# Strongyloidiasis


**Melody Ren and Andrea K. Boggild**

**Abstract** *Strongyloides stercoralis* is an intestinal nematode estimated to infect at least 100 million people worldwide, predominantly in subtropical and tropical regions. With a unique life cycle and expansion of global travel and migration, strongyloidiasis is increasingly encountered in temperate and even non-endemic regions of North America. Most people harboring the worm are asymptomatic, but if left untreated, and especially in immunocompromised hosts such as people coinfected with HTLV-1/HTLV-2, *Strongyloides* larvae can disseminate and lead to a high-mortality hyperinfection syndrome manifesting as Gram-negative or polymicrobial sepsis and/or meningitis, pneumonitis, and end-organ failure. Diagnosis is based on microscopic examination or PCR of stool or serologic testing. Ivermectin remains the mainstay of treatment, but complicated infections should be treated with the support of a physician expert in tropical medicine.

**Keywords** Disseminated strongyloidiasis · Helminthiases · Immunosuppression · Migrant health · *Strongyloides stercoralis*

## 1 Introduction

Strongyloidiasis is caused by the intestinal roundworm (nematode), *Strongyloides stercoralis*. There are over 50 species of *Strongyloides* that infect a wide range of hosts [1]. Two other species, *Strongyloides fuelleborni* subsp. *fuelleborni* and

M. Ren
Division of Infectious Diseases, Department of Medicine, University of Toronto, Toronto, ON, Canada

A. K. Boggild (✉)
Division of Infectious Diseases, Department of Medicine, University of Toronto, Toronto, ON, Canada

Tropical Disease Unit, Toronto General Hospital, Toronto, ON, Canada

Institute of Medical Science, University of Toronto, Toronto, ON, Canada
e-mail: andrea.boggild@utoronto.ca

© Springer Nature Switzerland AG 2021

J. E. Weatherhead (ed.), *Neglected Tropical Diseases - North America*, Neglected Tropical Diseases, https://doi.org/10.1007/978-3-030-63384-4_3

*Strongyloides fuelleborni* subsp. *kellyi*, are known to infect humans but have limited clinical importance and are restricted in their geographic distribution [2]. *Strongyloides fuelleborni* infects primates and has been documented to infect humans in parts of Africa as well as Papua New Guinea [3]. This chapter focuses on the human pathogen *Strongyloides stercoralis*.

## 2 Epidemiology

Worldwide it is estimated that up to 100 million people are infected with *Strongyloides* [4, 5]. However, many experts believe this is an underestimate as many countries suffer from a lack of reporting and infrastructure to support high sensitivity testing [1, 6–8]. Some estimate the global prevalence as closer to 370 million people infected; however, with a dearth of epidemiological data, *Strongyloides*-related morbidity and mortality remain poorly defined [6].

*Strongyloides* exists mainly in tropical and subtropical regions with pockets in temperate climates comprising over 70 countries worldwide [1]. It shares a geographic distribution with hookworm [9]. With increasing trends in worldwide travel and northward migration, more cases have been encountered in non-endemic regions including in North America.

In Canada, 2.5 million people are estimated to have simple intestinal strongyloidiasis, mostly reflecting individuals born in endemic countries with a small proportion related to travel [10]. Anywhere from 9–77% of immigrants and refugees in Canada are thought to be infected, and current Canadian guidelines recommend screening for refugees from Southeast Asia, from Africa, and for immigrants from endemic areas including South America, Africa, Southeast Asia, and the Caribbean [11, 12]. Additionally, there have been reports of endemic institutional strongyloidiasis [13].

In the United States, many of the patterns observed in the Canadian context extend including infection in individuals born in endemic countries, travel-related infections, and institutional endemics [14]. There are also pockets in the Appalachia and rural areas in the southeastern United States that are endemic for *Strongyloides* [15–17]. Most people infected in these regions are involved in farming or mining activities, where skin-to-soil contact is presumed to be substantial [7].

The distribution of *Strongyloides* in Latin America is ill defined including in Mexico [18]. Studies in Mexico traditionally have been focused on capturing data on a wide range of intestinal parasites and therefore have used study techniques with a low sensitivity for strongyloidiasis [19, 20]. With these limitations, community-based and health service studies have reported less than 10% prevalence of strongyloidiasis in Mexico [7].

However unclear the specific epidemiological data are regarding strongyloidiasis prevalence; one fact remains clear: *Strongyloides*, as with soil-transmitted helminths, disproportionately affects impoverished peoples without access to adequate water, sanitation, or opportunities for socioeconomic development [21].

## 3 Transmission

The life cycle of *Strongyloides stercoralis* is unique and allows for host autoinfection (Fig. 1). *Strongyloides stercoralis* exists in four stages: egg, noninfectious rhabditiform larvae (250–300 μm by light microscopy), infectious filariform larvae (measuring 550 μm), and adults, either male and female sexually reproducing in the environment or as parthenogenetic female worms in the intestinal tract (semitransparent colorless worms measuring 2.2 mm). Adult male worms do not exist in the human intestinal tract [22]. Infectious filariform larvae penetrate the host skin from the environment and access the venous or lymphatic systems and then migrate to the lungs. Larvae are able to penetrate alveoli and migrate through to the bronchial system until they reach the trachea and are coughed then swallowed into the host into the gastrointestinal tract. It takes 18–28 days for the larvae to reach the small bowel mucosa from the time of skin penetration. Larvae then develop into adult females that intercalate themselves (hence the moniker "thread worm") into the small bowel epithelium where they produce eggs. The eggs develop into noninfectious rhabditiform larvae in the gastrointestinal tract mucosa before moving into the bowel lumen. By the time rhabditiform larvae reach the end of the gastrointestinal tract they have two potential paths: they are either excreted and become free-living sexually reproductive adult male and female worms which produce eggs that then develop into noninfectious rhabditiform larvae and then infectious filariform larvae or they develop into filariform larvae while still in the bowel lumen and penetrate the intestinal mucosa or perianal skin completing the autoinfection cycle.

