Giardiasis (Last updated August 22, 2019; last reviewed August 22, 2019)

Panel's Recommendations

I. In children with HIV infection, what are the best interventions (compared with no intervention) to prevent initial episodes of giardiasis?

- Giardiasis can be prevented by practicing good hygiene, not drinking or swimming in water that may be contaminated, and not eating food that may be contaminated (**expert opinion**).
- Frequent hand washing can help reduce the incidence of diarrheal illnesses, including giardiasis (**strong, moderate**).
- Initiating combination antiretroviral therapy (ART) in children with HIV infection to reverse or prevent severe immunodeficiency is the primary intervention to prevent severe enteric giardiasis (**strong, very low**).

II. In children with HIV infection, what are the best interventions (compared with no intervention) to treat giardiasis?

- Tinidazole and nitazoxanide are preferred therapies; metronidazole is the alternative recommended treatment for giardiasis in children (**strong, moderate**).
- Dehydration and electrolyte abnormalities should be corrected (**expert opinion**).

III. In children with HIV infection, what are the best interventions (compared with no intervention) to prevent recurrent episodes of giardiasis?

- Recurrent episodes of giardiasis can be prevented by practicing good hygiene and avoiding contaminated food and water (**expert opinion**).
- Frequent hand washing can help reduce the incidence of diarrheal illnesses, including giardiasis (**strong, moderate**).

Rating System

Strength of Recommendation: Strong; Weak

Quality of Evidence: High; Moderate; Low; or Very Low

Epidemiology

Giardia duodenalis (also known as *Giardia lamblia* or *Giardia intestinalis*) has a worldwide distribution, and giardiasis due to *G. duodenalis* is the most common nationally reportable intestinal parasitic disease identified by public health laboratories in the United States.[1] Giardiasis surveillance data show a bimodal age distribution, with the greatest number of reported cases occurring in children aged 1 to 9 years and adults aged 35 to 44 years. In the United States, most cases are reported between early summer and early fall and are associated with recreational water activities (e.g., swimming) and camping.[1]

Humans are the principal reservoir of *G. duodenalis*. The parasite is found in many animals species, although the role of zoonotic transmission is still being unraveled.[2-4] *G. duodenalis* is a flagellated protozoan with two forms: trophozoites and cysts. The infectious and environmentally resistant form is the cyst. After ingestion, each *Giardia* cyst produces two trophozoites in the proximal portion of the small intestine. Detached trophozoites pass through the intestinal tract, and form smooth, oval-shaped, thin-walled infectious cysts that are passed in feces. Duration of cyst excretion is usually self-limited but can vary and excretion may last for months. Studies in adults have shown that ingestion of as few as 10 to 100 fecally derived cysts is sufficient to initiate infection.[5] *Giardia* cysts are infectious immediately upon being excreted in feces and remain viable for at least 3 months in water at 4°C.[6] Although freezing will not eliminate the infectivity of *Giardia* cysts completely, heating, drying, or submersing them in seawater likely will.[6,7]

Infection with *Giardia* can occur directly by the fecal-oral route or indirectly via ingestion of contaminated water or food, but water contaminated with *Giardia* cysts appears to be the major reservoir and vehicle for spread of the parasite.[1,8] Most waterborne giardiasis outbreaks have been related to ingestion of untreated or improperly treated surface water.[9,10] Drinking untreated mountain stream water is a risk for hikers. Person-to-person spread of giardiasis occurs frequently in child care centers and in families of children with diarrhea.[11-13] Antigiardial host defenses are B-cell dependent, with secretory immunoglobulin A playing a major role in immunity. Individuals with humoral immunodeficiencies, such as X-linked agammaglobulinemia and hypogammaglobulinemia, who develop giardiasis are predisposed to chronic symptomatic disease.[14]

sufficient to prevent transmission of *Giardia* from a patient with the infection to a susceptible person with HIV.

