have demonstrated that antibiotics shorten the overall duration of moderate-to-severe TD to a little over 24 h.

Anti-bacterial drugs have been shown to reduce initiation of therapy until the last unformed stool is passed in cases of TD by 1–3 days compared with no therapy or placebo, and combination of an antibiotic with loperamide further shortens duration of illness.

Fluoroquinolones such as ciprofloxacin or levofloxacin have been the primary antibiotics of choice for most destinations.

There is evidence that most *Campylobacter* are fluoroquinolone resistant and the use of macrolides such as azithromycin for treatment is recommended.

Azithromycin was shown to be more effective than ciprofloxacin for all cases of TD in travelers to Thailand, probably because of the high prevalence of *Campylobacter* in this region.

A review of nine randomized clinical trials and one Cochrane review assessing fluoroquinolone use for the treatment of TD found overall reductions in diarrhea duration compared with placebo and evidence from these studies showed no serious harm associated with fluoroquinolone use.

For all antibiotics, either single-dose therapy or treatment for up to 3 days is usually sufficient to allow resolution of symptoms.

Studies show that once daily therapy is as effective as 3-day therapies for TD due to noninvasive pathogens.

A 3-day therapy is recommended for patients presenting with fever or dysentery.

Table 4. Acute diarrhea antibiotic treatment recommendations

Antibiotic ^a	Dose	Treatment duration
Levofloxacin	500 mg by mouth	Single dose ^b or 3-day course
Ciprofloxacin	750 mg by mouth or 500 mg by mouth	Single dose ^b 3-day course
Ofloxacin	400 mg by mouth	Single dose ^b or 3-day course
Azithromycin ^{c,d}	1,000 mg by mouth or 500 mg by mouth	Single dose ^b 3-day course ^d
Rifaximin ^e	200 mg by mouth three times daily	3-days

ETEC, Enterotoxigenic *Escherichia coli*.

^aAntibiotic regimens may be combined with loperamide, 4 mg first dose, and then 2 mg dose after each loose stool, not to exceed 16 mg in a 24-h period.

^bIf symptoms are not resolved after 24 h, complete a 3-day course of antibiotics.

^cUse empirically as first line in Southeast Asia and India to cover fluoroquinolone-resistant *Campylobacter* or in other geographical areas if *Campylobacter* or resistant ETEC are suspected.

^dPreferred regimen for dysentery or febrile diarrhea.

^eDo not use if clinical suspicion for *Campylobacter*, *Salmonella*, *Shigella*, or other causes of invasive diarrhea.

Enteric infection by *Shigella dysenteriae* appears to be an exception, insofar as 5 days of therapy appears to be superior to single-dose or 3-day therapy.

Shigella sonnei has been found to have reduced susceptibility to azithromycin among isolates in the United States.

Although no studies looked at the efficacy of azithromycin vs. placebo, there were four randomized controlled trials that compared azithromycin to the fluoroquinolones in the treatment of TD. No difference was noted in efficacy between the two treatment groups.

Among adult student travelers to Mexico, a single dose 1,000 mg azithromycin was comparable to levofloxacin 500 mg in shortening the duration of illness.

Azithromycin is effective against *Shigella* spp., as well as noninvasive diarrheagenic *Escherichia coli*.

Rifaximin, a non-absorbable rifamycin-derived antibiotic, has been shown to be effective against diarrheagenic *E. coli*, which appear to be the most common bacterial pathogens in the Western Hemisphere.

In two studies evaluating rifaximin compared with placebo, rifaximin was associated with a higher percentage of travelers cured.

Two additional studies directly compared rifaximin with ciprofloxacin. There was no significant difference with respect to cure or treatment failure.

While individual self-treatment of TD among travelers has been common since the late 1980s, there are a few microbe-specific concerns with the use of empiric anti-bacterial therapy of TD.

The first is that anti-bacterial drugs appear to complicate enteric disease caused by Shiga-like toxin-producing *E. coli* by increasing the risk of hemolytic uremic syndrome.

Although this may occur more commonly in children, a meta-analysis did not show an association between anti-microbial therapy in adult patients with hemorrhagic colitis due to *E. coli* 0157:H7.

Another theoretical concern with antibiotic use is that for non-typhoidal Salmonella strains, there may be prolonged intestinal carriage.

A meta-analysis showed that antibiotic therapy does not appear to reduce the length of illness in immunocompetent adults and increases the period during which Salmonella was detected in stool.

Another perhaps more legitimate concern is that treatment with antibiotics will modify the microbiota. This may result in the development of C. difficile - associated diarrhea or colitis.

At present, the risk of acquired extended spectrum β -lactamase on the individual and community vs. the potential negative consequences of untreated TD has raised awareness and interest in the development of more data to inform management decisions.