The autoinfective capabilities of *Strongyloides stercoralis* enable it to complete its entire life cycle in the human host [23]. This biological imperative has two important implications. First, the number of *Strongyloides* parasites can increase within the human host without exogenous reinfection. This can lead to the clinical manifestations of severe complicated strongyloidiasis, disseminated strongyloidiasis, and hyperinfection, years after the initial infection. Second, *Strongyloides* can be theoretically transmitted from one person to another during close physical contact so infection can occur without the need for travel to an endemic region. For these reasons *Strongyloides* is rather unique among helminths as it can cause disease with significant mortality among persons who might not be easily identified by a history focused solely on the individual risk factors.

Transmission to humans most commonly occurs when filariform larvae in the sand or soil penetrate through intact human skin while walking barefoot. Children are also at risk of exposure when they play in contaminated soil without skin protection. Person-to-person transmission has been reported in institutional settings such as day care centers and psychiatric facilities, among men who have sex with men, and between solid organ donors and recipients via the donated organs [24, 25].

*Strongyloides* infection elicits a host immune response that is mostly mediated by the Th2 arm. There are also concurrent high levels of IL-4, IL-5, IL-10, IL-13, serum IgE, and often eosinophils. Acquired protective immunity has been demonstrated in

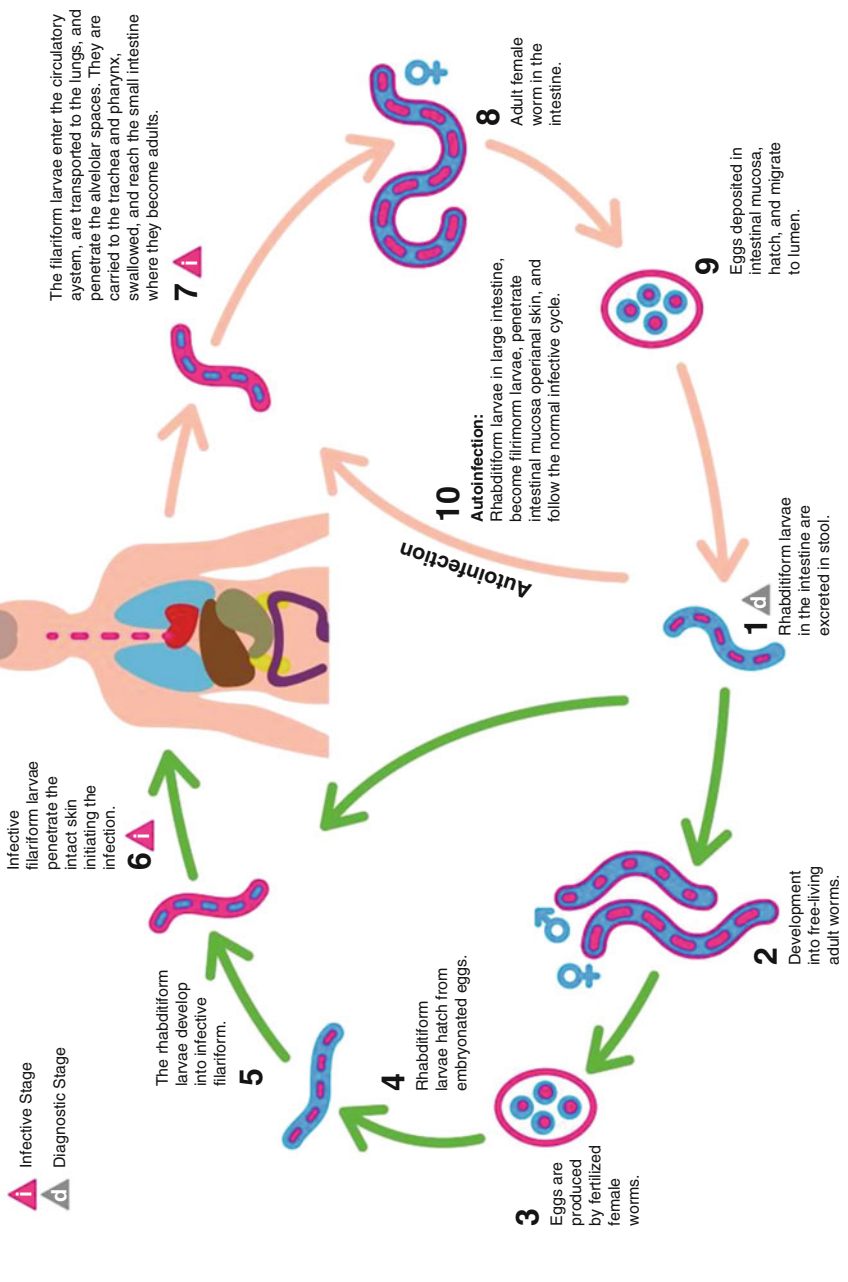


**Fig. 1** Life cycle of *Strongyloides* in humans [7]

animal models, though human antibody responses that aid in controlling the worm burden do not lead to worm eradication [26, 27].

The immune response to *Strongyloides* infection is especially important in human T-lymphotropic virus type 1 (HTLV-1) coinfection. HTLV-1 is a retrovirus that typically causes chronic asymptomatic infection [28]. It is most prevalent in Japan, West Africa, focally throughout the Caribbean islands, and certain countries of South America, particularly Peru [29]. HTLV-1 causes an impaired Th2 response, the major immune response to *Strongyloides*, which in turn leads to diminished circulating levels of IL-4 and IL-5, and a suboptimal eosinophil recruitment response, indicated by low peripheral blood eosinophils. This immunopathogenesis leads to increased susceptibility to simple intestinal strongyloidiasis and severe complicated strongyloidiasis as well as poor response to treatment with frequent relapses [30–35]. There is also evidence showing the deleterious relationship between HTLV-1 and *Strongyloides* is mutual, specifically that strongyloidiasis can promote HTLV-1 progression to T-cell leukemia/lymphoma [36].