Before traveling to areas where the water may be contaminated or the safety of drinking water doubtful, travelers, hikers, and campers should be advised of methods to make water safe for drinking. These measures include using bottled water, disinfecting water by heating it to a rolling boil for 1 minute, or using a filter that has been tested and rated to National Safety Foundation Standard 53 or Standard 58 for cyst and oocyst reduction. Waterborne outbreaks of giardiasis can be prevented with a combination of adequate filtration of water sources, chlorination, and maintenance of water distribution systems.[1,9] Travelers should also be advised of the potential for transmission of giardiasis during use of contaminated recreational water (e.g., lakes, rivers, inadequately treated swimming pools).

Preventing First Episode of Disease

No chemoprophylactic regimens are known to be effective in preventing giardiasis. However, because the risk of acquisition of giardiasis and the severity of infection increase with the severity of immunosuppression, ART to prevent or reverse severe immunodeficiency is a primary modality for giardiasis prevention in children with HIV. In the United States, it is standard practice to treat all children with HIV infection with ART.

Discontinuing Primary Prophylaxis

Not applicable.

Treatment Recommendations

Treating Disease

Effective ART and anti-parasitic therapy are the primary initial treatments for *Giardia* infections in children and adults with HIV infection.[21] Supportive care with hydration, correction of electrolyte abnormalities, and nutritional supplementation should be provided. Antimotility agents should be used with caution in young children. Patients with chronic diarrhea should be monitored for malabsorption leading to malnutrition.

The therapeutic efficacy of metronidazole against *Giardia* led to development of other nitroimidazole derivatives, such as tinidazole and secnidazole. These agents have the advantage of longer half-lives than metronidazole, making them suitable for single-daily-dose therapies. A single, 2-g dose (or the equivalent pediatric dosing of 50 mg/kg in a single dose) of tinidazole has demonstrated cure rates ranging from 80% to 100% and is also associated with improved medication adherence. Cure rates of patients with *Giardia* have been shown to be consistently higher with the use of tinidazole than with use of other anti-parasitic drugs such as metronidazole, nitazoxanide, mebendazole, albendazole and chloroquine.[45-47] Tinidazole is approved for use in children 3 years and older.The drug is available in tablets, which can be crushed in flavored syrup for patients unable to swallow tablets.

Nitazoxanide is approved in the United States for treatment of infections due to *G. duodenalis* in patients 1 year or older. A randomized, controlled clinical trial in adolescents and adults without HIV infection in Egypt demonstrated nitazoxanide's efficacy against placebo.[48] Nitazoxanide has been compared with metronidazole and mebendazole to treat giardiasis in children and was found to be equally effective, with eradication rates for *G. duodenalis* of 71% to 81% with nitazoxanide treatment.[49]

Metronidazole was determined to be therapeutic against giardiasis in 1962. Since then, clinicians have used metronidazole and other nitroimidazoles as the mainstay of therapy of giardiasis. Metronidazole is the drug most often used for giardiasis treatment worldwide. Children have been included in many of the clinical trials of metronidazole, with outcomes similar to those in adults (median efficacy, 94%) with 5- day to 10-day regimens.[50] Metronidazole is not available in a standard liquid form, but a suspension can be prepared by thoroughly crushing metronidazole tablets, using glycerin as a lubricant, and suspending the mixture in

flavored syrup.[51] Despite widespread and accepted use of metronidazole against *Giardia*, it has not been approved by the U.S. Food and Drug Administration for this indication.

Quinacrine has been used in combination therapy for cases in which treatment failure was suspected.[52] The severity of side effects prevented clinicians from using quinacrine as an initial therapeutic choice or first-line alternative, particularly in children. A bitter taste and vomiting led to the drug's lower efficacy in children, probably because of poor medication adherence.[53] Quinacrine is no longer available in the United States and has been discontinued by the manufacturer.[54,55]

Monitoring and Adverse Events (Including IRIS)

Patients with chronic diarrhea should be closely monitored for signs and symptoms of volume depletion, electrolyte and weight loss, and malnutrition. In severely ill patients, total parenteral nutrition may be indicated.