The evidence is strong for anti-microbial treatment of specific parasitic causes of acute diarrheal infection such as metronidazole, tinidazole, or nitazoxanide for Giardia infections, metronidazole or tinidazole for Entameba histolytica, nitazoxanide for Cryptosporidiosis, trimethoprim/sulfamethoxazole for Cyclosporiasis or Cystisporiasis, albendazole for Enterocyotzoan bienusi, or iodoquinol for Diemtameba fragilis.

With the advent of new molecular diagnostics, more specific diagnoses including parasitic etiologies may be made more promptly, guiding the targeted use of anti-microbial therapy.

EVALUATION OF PERSISTING SYMPTOMS

Recommendations

- 11.** Serological and clinical lab testing in individuals with persistent diarrheal symptoms (between 14 and 30 days) is not recommended.
- 12.** Endoscopic evaluation is not recommended in individuals with persisting symptoms (between 14 and 30 days) and negative stool work-up.

Summary of evidence

In the evaluation of the patient with persistent symptoms, a thorough and directed history is essential.

Among patients with persistent symptoms (between 14 and 30 days), the role of clinical laboratory studies and endoscopy is uncertain and should be dictated by clinical suspicion and disease severity, within the context of most likely etiologies.

An initial diagnostic evaluation in the patient with persistent symptoms should include tests for the presence of microbial pathogens.

Even some of the newer methods, such as enzyme-linked immunoassays and direct immunofluorescence staining, which increase sensitivity, may not be able to distinguish, e.g., between the pathogen *Entamoeba histolytica* and a non-pathogenic but microscopically indistinguishable *Entamoeba dispar*.

Colonoscopy has been considered in the evaluation of the patient with persistent Diarrhea.

While not considered in these guidelines, the work-up of chronic diarrhea is briefly considered and should include the differential diagnoses such as celiac disease, Crohn's disease, eosinophilic gastroenteritis, and Whipple's disease.

Gastrointestinal endoscopy and relevant serological assays may contribute to the diagnosis and management if sustained or progressive weight loss is a prominent feature, and upper endoscopy may be considered, especially if empiric therapy and symptomatic measures have not helped.

A review of 18 primary studies looking at the diagnostic value of colonoscopy in patients with chronic diarrhea, as well as a review of nine published guidelines provides the basis for a colonoscopy recommendation in such Patients.

In the situation of chronic diarrhea and abdominal symptoms occurring after a bout of infectious diarrhea, a diagnosis of post infectious irritable bowel syndrome must be considered.

PREVENTION

Counseling

Recommendations

13. Patient level counseling on prevention of acute enteric infection is not routinely recommended but may be considered in the individual or close-contacts of the individual who is at high risk for complications.

Individuals should undergo pre travel counseling regarding high risk food/beverage avoidance to prevent TD.

Summary of evidence

Non-travel setting: One in six US citizens get sick from a foodborne illness each year, and a majority of these illness will be from contaminated food consumed in the United States (e.g., non-travel associated)

Food safety is a major public health effort that involves multiple Federal, State, and local agencies including the Food and Drug Administration, US Department of Agriculture, US Food Inspection Service, and state and local health departments, all of which focus on the potential risks for large outbreaks associated with centralization of food processing and reliance on imported foods.

However, for vulnerable patient populations who are at increased risk for severe disease and complications associated with acute foodborne illness, including pregnant women, elderly, and those with immune deficiency due to HIV or immunotherapeutic, situational individual patient level counseling may be appropriate

Traveler setting:

In the realm of travel medicine, Shlim reviewed the evidence for the effectiveness of personal hygiene precautions in prevention of TD.

In the eight studies identified in this 2005 review, seven found no correlation between the types of food selected by the traveler and the risk of acquiring traveler's diarrhea.

The sum total of these errors leads to abundant opportunities for the spread of enteric pathogens, whether from employees' hands, flies, or contaminated meat and produce, with ample time available for bacterial growth to reach infective levels.

In summary, the evidence of counseling effectiveness on TD risk reduction related to food and water indiscretion is mixed and lacks recent high-quality studies.

Hand washing

Recommendation

15. Frequent and effective hand washing and alcohol-based hand sanitizers are of limited value in preventing most forms of traveler's diarrhea but may be useful where low-dose pathogens are responsible for the illness as for an example during a cruise ship outbreak of norovirus infection, institutional outbreak, or in endemic diarrhea prevention.

Summary of evidence .

Traveler setting: The evidence of hand washing and use of alcohol-based hand sanitizers in preventing TD is mixed.

Theoretically, they would be most effective in prevention of enteric infection caused by pathogens causing illness at low inoculum doses.

Hand washing should be effective in reducing these highly communicable pathogens and should be aggressively pursued in settings where one of these is likely to occur.

For cruise travelers regular hand washing can be useful in case there is apparent or inapparent transmission of norovirus infection.