Human immunodeficiency virus (HIV) and *Strongyloides* have overlapping geographies in low- and middle-income countries with millions of people predicted to be coinfected [37]. When AIDS was first described, there were concerns about an impending outbreak of disseminated strongyloidiasis, and the infection was initially included as an AIDS-defining illness prior to the identification of HIV [38]. At that time, it was hypothesized that the impaired cell-mediated immunity would allow for increased worm proliferation and subsequent dissemination. In 1987, the infection was removed from the revised AIDS classification as it was rarely described [39, 40]. Since then the general consensus has been that HIV is not associated with a higher risk of developing *Strongyloides* hyperinfection [41]. This could be because HIV primarily causes the loss of Th1 activity and may impact Th2 activity to a lesser degree and possibly even augment Th2 activity [42]. There have, however, been reports of severe complicated strongyloidiasis as part of an immune reconstitution phenomenon after initiating anti-retroviral therapy in patients [43, 44].

## 4 Clinical Manifestations

Strongyloidiasis has three major clinical manifestation profiles:

1. Simple intestinal strongyloidiasis, which can have an acute and chronic phase
2. Hyperinfection, one end of the spectrum of severe complicated strongyloidiasis
3. Dissemination, the other end of the spectrum of severe complicated strongyloidiasis

Simple intestinal strongyloidiasis occurs when *Strongyloides stercoralis* is confined to its typical life cycle in the human body while the host's cell-mediated immunity keeps the worm burden under control. In the acute phase, symptoms can occur that are consistent with the migration patterns of the parasite [23]. After skin penetration, larvae can cause a pruritic papular rash. The specific cutaneous finding

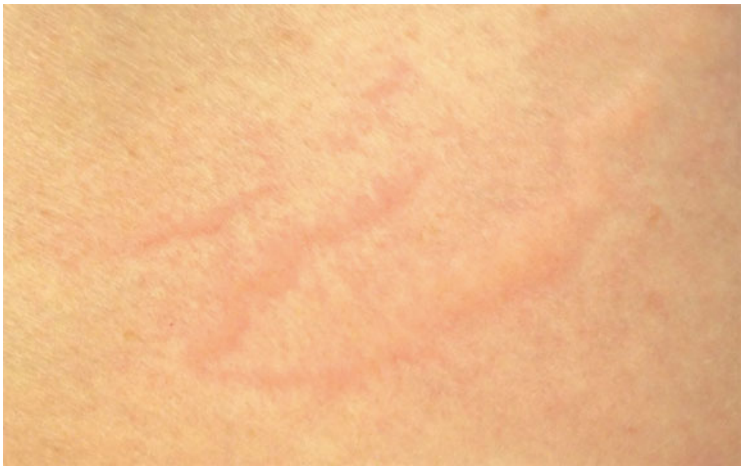

**Fig. 2** Larva currens rash of strongyloidiasis [12]. CMAJ has granted permission for reproduction

of larva currens, a serpiginous rash that can move up to 10 cm/h, is pathognomonic for *Strongyloides* infection (Fig. 2). Larva currens is a manifestation of the migrating infectious filariform larvae through the skin and usually occurs on the buttock, groin, or trunk; however, larva currens can affect all areas of the skin and is often one of the manifestations that triggers clinical teams to consider the diagnosis in those who are critically ill with exuberant autoinfection and diffuse serpiginous eruptions. When larvae enter the lungs, they can lead to cough or wheezing, and once in the GI tract, can cause abdominal pain and diarrhea. While penetrating the lungs and other host tissues, larvae incite a high-grade peripheral eosinophilia in 75–80% of cases of acute infection. In the chronic phase of simple intestinal strongyloidiasis, most patients are asymptomatic as the parasite is being regulated by the host immune system. Some patients can have symptoms that are similar to those in the acute phase as *Strongyloides* completes repeated autoinfection cycles in its host. These symptoms include recurrent maculopapular or urticarial rash or larva currens, recurrent asthma or a Loeffler-like syndrome, refractory gastritis, abdominal pain, vomiting, diarrhea, pruritus ani, and an isolated intermittent eosinophilia.

Severe complicated strongyloidiasis represents two states, hyperinfection and dissemination, both of which are usually associated with an impairment of the host cell-mediated immunity arising from corticosteroid use, HTLV-1 coinfection, solid organ and bone marrow transplant, hematologic malignancy, hypogammaglobulinemia, heavy alcohol use, end-stage renal disease, or malnutrition. Eosinophilia is typically absent in cases of severe complicated strongyloidiasis as well as in immunocompromised hosts [45]. In *Strongyloides* hyperinfection, the worm burden is increased from baseline but remains within the organ systems it typically infects including the gut, lung, and skin. Most patients in this stage of illness will remain ambulatory or only intermittently fulfill admission criteria for hospitalization. Gram-negative bacteremia may be detected in a portion of such

patients. Risk factors specific to hyperinfection outside of immunosuppression include prolonged burden of autoinfection [8].

In disseminated strongyloidiasis, the worm burden has increased to the point that larvae and possibly other stages including adults and/or eggs can be detected in off-target organ systems that are not within the typical migratory pattern of *Strongyloides*, such as the central nervous system, renal collecting system, and liver. Specific impairment of the Th2 immune response can lead to dissemination [46, 47]. In these cases filariform larvae are detectable at distant sites and complications include polymicrobial bacteremia, meningitis, and sepsis as a result of fecal flora being tracked throughout the body. The mortality of disseminated strongyloidiasis is quoted to be at least 85% and 100% if left untreated [48].

