Strongyloidiasis Microlearning FAQ & Supplemental Information

MINNESOTA CENTER OF EXCELLENCE IN NEWCOMER HEALTH MICROLEARNING SERIES

Infection and symptoms

How does *Strongyloides* infection spread?

Most infections are acquired through environmental transmission (skin contact with contaminated soil). Person-to-person transmission can occur, but it is considered rare and includes organ transplantation and spread within facilities that provide both medical and personal care services such as long-term care facilities and daycare centers. It may also be spread fecal-orally with potential for sexual transmission.

Where is *Strongyloides* endemic?

Strongyloides is mostly found in tropical and subtropical areas, but may occur anywhere. Limited foci of transmission have been found in warm, nontropical climates, including Southern Europe, Southeastern/Appalachian regions in the U.S. (~4% prevalence), and the Torres Strait Islands in Australia.

What is the difference between strongyloidiasis "hyperinfection" and "disseminated infection"?

"Hyperinfection" is an increased larval migration within the organs normally involved in the chronic autoinfection cycle (GI tract, skin, lungs). This scenario has high parasitic burden, but clinically needs a high index of suspicion to consider the diagnosis. It can also present as gram-negative sepsis due to the invasion of enteric bacteria through bowel mucosa into the circulation facilitated by larvae penetration.

"Disseminated infection" is a hyperinfection syndrome with spread of larvae to organs outside of those involved in the autoinfection cycle (e.g., CNS, liver, heart, urinary tract, and endocrine organs).

Predisposing conditions for hyperinfection and dissemination are decreased cell-mediated immunity, including corticosteroid therapy (prednisone 20mg or higher for ≥ 6 days), HTLV-1, HIV/AIDS, malignancy/chemotherapy, malnutrition, organ transplant, COPD, renal failure, and alcoholism. The mortality rate in immunocompromised persons with disseminated infection may be >60–85%.

Diagnosis

How is strongyloidiasis diagnosed?

Diagnosis can be performed through stool testing or serology. To screen for asymptomatic infection, serology is used.

Do *Strongyloides* antibodies change over time?

Since antibodies can persist for some time, it can be difficult to distinguish between active cases and historical cases. Titers decline following effective treatment, and a significant proportion of people become antibody negative within 6 months after successful treatment.

Can *Strongyloides* serology results be falsely negative?

Strongyloides IgG maybe falsely negative in immunocompromised patients.

Can *Strongyloides* serology results be falsely positive?

Strongyloides IgG has a broad cross-positivity with other helminths (e.g., filarial parasites, schistosomes, and Ascaris lumbricoides) and therefore serology can be falsely positive if someone has another helminth infection.

What to do with equivocal *Strongyloides* serology results?

CDC performs reference serologic testing (using more sensitive and specific serologic tests with recombinant antigens) to confirm test results, which are occasionally difficult to interpret or equivocal. However, given the limited availability of this test, treatment is usually recommended for equivocal *Strongyloides* serology. For more information, refer to CDC: Clinical Overview of Strongyloides (https://www.cdc.gov/strongyloides/hcp/clinical-overview/index.html).

Treatment

When was presumptive overseas treatment with ivermectin for strongyloidiasis initiated?

Presumptive overseas ivermectin treatment was initiated in 2005 and included refugees from North Africa, Asia, and the Middle East. In 2019 guidelines were updated and added refugees from Latin American and Caribbean.

Any presumptive anti-helminthic treatment(s) received pre-departure should be documented in overseas medical records. For more information, refer to CDC: Guidance for Overseas Presumptive Treatment of Strongyloidiasis, Schistosomiasis, and Soil-Transmitted Helminth Infections for Refugees Resettling to the United States (https://www.cdc.gov/immigrant-refugee-health/hcp/overseas-guidance/intestinal-parasite-guidelines.html).

Refugees who meet the following criteria likely did not receive presumptive overseas Ivermectin treatment for strongyloidiasis:

- All Sub-Saharan refugees who originated from or resided in countries where *Loa loa* is endemic (i.e., Angola, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of Congo, Equatoria Guinea, Gabon, Nigeria, and South Sudan).
- Pregnant women.
- Children weighing < 15 kg or measuring < 90 cm.
- **NOTE:** Asylees, Special Immigrant Visa-holders, certified victims of human trafficking, and parolees do not undergo the same overseas medical exams as refugees and therefore do not receive the same medical treatments.

What is the optimal dose of Ivermectin for uncomplicated strongyloidiasis?

The optimal dosage schedule of ivermectin is a single dose (200 mcg/kg) for uncomplicated chronic strongyloidiasis (Buonfrate D, et al. Lancet Infect Dis. 2019 Nov;19(11):1181-1190. PMID: 31558376).

What is the treatment duration of Ivermectin for severe cases of strongyloidiasis?

Duration of treatment in severe disease (hyperinfection or disseminated infection) is variable and often individualized based on underlying degree of immunosuppression and treatment response (clinical resolution of symptoms and clearance of infection). Oral ivermectin 200 µg/kg per day is usually given for a minimum of two weeks, or until symptoms have resolved and stool and/or sputum are negative for two weeks (this includes one autoinfection cycle). Additionally, immunosuppression should be stopped or reduced, if possible. Patients in whom treatment fails to elicit a response should undergo screening for HTLV-1 infection. Contact infectious diseases expert for additional management recommendations after diagnosis of severe infection is made.

What is the management strategy of strongyloidiasis infection when at risk for Loa-Loa co-infection?

