Complicated and fatal *Strongyloides* infection in Canadians: risk factors, diagnosis and management

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**Abstract**

*Strongyloides stercoralis*, which is caused by the nematode *Strongyloides stercoralis*, is a common and persistent infection, particularly in developing countries. In the setting of compromised cellular immunity, it can result in fulminant dissemination with case-fatality rates of over 70%. The majority of new Canadian immigrants come from countries where *Strongyloides* is highly endemic; therefore, the burden of *Strongyloides* may be underappreciated in Canada. Because early diagnosis and therapy can have a marked impact on disease outcome, screening for this infection should be considered mandatory for patients who have a history of travel or residence in a disease-endemic area and risk factors for disseminated disease (e.g., corticosteroid use and human T-lymphotropic virus type 1 infection).

**Epidemiology**

*Strongyloides stercoralis* is a common intestinal nematode that affects 30–100 million people worldwide; it is endemic in Africa, Asia, Southeast Asia, and Central and South America.1,2 Human infection occurs when infective (filariform) larvae penetrate intact skin. This most commonly happens when the host’s bare feet come in direct contact with soil contaminated with infective *Strongyloides* larvae (Fig. 2). Once infected, most people have an asymptomatic, chronic infection of the gastrointestinal tract. However, because of the unique ability of *S. stercoralis* to complete its life cycle within the human host, the burden of worms can dramatically increase through a cycle of autoinfection. Autoinfection can lead to disease persistence as well as to hyperinfection syndrome, where the disease is disseminated amid impaired cellular immunity.

![Fig. 1: *Strongyloides stercoralis* larva tracks on a blood agar plate from the bronchoalveolar lavage of a patient with disseminated strongyloidiasis.](image)
Although strongyloidiasis has traditionally been considered a tropical disease, increased worldwide travel and migration challenge this view. Canada’s immigrant population, for example, has changed significantly over the past several decades. Before 1961, only 5.3% of Canadian immigrants were from countries where *Strongyloides* infection is endemic. In contrast, 2001 Census data indicate that 77.5% of immigrants coming to Canada over the 10-year...
period between 1991 and 2001 were from Strongyloides-endemic countries. Furthermore, ethnic minorities born in Canada are also at increased risk for strongyloidiasis, since they are more likely to visit friends and relatives in disease-endemic countries. Although the worldwide prevalence of Strongyloides is unknown, estimates are available from seroprevalence studies of high-risk populations. One study found that Southeast Asian refugees arriving in Canada had seroprevalence rates between 11.8% (Vietnamese) and 76.6% (Cambodians). According to Statistics Canada, 43.7% of Toronto’s total population in 2001 was composed of foreign-born people, with the majority arriving from Strongyloides-endemic areas, including Southeast Asia, the Indian subcontinent and China. This suggests that strongyloidiasis may be an unrecognized infection among the Canadian population.

This contention is supported by observations of cases of disseminated strongyloidiasis in Canada. Over a 7-month period in 2002, a series of 10 consecutive cases of disseminated or fatal Strongyloides infection were identified in 2 academic hospitals in Toronto (see the online table at www.cmaj.ca/cgi/content/full/171/5/479/DC1). These cases highlight the epidemiology, risk factors, and diagnostic and management challenges associated with strongyloidiasis in areas where the disease is not endemic, such as Canada. Of these 10 cases, 7 were male, and the mean age was 64.6 (range 24–89) years. All of the patients were immigrants to Canada who acquired strongyloidiasis in their country of origin (3 in Asia, 6 in the Caribbean and 1 in Africa). One patient had lived in Canada for 56 years before symptoms developed. None acquired infection during travel to disease-endemic areas, with infection in Canadian travellers has been reported. With respect to risk factors, corticosteroid use was documented in 4 of these 10 patients and positive human T-lymphotropic virus-1 (HTLV-1) serology was found in 3. Seven patients had disseminated infection with an associated mortality of 71%.

Clinical manifestations

Table 1 outlines the common presenting symptoms based on the host’s immune status. Gastrointestinal symptoms are the most common, and the respiratory tract is the system most frequently affected outside the gastrointestinal tract. Gram-negative or polymicrobial bacteremia from migration of larvae through the bowel wall is another common presentation of disseminated infection.

In the case of drug-induced or disease-associated defects in cellular immunity, autoinfection may lead to a massive increase in parasite burden and dissemination to almost all organ systems, including the lungs, liver and central nervous system. One study estimated that disseminated strongyloidiasis occurs in 1.5%–2.5% of infected patients. However, this number should be interpreted with caution, as the prevalence of Strongyloides infection is difficult to assess and is dependent upon geography, host immune status, test characteristics of available diagnostic assays and other factors. Nonetheless, it is generally agreed that disseminated strongyloidiasis has a high associated rate of death, with one review demonstrating a rate of 86%.

Risk factors for dissemination

The association between impaired cellular immunity and a hyperinfective state was first reported in 1966. Risk factors for dissemination are shown in Box 1. Details of these mechanisms remain unclear, as there are have been cases of hyperinfection in people with no identifiable immunodeficiency.