Due to its ability to autoinfect its host, it is important for clinicians to know that the clinical manifestations of strongyloidiasis can occur over 50 years after the time of presumed exposure [4, 49].

## 5 Diagnosis

Due to the nonspecific or absent nature of symptoms, clinical diagnosis of *Strongyloides* infection is challenging. Mild eosinophilia that accompanies gastrointestinal symptoms such as abdominal pain, bloating, and diarrhea can occur with many other helminthiases including schistosomiasis, ascariasis, and hookworm infection. The exception is in the setting of larva currens—the rapidly migrating serpiginous skin eruption—which is stereotypical of strongyloidiasis. Laboratory diagnosis of strongyloidiasis is an evolving science, and like all areas of microbiology, molecular techniques are being increasingly utilized in diagnostic algorithms.

The main currently available diagnostic testing for strongyloidiasis includes serology, microscopy- or molecular-based stool ova and parasite testing, stool agar culture, and microscopic ova and parasite testing on other body fluids including sputum, endotracheal aspirates, urine, cerebral spinal fluid (CSF), and tissue. Stool PCR testing remains generally confined to reference laboratories.

There are several high sensitivity enzyme immunoassay-based serologic tests for strongyloidiasis available in North America [50, 51]. The overall reported sensitivity of serologic assays in acute and chronic *Strongyloides* infections are 73% and 98%, respectively; however, this performance can be drastically reduced in situations of immunosuppression such as HTLV-1 infection, immune ablating medications, and hematologic malignancy [52–54]. The sensitivity of serology is also reduced in disseminated infection. The specificity of *Strongyloides* serology is typically limited by a high degree of cross-reactivity with other helminthiases, in particular filariasis. Additionally, a positive serologic test cannot be used to differentiate between simple intestinal infection, hyperinfection, or dissemination.

In contrast to serology, microscopy-based stool ova and parasite testing has a low sensitivity and a high specificity; however, performance can be optimized through collection of multiple stools over the course of several days due to low or intermittent

larval shedding [50, 55]. A single stool specimen can miss up to 70% of cases; however, in some studies >90% sensitivity is achieved if seven or more stool samples are examined consecutively [56–58]. Several techniques have been developed to improve the performance of stool testing such as formalin-ethyl acetate concentration, Baermann concentration, and Harada-Mori filter paper culture. The formalin-ethyl acetate concentration technique increases the larvae yield but kills the larvae rendering them immotile and therefore more difficult to detect at low magnification. The Baermann concentration and Harada-Mori filter paper culture both capitalize on the larval propensity to migrate into warm water; however, neither is commonly used in diagnostic parasitology laboratories. In accordance to the life cycle of *Strongyloides stercoralis*, the long pre-patency generally leads to negative stool testing within the first month of infection while larvae migrate through the human host before reaching the bowel and maturing to reproductive adults [59].

Stool agar culture consists of plating a fresh stool specimen on agar and then incubating in the presence of UV light to help identify and preserve larvae and adult worms. A positive stool agar culture is indicated by gross examination of tracts left by organisms as they crawl across the agar or microscopic examination of agar for different stages. Stool agar culture is highly specific and can be more sensitive than direct stool microscopic examination. However, sensitivity is low in non-endemic settings such as much of North America where microbiological and specialized parasitological testing is usually regionalized, leading to delays between specimen collection by the patient and ultimate inoculation onto agar in the laboratory. Such testing can be plagued with logistical challenges requiring 2–3 days of incubation, expensive equipment, and specialized technical knowledge, which is waning over time with attrition of expert microscopists [51, 57, 60].

Ova and parasite testing on other bodily fluids such as sputum, urine, CSF, and tissue can be used in severe complicated strongyloidiasis when larval burden is high. Prolonged shedding can occur in these fluids and be monitored for parasite stage, density, and drug effect, all of which influence clinical management decisions [50].

The use of stool PCR has generated mixed conclusions across geographic regions and patient populations in which it has been validated. Studies have demonstrated a lack of performance advantage of stool PCR over traditional microscopy or stool agar plate culture, with extremely poor sensitivity when worm burden is low [50, 61–63]. Other studies have indicated that PCR testing of stool offers performance characteristics justifying its implementation including sensitivity and specificity of up to 100% [64, 65]. Ultimately, stool PCR necessitates further validation across regions and laboratory settings but has the potential for far-reaching diagnostic impacts.

## *5.1 Screening Guidelines*

The following approach is recommended to screening for strongyloidiasis in the North American context:

**Table 1** Tests for diagnosis of strongyloidiasis. Adapted from [10] (also available as an app on: https://apps.apple.com/ca/app/the-strongy-app/id1260973695)

| Clinical scenario | Recommended test |
|---|---|
| Asymptomatic patient | Serology |
| Immunocompromised patient | Serology<br>Stool ova and parasite examination |
| Suspected hyperinfection or dissemination | Serology<br>Stool ova and parasite examination<br>Sputum, urine, CSF, and/or tissue ova and parasite examination |

1. Consider screening anyone with a cumulative exposure of greater than 2–-6 months in endemic areas or in anyone with compatible clinical manifestations. It is of particular importance that anyone who fulfills such criteria is screened prior to starting immunosuppression that can lead to severe complicated strongyloidiasis.
2. Screen family members of a positive index cases with common exposures, even if asymptomatic.
3. Use the appropriate tests for diagnosis. See Table 1.