Adverse effects reported with tinidazole are not as common as with metronidazole but do include bitter taste, vertigo, and GI upset.[50]

Nitazoxanide is generally well tolerated with no significant adverse events noted in human trials. Adverse events have been mild and transient and principally related to the GI tract, such as abdominal pain, diarrhea, and nausea. Nitazoxanide has been well tolerated up to the maximum dose of 4 g when taken with or without food, but the frequency of GI side effects increases significantly with the dose level.[49]

The most common side effects of metronidazole treatment include headache, vertigo, nausea, and a metallic taste. Nausea occurs in 5% to 15% of patients given standard multiday courses. In addition, pancreatitis, central nervous system toxicity at high doses, and transient, reversible neutropenia have been attributed to metronidazole.[50]

Among patients taking quinacrine, 4% to 5% had yellow/orange discoloration of the skin, sclerae, and urine beginning about 1 week after starting treatment, and continuing up to 4 months after the drug was discontinued. Other common side effects of quinacrine included nausea, vomiting, headache, and dizziness. Quinacrine can precipitate hemolysis in glucose-6-phosphate dehydrogenase (G6PD)-deficient individuals.[53]

Immune reconstitution inflammatory syndrome has not been associated with giardiasis or its treatment.

Managing Treatment Failure

The most important steps for management of giardiasis treatment failure are supportive treatment, optimal use of ART to achieve full virologic suppression, and modification of antiparasitic therapy. Treatment failures have been reported with all of the common anti-*Giardia* agents. It is important that clinicians differentiate between resistance to treatment and reinfection, which is common in *Giardia* endemic regions and situations where poor hygiene facilitates fecal-oral transmission. Resistance to most anti-*Giardia* agents has been documented, but there is no consistent correlation between *in vitro* resistance and clinical failure.[50] Clinically resistant strains have been treated with longer repeated courses or higher doses of the original agent or a drug from a different class to avoid potential cross-resistance. Using combination regimens that include metronidazole-albendazole, metronidazole-quinacrine, or other active drugs or giving a nitroimidazole plus quinacrine for at least 2 weeks have both proven successful against refractory infection. Combination therapy with albendazole-praziquantel, nitazoxanide–albendazole, and bacitracin –neomycin has been investigated in clinical trials. However, randomized controlled trials of combination therapy are limited and the optimal combinations need to be clarified, particularly in cases of treatment failure associated with suspected drug tolerance.[56] In patients with AIDS who have severe giardiasis, prolonged or combination therapy may be necessary.[52,57]

Preventing Recurrence

No known pharmacologic interventions effectively prevent recurrence of giardiasis. Reinfection is frequent in endemic areas, or in situations where hygiene is poor or contaminated water (e.g., in private wells) is not adequately treated. Reinfection can be prevented by consistently practicing good hand hygiene, but

particularly after defecation and handling of soiled diapers. Hand hygiene should also be practiced before preparing and eating food.[12] To reduce risk of disease transmission, children with diarrhea should be excluded from child care settings until the diarrhea has stopped. Children with giardiasis should not frequent recreational water venues for 2 weeks after symptoms resolve. Additional information about recreational water illnesses and how to stop them from spreading is available at https://www.cdc.gov/healthywater/swimming/ and at https://www.cdc.gov/parasites/giardia/prevention-control.html.

Discontinuing Secondary Prophylaxis

Not applicable.

Recommendations

I. In children with HIV infection, what are the best interventions (compared with no intervention) to prevent initial episodes of giardiasis?

- Giardiasis can be prevented by practicing good hygiene, not drinking or swimming in water that may be contaminated, and not eating food that may be contaminated (**expert opinion**).

  Because giardiasis results from ingestion of infectious cysts that are passed in the feces of infected individuals that may contaminate food or water, careful hand washing and washing of fruits and vegetables are recommended.