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**Table 1: Typical clinical manifestations and treatment of strongyloidiasis in immunocompetent and immunosuppressed hosts**

| Host                  | Common signs and symptoms                                      | Eosinophilia                      | Treatment                                      |
|-----------------------|-----------------------------------------------------------------|-----------------------------------|------------------------------------------------|
| Normal immune system  | Gastrointestinal (most common): progressive weight loss, diarrhea, abdominal pain, vomiting | Usually present in > 70% of cases | Single drug: albendazole 400 mg twice daily × 7 d OR ivermectin 200 µg/kg daily × 1–2 d |
|                       | Dermatologic: larva currens (perianal, rapidly moving and pruritic linear eruption due to migration of larvae); this symptom is pathognomonic of strongyloidiasis |                                    |                                                |
|                       | Respiratory (most common outside the gastrointestinal tract): dyspnea, wheezing, hemoptysis, cough, respiratory distress |                                    |                                                |
|                       | Fever                                                           | Often absent                      | Combination therapy: albendazole 400 mg twice daily × 7 d AND ivermectin 200 µg/kg daily × 1–2 d |
|                       | Gram-negative/polymicrobial bacteremia due to migration of larvae through the bowel wall |                                    | In cases of disseminated strongyloidiasis, albendazole and ivermectin are continued until there is evidence that the parasite is cleared |

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CMAJ • AUG. 31, 2004; 171 (5) 481
Corticosteroids, which target T cells, have been documented as an important factor in the subsequent development of hyperinfection.15,16,21,33,34 Hematologic cancers make up the majority of malignant diseases associated with hyperinfection, accounting for 20 of 22 malignant disease in one review.13 In general, malignant disease alone is rarely the sole factor for dissemination.13,35 The majority of patients who experience disseminated strongyloidiasis do so after they have received immunosuppressive therapy, usually prednisone, as treatment for their disease. Thus, although patients with hematologic cancer are known to have degrees of immune deficiency,36 the high frequency of corticosteroid use in this population confounds the strength of the association between disseminated strongyloidiasis and hematologic malignant disease.

Another major risk factor is HTLV-1 coinfection. HTLV-1 is a retrovirus associated with adult T-cell leukemia and HTLV-1-associated myelopathy,37 with adult T-cell leukemia developing in 3%–5% of HTLV-1 carriers after a long period of latency.38 This latent or preleukemic phase is reported to be up to 30 years shorter in HTLV-1 carriers who are coinfected with Strongyloides than in other HTLV-1-infected people.39–42 Monoclonal proliferation of the HTLV-1-infected cells has been shown to occur in coinfected patients but not in asymptomatic HTLV-1 carriers who do not have strongyloidiasis.43,44 Furthermore, the results of a recent study have shown that the Strongyloides antigen is implicated in T-cell proliferation and ultimately accelerates leukemogenesis.37 Successful treatment of strongyloidiasis may reverse clonal expansion by decreasing the HTLV-1 proviral load.38 This relationship appears to be bidirectional: not only does Strongyloides infection have an effect on the development of HTLV-1-associated malignant disease, but HTLV-1 inhibits cellular responses to Strongyloides infection.45–52

In a review of 27 cases in the West Indies,1 HTLV-1 infection was the most common condition (71%) predisposing to dissemination. As well, 6 of the 7 patients who died were HTLV-1 positive, which suggests that coinfection is a marker of a poor prognosis. Given the significant correlation between HTLV-1 and strongyloidiasis in regions where the latter is endemic, such as the West Indies and Japan,48 it has been suggested that each disease should prompt diagnostic efforts for the other.1

### Diagnosis and management

A suggested diagnostic approach is shown in Table 2, which highlights the most likely clinical presentations encountered where one should suspect Strongyloides infection, followed by the appropriate diagnostic investigations.

### Box 1: Risk factors for disseminated strongyloidiasis

**Major risk factors**
- Immunosuppressive therapy (particularly corticosteroids)
- Transplantation
- Hematologic malignant disease
- Human T-lymphotropic virus-1 infection

**Additional risk factors**
- Malnutrition
- Diabetes mellitus
- Chronic renal failure
- Chronic alcohol consumption

Note: Some cases may have no identifiable risk factors for immunodeficiency.

### Table 2: Diagnostic procedure for strongyloidiasis in people who have travelled to or lived in disease-endemic areas

| Presentation | Diagnostic procedure |
|--------------|----------------------|
| Patient has gastrointestinal symptoms compatible with uncomplicated strongyloidiasis (weight loss, diarrhea, abdominal pain, vomiting) | 3 serial stool samples screened for ova and parasites **AND** enzyme-linked immunosorbent assay for *S. stercoralis* serology |
| OR | |
| Patient is asymptomatic but may be receiving corticosteroids or other immunosuppressive therapy in the near future | |
| Patient is unwell and has pulmonary symptoms (wheezing, respiratory distress), gram-negative/polymicrobial sepsis and risk factors for disseminated disease (see Box 1) | Blood and sputum cultures for *S. stercoralis*, and culture other specimens based on suspected organ involvement (e.g., CSF) **AND** 3 serial stool samples screened for ova and parasites **AND** enzyme-linked immunosorbent assay for *S. stercoralis* serology |

Note: CSF = cerebrospinal fluid.

*Strongyloidiasis should be recognized and treated before initiating immunosuppressive therapy, since once the disease disseminates it carries a high fatality rate regardless of therapeutic intervention.*
Complicated strongyloidiasis in Canadians

Competing interests: None declared.

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This article has been peer reviewed.

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