### *5.2 Differential Diagnosis*

It is prudent to consider other migratory helminthiases in the differential diagnosis of gut and/or cutaneous symptomatology suggestive of strongyloidiasis, including toxocariasis, gnathostomiasis, filariasis, and angiostrongyliasis. These other helminths can present with symptoms similar to strongyloidiasis and can also cross-react with *Strongyloides* serological testing.

## 6 Treatment

### *6.1 Available Pharmacologic Treatment*

The goal of pharmacologic treatment of strongyloidiasis is complete eradication of the parasite (i.e., curative intent) due to the autoinfection process. This is in contrast to other soil-transmitted helminths where decreasing parasite burden is adequate to achieve clinical cure. Three antihelminthics exist to theoretically achieve this goal including ivermectin, albendazole, and thiabendazole.

Ivermectin dosed at 200 mcg/kg orally is first-line treatment for strongyloidiasis. It is safe and well tolerated and imparts its effects on ion channels in the cell membrane causing parasite paralysis. In cases where oral administration is not

feasible—particularly in the setting of disseminated strongyloidiasis—subcutaneous and parenteral ivermectin has been used with success [66–69]. A 2016 Cochrane meta-analysis found no difference comparing one dose versus two doses of ivermectin in simple intestinal strongyloidiasis that was re-demonstrated in a 2019 RCT comparing one versus four doses in immunocompetent patients in non-endemic regions [70, 71]. The two-dose regimen was based on theoretical idea that a 14-day interval between two doses would target the pre-patent infection arising from autoinfection [48]. Prior to ivermectin administration, the risk of microfilaremic loiasis needs to be assessed as ivermectin has been associated with severe fatal encephalopathy in untreated high-microfilaremic *Loa loa* infection [72]. A diagnosis of *Loa loa* should be considered in those who are born or have prolonged residency in countries of the central African rainforest including Cameroon, Equatorial Guinea, Gabon, Central African Republic, the Democratic Republic of the Congo, Nigeria, Chad, South Sudan, and northern Angola. Daytime blood film for microfilaria examination should then be performed in these patients prior to administration of ivermectin.

Albendazole 400 mg orally every 12 h for 7 days is a less effective alternative for strongyloidiasis treatment [10, 48, 70], and based on smaller scale data, thiabendazole has a similar efficacy to ivermectin but with a much worse safety and tolerability profile [73].

Ivermectin and albendazole are pregnancy category C drugs; however, the benefits of treatment likely outweigh the risk in cases of hyperinfection and dissemination. A recent systematic review and meta-analysis of use of antihelminthics in pregnancy noted no signal toward adverse maternal outcomes or safety events following gestational ivermectin use [74].

## *6.2 Treatment Approach*

The following list of interventions should be considered for all patients diagnosed with strongyloidiasis:

1. Consult an expert in migrant health or tropical infectious diseases.
2. Administer pharmacologic treatment based on the patient's clinical manifestations

    a. Simple intestinal or asymptomatic strongyloidiasis: ivermectin 200 mcg/kg orally in two doses separated by 14 days

        If the patients is undergoing imminent immunosuppression with a history of exposure to endemic regions, consider empiric treatment with ivermectin prior to the return of serology.

    b. Mild hyperinfection: empiric ivermectin 200 mcg/kg orally on day 1 and day

14 PLUS albendazole 400 mg orally BID daily for 7 days; or ivermectin 200 mcg/kg orally daily for 7 days

c. Dissemination: empiric ivermectin 200 mcg/kg orally or subcutaneously daily plus albendazole 400 mg orally BID daily until cessation of larval shedding (i.e., repeat sputum and stool ova and parasite testing are negative) and clinical improvement

Also start broad-spectrum antibiotics to cover polymicrobial sepsis.
If possible, lower the degree of immunosuppression in the patient.

3. Consider testing for HTLV-1 in those at risk

   a. If HTLV-1 positive, consider two daily doses of ivermectin every 2–6 weeks to keep larvae suppressed.

4. Arrange for follow-up for repeat serology in 9–12 months after treatment. A greater than 60% reduction in the antibody titer or serologic optical density indicates successful treatment [75, 76].

## 7 Prevention

In North America, most cases of strongyloidiasis will be encountered in healthcare settings, and prevention measures need to be taken for infection control as nosocomial transmission has been previously described [14, 77–80]. Contact precautions should be instituted for patients with suspected or confirmed strongyloidiasis and the laboratory workers processing their microbiology samples. Agar plates of specimens from patients with disseminated strongyloidiasis should be handled with gloves and sealed with Parafilm® tape [10].

Worldwide, experts agree that strongyloidiasis remains a neglected tropical disease that warrants expanded public health efforts and research coordination in order to manage the disease burden [6, 57, 81–83].

## References

1. Olsen A et al (2009) Strongyloidiasis – the most neglected of the neglected tropical diseases? Trans R Soc Trop Med Hyg 103(10):967–972. https://doi.org/10.1016/j.trstmh.2009.02.013
2. Dorris M et al (2002) Molecular phylogenetic analysis of the genus strongyloides and related nematodes. Int J Parasitol 32(12):1507–1517. https://doi.org/10.1016/s0020-7519(02)00156-x
3. Ashford Rw et al (1978) Strongyloides infection associated with acute infantile disease in Papua new guinea. Trans R Soc Trop Med Hyg 72(5):554. https://doi.org/10.1016/0035-9203(78)90193-1
4. Lim S (2004) Complicated and fatal strongyloides infection in canadians: risk factors, diagnosis and management. Can Med Assoc J 171(5):479–484. https://doi.org/10.1503/cmaj.1031698