Alcohol-based hand sanitizers often have anti-viral properties.

In developing regions the presence of soap in homes is associated with reduced diarrhea rates in local populations living in unhygienic areas.

Hygiene including hand washing undoubtedly has a greater effect in preventing diarrhea in wilderness backpackers who may have exposures more resembling endemic settings in the developing world than those seen with typical travelers staying in clean hotels.

Prophylaxis

Recommendations

16. Bismuth subsalicylates have moderate effectiveness and may be considered for travelers who do not have any contraindications to use and can adhere to the frequent dosing requirements.
17. Probiotics, prebiotics, and synbiotics for prevention of traveler's diarrhea are not recommended.
18. Antibiotic chemoprophylaxis has moderate to good effectiveness and may be considered in high-risk groups for short term use.

Summary of evidence

Traveler setting: Prevention of TD is challenging because of the ubiquitous exposures to individuals through contaminated food, water, and generally unhygienic conditions among much of the developing world.

Although vaccines for many of the agents commonly associated with TD are under development, these are considered a long-term solution and might likely suffer from the lack of utilization as has been seen with most travel-associated vaccines.

Bismuth subsalicylate . BSS has been shown in several studies to reduce the frequency of TD when used during period of risk for 3 weeks.

The drug provides at least 60% protection in a dose of 2.1 g per day .

The recommended dose of BSS for TD prevention is two tablets four daily doses at mealtimes and at bedtime.

Both the dose and the interval of administration appear to be important as 2.1 and 1.05 g given two times a day led to reduced levels of protection, 41% and 35%, respectively.

The chemoprophylactic dose of BSS leads to important absorption of salicylate and should not be used when other salicylates are being taken.

BSS use has been shown to reduce the occurrence of TD if taken in proper daily dose for up to 3 weeks. Most authorities recommend that chemoprophylaxis could be used for trips up to 2 weeks, Chemoprophylaxis should not be used for longer trips.

Persons with underlying inflammatory bowel disease or HIV infection should not receive BSS because of the fear of excessive absorption of this generally poorly absorbed bismuth compound leading to bismuth encephalopathy.

Probiotic/prebiotic/synbiotics .

The use of probiotics, prebiotics, and synbiotics to prevent acute diarrheal infection is an appealing concept because of their ease of use and relative safety.

The data, however, supporting their use in preventing infectious diarrhea is not consistently strong and at this point we do not recommend them for this purpose.

Although two meta-analyses suggest a marginal benefit of probiotics in prevention of TD, both suggest there is insufficient evidence for extrapolation to global recommendations for their use.

Antibiotics

Anti-microbial prophylaxis has been considered an option to prevent infection.

studies that have examined the cost benefit of chemoprophylaxis for the prevention of TD have recommended against prophylaxis except in high-risk groups. While debate continues, the standard practice and recommendation has remained unchanged for 20 years.

Two recent developments are challenging the general recommendation against use of chemoprophylaxis.

First, postinfectious irritable bowel syndrome has been recognized as an important chronic health consequence, occurring in a sizeable proportion of those who experience an episode of TD, particularly among those with bacterial infection and a more severe clinical presentation.

Second, rifaximin, a non-absorbable antibiotic, has been developed and may provide a safer alternative for prophylaxis than fluoroquinolones, which are known to be quite effective but may have an unacceptable safety profile.

With respect to rifaximin chemoprophylaxis, two studies (Armstrong et al. and Flores et al.) did not show that chemoprophylaxis with rifaximin reached a statistically significant difference in preventing TD compared with placebo. In both studies the incidence of TD in the control group was relatively low (8/48 or 17% and 9/47 or 19%, respectively).

Most recently, an effectiveness study by Zanger et al. reported moderate protection with rifaximin for up to 28 days to the South and Southeast Asian regions.

However, a study by Taylor et al. suggests that rifaximin may be effective against shigellosis, which is a common invasive TD pathogen.

There were no serious adverse drug-associated safety adverse events reported among these published studies.

While no recent studies have been conducted, fluoroquinolones consistently demonstrate a higher effectiveness in the prevention of TD with a summary pooled estimate of 88% (95% CI: 80–93%) protective efficacy.

The emergence of fluoroquinolone resistance to commonly encountered TD pathogens may be a factor today if these studies were replicated.

The evidence to date suggests moderate to good efficacy of rifaximin and fluoroquinolones for chemoprophylaxis.

However, until such studies are carried out, which adequately assess the risk and benefits of this strategy in reduction of acute and chronic consequences while balance the negative consequences of antibiotic use,

Recommendations for use in the traveler setting should be restrictive and used in short durations.

The traveler who is at high risk for TD and susceptible to potentially serious health consequences, or whose illness may critically impact the intended purpose of travel, may benefit from antibiotic chemoprophylaxis.