- Frequent hand washing can help reduce the incidence of diarrheal illnesses, including giardiasis (**strong, moderate**).

  A randomized trial of an intensive hand washing intervention (i.e., handwashing after defecation, after cleaning infants who had defecated, before preparing food, before eating, and before and after sex) in 148 adults with HIV infection in the United States resulted in fewer episodes of diarrheal illness and *Giardia* infections during a one year period, demonstrating the effectiveness of hand washing.[44]

- Combination antiretroviral therapy of children with HIV infection to reverse or prevent severe immunodeficiency is the primary mode of prevention of severe enteric giardiasis (**strong, very low**).

  A case-control study comparing giardiasis in adults with HIV infection in Brazil before and after the introduction of ART demonstrated that the incidence of enteric diseases caused by *Giardia* decreased after the introduction of ART.[21] Given the evidence, it is reasonable to recommend initiation of ART and immune reconstitution as a primary mode of giardiasis prevention.

II. In children with HIV infection, what are the best interventions (compared with no intervention) to treat giardiasis?

- Tinidazole and nitazoxanide are preferred, and metronidazole is the alternative recommended treatment for giardiasis in children (**strong, moderate**).

  Clinical trials in children without HIV infection have demonstrated the efficacy of single dose tinidazole in comparison to other anti-parasitic drugs such as nitazoxanide, mebendazole, albendazole and chloroquine.[45-47] Tinidazole can be used in children 3 years and older. Nitazoxanide can be used in children 1 year or older. Metronidazole is inexpensive and widely available and has been used by clinicians as the mainstay of therapy of giardiasis. Metronidazole has been shown to be less efficacious than tinidazole, but comparable to nitazoxanide.[7,45,58]

- Dehydration and electrolyte abnormalities should be corrected (**expert opinion**).

  There are no studies that address this specific management issue in giardiasis. However, recognition and management of hydration status and electrolyte imbalance are key to management of infectious diarrhea.

III. In children with HIV infection, what are the best interventions (compared with no intervention) to prevent recurrent episodes of giardiasis?

- Recurrent episodes of giardiasis can be prevented by practicing good hygiene and avoiding contaminated food and water (**expert opinion**).
- Frequent hand washing can help reduce the incidence of diarrheal illnesses, including giardiasis (**strong, moderate**).

  Good hygiene, including frequent hand washing and avoiding contaminated food and water, are recommended to prevent both initial and recurrent *Giardia* infections.

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Dosing Recommendations for Prevention and Treatment of Giardiasis

Indication	First Choice	Alternative	Comments/Special Issues
Primary Prophylaxis	ART to avoid advanced immunodeficiency	N/A	N/A
Secondary Prophylaxis	N/A	N/A	N/A
Treatment	Tinidazole 50 mg/kg orally, administered as one dose given with food (maximum dosage tinidazole 2 g). **Note:** Based on data from children who are HIV-negative. Nitazoxanide: • Aged 1–3 Years: Nitazoxanide 100 mg by mouth every 12 hours with food for 3 days • Aged 4–11 Years: Nitazoxanide 200 mg by mouth every 12 hours with food for 3 days • Aged ≥12 Years: Nitazoxanide 500 mg by mouth every 12 hours with food for 3 days • **Note:** Based on data from children who are HIV-negative	Metronidazole 5 mg/kg by mouth every 8 hours for 5–7 days. **Note:** Based on data from children who are HIV-negative.	Tinidazole is FDA-approved in the United States for children aged ≥3 years. It is available in tablets that can be crushed. Metronidazole has a high frequency of GI side effects. A pediatric suspension of metronidazole is not commercially available but can be compounded from tablets. Metronidazole is not FDA-approved for the treatment of giardiasis. Supportive Care: • Hydration • Correction of electrolyte abnormalities • Nutritional support Antimotility agents (e.g., loperamide) should be used with caution in young children.

Key: ART = antiretroviral therapy; FDA = U.S. Food and Drug Administration; GI = gastrointestinal