5. Bethony J et al (2006) Soil-transmitted helminth infections: ascariasis, trichuriasis, and hookworm. Lancet 367(9521):1521–1532. https://doi.org/10.1016/s0140-6736(06)68653-4
6. Bisoffi Z et al (2013) Strongyloides stercoralis: a plea for action. PLoS Negl Trop Dis 7 (5):2214. https://doi.org/10.1371/journal.pntd.0002214
7. Schär F et al (2013) Strongyloides stercoralis: global distribution and risk factors. PLoS Negl Trop Dis 7(7):2288. https://doi.org/10.1371/journal.pntd.0002288
8. Montes M et al (2010) Strongyloides stercoralis: there but not seen. Curr Opin Infect Dis 23 (5):500–504. https://doi.org/10.1097/qco.0b013e32833df718
9. Becker SL et al (2011) Diagnosis, clinical features, and self-reported morbidity of strongyloides stercoralis and hookworm infection in a co-endemic setting. PLoS Negl Trop Dis 5(8):1292. https://doi.org/10.1371/journal.pntd.0001292
10. Boggild AK et al (2016) CATMAT statement on disseminated strongyloidiasis: prevention, assessment and management guidelines. Can Commun Dis Rep 42(1):12–19. https://doi.org/10.14745/ccdr.v42i01a03
11. Pottie K et al (2010) Evidence-based clinical guidelines for immigrants and refugees. Can Med Assoc J 183(12):090313. https://doi.org/10.1503/cmaj.090313
12. Thompson C, Boggild AK (2015) Strongyloidiasis in Immigrants and Refugees in Canada. Can Med Assoc J 187(18):1389. https://doi.org/10.1503/cmaj.141441
13. Proctor EM et al (1987) Endemic institutional strongyloidiasis in British Columbia. Can Med Assoc J 136(11):1173–1176
14. Notes from the field: strongyloides infection among patients at a long-term care facility--Florida, 2010-2012. MMWR Morb Mortal Wkly Rep 2013;62(42):844
15. Croker C et al (2010) Strongyloidiasis-related deaths in the United States, 1991–2006. Am J Trop Med Hyg 83(2):422–426. https://doi.org/10.4269/ajtmh.2010.09-0750
16. Milder JE et al (1981) Clinical features of strongyloides stercoralis infection in an endemic area of the United States. Gastroenterology 80(6):1481–1488. https://doi.org/10.1016/0016-5085(81)90261-4
17. Notes from the field: strongyloidiasis in a rural setting--Southeastern Kentucky, 2013. Centers for Disease Control and Prevention MMWR Morb Mortal Wkly Rep 2013;62(42):843
18. Buonfrate D et al (2014) Prevalence of strongyloidiasis in Latin America: a systematic review of the literature. Epidemiol Infect 143(3):452–460. https://doi.org/10.1017/s0950268814001563
19. Guarner J et al (1997) Frequency of intestinal parasites in adult cancer patients in Mexico. Arch Med Res 20(2):219–222
20. Faulkner CT et al (2003) Prevalence of endoparasitic infection in children and its relation with cholera prevention efforts in Mexico. Rev Panam Salud Publica 14(1):31–41. https://doi.org/10.1590/s1020-49892003000600006
21. Albonico M et al (2008) Controlling soil-transmitted helminthiasis in pre-school-age children through preventive chemotherapy. PLoS Negl Trop Dis 2(3):126. https://doi.org/10.1371/journal.pntd.0000126
22. Grove DI (1996) Human Strongyloidiasis. Adv Parasitol 38:251–309. https://doi.org/10.1016/s0065-308x(08)60036-6
23. Greaves D et al (2013) Strongyloides stercoralis infection. BMJ 347(3):4610. https://doi.org/10.1136/bmj.f4610
24. Gatti S et al (2000) Intestinal parasitic infections in an institution for the mentally retarded. Ann Trop Med Parasitol 94(5):453–460. https://doi.org/10.1080/00034983.2000.11813564
25. Hasan A, Le M, Pasko J et al (2013) Transmission of Strongyloides stercoralis through transplantation of solid organs—Pennsylvania, 2012. MMWR Morb Mortal Wkly Rep 62:264–266
26. Iriemenam NC et al (2010) Strongyloides stercoralis and the immune response. Parasitol Int 59 (1):9–14. https://doi.org/10.1016/j.parint.2009.10.009
27. Bonne-Année S et al (2011) Innate and adaptive immunity to the nematode strongyloides stercoralis in a mouse model. Immunol Res 51(2-3):205–214. https://doi.org/10.1007/s12026-011-8258-2