Refugees coming from countries in which *Loa loa* is endemic do not receive presumptive treatment for *Strongyloides* before departure as they are at risk for complications from treatment if they have a pre-existing *Loa loa* infection. These individuals can either be tested for *Strongyloides* and if positive, then undergo evaluation for *Loa loa* infection before receiving *Strongyloides* treatment with ivermectin OR be tested for *Loa loa* and if negative receive presumptive ivermectin therapy. To evaluate for *Loa loa* infection, obtain a single thin & thick Giemsa-stained blood smear between 10 a.m. to 2 p.m. to rule out filaremia. If *Loa loa* infection cannot be excluded, a high dose of albendazole (400mg twice daily for 7 days) is an acceptable alternative treatment for strongyloidiasis and is considered safe with *Loa Loa* co-infection. If blood smear for *Loa loa* confirms filaremia, seek advice from the CDC for further management. For more information, refer to CDC: About Loiasis (https://www.cdc.gov/filarial-worms/about/loiasis.html).

What do I do if the patient is not able to tolerate ivermectin oral therapy?

Published case reports have demonstrated efficacy with rectal ivermectin administration (Lichtenberger P, et al. Transpl Infect Dis. 2009 Apr;11(2):137-42. PMID: 19144097). If oral and/or rectal administrations are not possible, there have been instances where Investigational New Drug (IND) exemptions for the veterinary subcutaneous formulation of ivermectin have been granted by the FDA (Barrett J, et al. J Antimicrob Chemother. 2016 Jan;71(1):220-5. PMID: 26462990). Contact infectious diseases expert. For more information, refer to CDC: Clinical Care of Strongyloides (https://www.cdc.gov/strongyloides/hcp/clinical-care/index.html).

Complications and other parasitic infections

What is the difference between “cutaneous larva migrans/ground itch/creeping eruption” and “larva currens syndrome”?

They are all pruritic, erythematous, edematous, serpiginous urticarial rashes that are the result of reaction from certain helminthic invasions through the skin.

- "Cutaneous larva migrans" (or ground itch or creeping eruption) caused by Hookworm spp or *Strongyloides* spp at the initial site of larval skin entry, has typical location on feet/lower legs (or any point of contact with soil) and advances by 1-2 cm per day, and usually last for 2-8 weeks.
- "Larva currens" (or running or racing larva) is a distinctive form of cutaneous larva migrans caused by *Strongyloides* as a result of chronic autoinfection. Rash is recurrent with typical location on the perianal, buttock, thighs, and lower trunk/abdomen areas, rapid migration (5-15cm/hr) which is pathognomonic, and lesions last only for a few hours, and have wider band of urticaria.

What is Loffler's syndrome and which other parasitic infection can cause the same symptoms?

Löffler's syndrome is an eosinophilic pneumonia caused by accumulation of eosinophils in the lung as a response to a parasitic infection. It is defined by transient pulmonary infiltrates with eosinophilia, which can mimic COPD or asthma flares. Wheezing or pneumonitis that worsens, despite antibiotics or corticosteroids may be a tip-off. It can be caused by migrating larvae of *Strongyloides stercoralis*, but also Hookworm spp (*Ancylostoma duodenale*, *Necator americanus*) and *Ascaris lumbricoides*. Differential diagnoses also include tropical pulmonary eosinophilia filarial infection (*Wuchereria bancrofti*, *Brugia malayi*, *brugia timori*) caused by a type 1 hypersensitivity reaction to the microfilariae tapped within the lung parenchyma.

Special considerations for treatment

Is the testing of newborns and infants recommended?

Testing of newborns and young infants is not recommended given the low risk of infection. Infected mothers are known to pass IgG to their infants (and cause false positive test), but the duration of infant IgG positivity from maternal-fetal immunoglobulin transmission is unknown. However, if the infant has soil contact with skin (crawling, sitting, and lying on earth), then testing is recommended.

Is presumptive treatment for young children recommended?

Even though presumptive treatment is not recommended for children <1 year, treatment of young children with positive infection is recommended. The goal of treatment is to prevent development of symptomatic infection and related complications later in life with immunosuppression. Hyperinfection syndrome has rarely been reported in pediatric literature and is not well understood in children.

Currently, ivermectin use is contraindicated in children weighing < 15 kg. Systematic review suggests that oral ivermectin in children weighing less than 15 kilograms is safe (Jittamala P, et al. PLoS Negl Trop Dis. 2023 Jan 6;17(1). Erratum for: PLoS Negl Trop Dis. 2021 Mar 17;15(3). PMID: 36607893). Prior to initiating treatment in children who weigh <15 kg, consider contacting an infectious diseases expert.

Is treatment for *Strongyloides* recommended for pregnant persons?

Presumptive treatment is not recommended for pregnant persons and withholding treatment until delivery is typically recommended among asymptomatic pregnant women with positive serology. However, if a pregnant person with strongyloidiasis receives immunosuppressive medication during pregnancy, they are at risk of hyperinfection syndrome. Treatment is recommended for symptomatic pregnant women OR asymptomatic pregnant women receiving immunosuppressing medications or who are planning to use immunosuppressing medications (e.g., corticosteroids for preterm labor).

Limited information following use of ivermectin and albendazole during pregnancy is available. Because of this, both medications are relative contraindications during pregnancy. The risk of treatment must be balanced with the risk of disease progression (e.g., developing hyperinfection and adverse pregnancy outcome) in the absence of treatment.

Ivermectin is the preferred drug outside pregnancy, and it should also be considered in case of severe infection or in the setting of immunosuppressive treatment during pregnancy.

Albendazole seems to have a more established safety profile but has lower efficacy. If albendazole was given during pregnancy, then repeat treatment with ivermectin after delivery may be considered. If there are questions about adequacy of treatment during pregnancy, consider contacting an infectious diseases expert for management recommendations.

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