28. Verdonck K et al (2007) Human T-lymphotropic virus 1: recent knowledge about an ancient infection. Lancet Infect Dis 7(4):266–281. https://doi.org/10.1016/s1473-3099(07)70081-6
29. Proietti FA et al (2005) Global epidemiology of HTLV-I infection and associated diseases. Oncogene 24(39):6058–6068. https://doi.org/10.1038/sj.onc.1208968
30. Porto AF et al (2001) HTLV-1 decreases Th2 type of immune response in patients with strongyloidiasis. Parasite Immunol 23(9):503–507. https://doi.org/10.1046/j.1365-3024.2001.00407.x
31. Montes M et al (2009) Regulatory T cell expansion in HTLV-1 and strongyloidiasis co-infection is associated with reduced IL-5 responses to strongyloides stercoralis antigen. PLoS Negl Trop Dis 3(6):456. https://doi.org/10.1371/journal.pntd.0000456
32. Peters L et al (2009) Secondary strongyloides stercoralis prophylaxis in patients with human T-cell lymphotropic virus type 1 infection: report of two cases. Int J Infect Dis 13(6):9. https://doi.org/10.1016/j.ijid.2009.02.009
33. Gotuzzo E et al (1999) Strongyloides stercoralis hyperinfection associated with human T cell lymphotropic virus type-1 infection in Peru. Am J Trop Med Hyg 60(1):146–149. https://doi.org/10.4269/ajtmh.1999.60.146
34. Terashima A et al (2002) Treatment failure in intestinal strongyloidiasis: an indicator of HTLV-I infection. Int J Infect Dis 6(1):28–30. https://doi.org/10.1016/s1201-9712(02)90132-3
35. Satoh M et al (2002) Reduced efficacy of treatment of strongyloidiasis in HTLV-I carriers related to enhanced expression of IFN-γ and TGF-β1. Clin Exp Immunol 127(2):354–359. https://doi.org/10.1046/j.1365-2249.2002.01733.x
36. Salles F et al (2013) Treatment of Strongyloidiasis in HTLV-1 and strongyloides stercoralis coinfected patients is associated with increased TNFα and decreased soluble IL2 receptor levels. Trans R Soc Trop Med Hyg 107(8):526–529. https://doi.org/10.1093/trstmh/trt052
37. Grove DI (2004) Strongyloides stercoralis. Textbook – atlas of intestinal infections in AIDS. Springer, New York, pp 367–371
38. Centers for Disease Control (1982) Update: acquired immunodeficiency syndrome – United States. MMWR 31:557–580
39. Centers for Disease Control (1987) Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. MMWR 36(1S):3S–15S
40. Lucas SB (1990) Missing infections in AIDS. Trans R Soc Trop Med Hyg 84:34–38. https://doi.org/10.1016/0035-9203(90)90453-l
41. Viney ME et al (2004) Why does HIV infection not lead to disseminated strongyloidiasis? J Infect Dis 190(12):2175–2180. https://doi.org/10.1086/425935
42. Siegel MO, Simon GL (2012) Is human immunodeficiency virus infection a risk factor for strongyloides stercoralis hyperinfection and dissemination. PLoS Negl Trop Dis 6(7). https://doi.org/10.1371/journal.pntd.0001581
43. Taylor CL, Ustianowski AP (2008) Immune reconstitution syndrome to strongyloides stercoralis infection. AIDS 22(8):998. https://doi.org/10.1097/qad.0b013e3282ffdeba
44. Brown M et al (2006) Dissemination of strongyloides stercoralis as an immune restoration phenomenon in an HIV-1-infected man on antiretroviral therapy. Int J STD AIDS 17(8):560–561. https://doi.org/10.1258/095646206778145712
45. Grove DI (1989) Clinical manifestations. In: Grove DI (ed) Strongyloidiasis: a major roundworm infection of man. Philadelphia (Pennsylvania). Taylor & Francis, Philadelphia, pp 155–173
46. Gyorkos TW et al (1990) Seroepidemiology of strongyloides infection in the Southeast Asian refugee population in Canada. Am J Epidemiol 132(2):257–264. https://doi.org/10.1093/oxfordjournals.aje.a115655
47. Mejia R, Nutman TB (2012) Screening, prevention, and treatment for hyperinfection syndrome and disseminated infections caused by strongyloides stercoralis. Curr Opin Infect Dis 25(4):458–463. https://doi.org/10.1097/qco.0b013e3283551dbd

48. Suputtamongkol Y et al (2011) Efficacy and safety of single and double doses of ivermectin versus 7-day high dose albendazole for chronic strongyloidiasis. PLoS Negl Trop Dis 5 (5):1044. https://doi.org/10.1371/journal.pntd.0001044
49. Bailey KE et al (2015) Chronic larva currens following tourist travel to the Gambia and Southeast Asia over 20 years ago. J Cutan Med Surg 19(4):412–415. https://doi.org/10.1177/1203475415575247
50. Dong MD et al (2016) Strongyloidiasis in Ontario: performance of diagnostic tests over a 14-month period. Travel Med Infect Dis 14(6):625–629. https://doi.org/10.1016/j.tmaid.2016.10.011
51. Bisoffi Z et al (2014) Diagnostic accuracy of five serologic tests for strongyloides stercoralis infection. PLoS Negl Trop Dis 8(1):2640. https://doi.org/10.1371/journal.pntd.0002640
52. Sudarshi S et al (2003) Clinical presentation and diagnostic sensitivity of laboratory tests for strongyloides stercoralis in travellers compared with immigrants in a non-endemic country. Trop Med Int Health 8(8):728–732. https://doi.org/10.1046/j.1365-3156.2003.01069.x
53. Porto AF et al (2001) Influence of human T-cell lymphocytotropic virus type 1 infection on serologic and skin tests for strongyloidiasis. Am J Trop Med Hyg 65(5):610–613. https://doi.org/10.4269/ajtmh.2001.65.610
54. Schaffel R et al (2001) The value of an immunoenzymatic test (enzyme-linked immunosorbent assay) for the diagnosis of strongyloidiasis in patients immunosuppressed by hematologic malignancies. Am J Trop Med Hyg 65(4):346–350. https://doi.org/10.4269/ajtmh.2001.65.346
55. Sato Y et al (1995) Efficacy of stool examination for detection of strongyloides infection. Am J Trop Med Hyg 53(3):248–250. https://doi.org/10.4269/ajtmh.1995.53.248
56. Nielsen PB, Mojon M (1987) Improved diagnosis of strongyloides stercoralis by seven consecutive stool specimens. Zentralblatt Bakteriol Mikrobiol Hyg 263(4):616–618. https://doi.org/10.1016/s0176-6724(87)80207-9
57. Ericsson CD et al (2001) Diagnosis of strongyloides stercoralis infection. Clin Infect Dis 33 (7):1040–1047. https://doi.org/10.1086/322707
58. Liu LX, Weller PF (1993) Strongyloidiasis and other intestinal nematode infections. Infect Dis Clin N Am 7:655–682
59. Freedman DO (1991) Experimental infection of human subjects with strongyloides species. Clin Infect Dis 13(6):1221–1226. https://doi.org/10.1093/clinids/13.6.1221
60. Anderson NW et al (2014) Comparison of three immunoassays for detection of antibodies to strongyloides stercoralis. Clin Vaccine Immunol 21(5):732–736. https://doi.org/10.1128/cvi.00041-14
61. Buonfrate D et al (2018) Accuracy of molecular biology techniques for the diagnosis of strongyloides stercoralis infection—a systematic review and meta-analysis. PLoS Negl Trop Dis 12(2). https://doi.org/10.1371/journal.pntd.0006229
62. Sultana Y et al (2013) Real-time polymerase chain reaction for detection of strongyloides stercoralis in stool. Am J Trop Med Hyg 88(6):1048–1051. https://doi.org/10.4269/ajtmh.12-0437
63. Knopp S et al (2014) Diagnostic accuracy of Kato–Katz, FLOTAC, Baermann, and PCR methods for the detection of light-intensity hookworm and strongyloides stercoralis infections in Tanzania. Am J Trop Med Hyg 90(3):535–545. https://doi.org/10.4269/ajtmh.13-0268
64. Becker SL et al (2015) Real-time PCR for detection of strongyloides stercoralis in human stool samples from Côte d'Ivoire: diagnostic accuracy, inter-laboratory comparison and patterns of hookworm co-infection. Acta Trop 150:210–217. https://doi.org/10.1016/j.actatropica.2015.07.019
65. Verweij JJ et al (2009) Molecular diagnosis of strongyloides stercoralis in faecal samples using real-time PCR. Trans R Soc Trop Med Hyg 103(4):342–346. https://doi.org/10.1016/j.trstmh.2008.12.001
66. Turner SA et al (2005) Parenteral administration of ivermectin in a patient with disseminated strongyloidiasis. Am J Trop Med Hyg 73(5):911–914. https://doi.org/10.4269/ajtmh.2005.73.911

67. Leung V et al (2008) Failure of subcutaneous ivermectin in treating strongyloides hyperinfection. Am J Trop Med Hyg 79(6):853–855. https://doi.org/10.4269/ajtmh.2008.79.853
68. Salluh JIF et al (2005) Successful use of parenteral ivermectin in an immunosuppressed patient with disseminated strongyloidiasis and septic shock. Intensive Care Med 31(9):1292–1292. https://doi.org/10.1007/s00134-005-2725-y
69. Chiodini P et al (2000) Parenteral ivermectin in strongyloides hyperinfection. Lancet 355 (9197):43–44. https://doi.org/10.1016/s0140-6736(99)02744-0
70. Henriquez-Camacho C et al (2016) Ivermectin versus albendazole or thiabendazole for strongyloides stercoralis infection. Cochrane Database Syst Rev 11:CD007745. https://doi.org/10.1002/14651858.cd007745.pub3.
71. Buonfrate D et al (2019) Multiple-dose versus single-dose ivermectin for strongyloides stercoralis infection (strong treat 1 to 4): a multicentre, open-label, phase 3, randomised controlled superiority trial. Lancet Infect Dis 19(11):1181–1190. https://doi.org/10.1016/s1473-3099(19)30289-0
72. Boussinesq M et al (2003) Clinical picture, epidemiology and outcome of Loa-associated serious adverse events related to mass ivermectin treatment of onchocerciasis in Cameroon. Filar J 2(Suppl 1):2883. https://doi.org/10.1186/1475-2883-2-s1-s4
73. Bisoffi Z et al (2011) Randomized clinical trial on ivermectin versus thiabendazole for the treatment of strongyloidiasis. PLoS Negl Trop Dis 5(7). https://doi.org/10.1371/journal.pntd.0001254
74. Lau R et al (2019) Treatment of soil-transmitted helminth infections in pregnancy: a systematic review and meta-analysis of maternal outcomes. J Travel Med 27:79. https://doi.org/10.1093/jtm/taz079
75. Page WA et al (2006) Utility of serological follow-up of chronic strongyloidiasis after anthelminthic chemotherapy. Trans R Soc Trop Med Hyg 100(11):1056–1062. https://doi.org/10.1016/j.trstmh.2005.12.006
76. Loutfy MR et al (2002) Serology and eosinophil count in the diagnosis and management of strongyloidiasis in a non-endemic area. Am J Trop Med Hyg 66(6):749–752. https://doi.org/10.4269/ajtmh.2002.66.749
77. Maraha B et al (2001) The risk of strongyloides stercoralis transmission from patients with disseminated strongyloidiasis to the medical staff. J Hosp Infect 49(3):222–224. https://doi.org/10.1053/jhin.2001.1075
78. Hauber HP et al (2005) Fatal outcome of a hyperinfection syndrome despite successful eradication of strongyloides with subcutaneous ivermectin. Infection 33(5-6):383–386. https://doi.org/10.1007/s15010-005-5060-x
79. Braun TI (1988) Strongyloidiasis in an institution for mentally retarded adults. Arch Intern Med 148(3):634. https://doi.org/10.1001/archinte.1988.00380030140024
80. Jones JM, Hill C, Briggs G et al (2016) Notes from the field: strongyloidiasis at a long-term-care facility for the developmentally disabled-Arizona 2015. MMWR 65:609
81. Satoh M, Kokaze A (2004) Treatment strategies in controlling strongyloidiasis. Expert Opin Pharmacother 5(11):2293–2301. https://doi.org/10.1517/14656566.5.11.2293
82. Gabrielli A-F et al (2011) Preventive chemotherapy in human helminthiasis: theoretical and operational aspects. Trans R Soc Trop Med Hyg 105(12):683–693. https://doi.org/10.1016/j.trstmh.2011.08.013
83. Krolewiecki AJ et al (2013) A public health response against strongyloides stercoralis: time to look at soil-transmitted helminthiasis in full. PLoS Negl Trop Dis 7(5). https://doi.org/10.1371/journal.pntd.0002165