Parasitic Infections Associated with HIV/AIDS in the Caribbean

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This review article seeks to highlight the significance for the Caribbean of major parasitic infections associated with AIDS, encourage awareness of these opportunistic parasites, and promote familiarity with appropriate diagnostic techniques and their clinical relevance. Specific agents considered include Pneumocystis carinii; Toxoplasma gondii; the enteric coccidians Cryptosporidium spp., Isospora belli, and Cyclospora cayetanensis; the hemoflagellates Leishmania spp. and Trypanosoma cruzi; the fungi Histoplasma capsulatum and Cryptococcus neoformans; the nematode Strongyloides stercoralis; and the mite Sarcoptes scabiei.

These disease agents can be divided into two groups, the immune-regulated "endogenous" parasites (the protozoans P. carinii and T. gondii, and possibly the roundworm S. stercoralis) and intracellular parasites (including the enteric coccidia, hemoflagellates, and fungi). Both in the Caribbean and elsewhere, the endogenous parasites (particularly P. carinii and T. gondii) are the most troublesome for AIDS patients, partly because they are likely to be transmitted and establish a benign immunoregulated presence early in the subject's life. Indeed, health management programs for AIDS patients often routinely include P. carinii prophylaxis, since nearly all such patients who survive long enough are expected to experience an episode of acute P. carinii infection. In contrast, there is no known epidemiologic association between AIDS and strongyloidiasis in the Caribbean, and the prevalence there of potentially opportunistic hemoflagellates such as Leishmania spp. and Trypanosoma cruzi is relatively low.

Since identification of the acquired immune deficiency syndrome (AIDS) as a novel disorder in 1981, HIV infections have claimed the lives of more than 3,000 individuals in the Caribbean area (1). Impaired cellular immunity, related to the affinity of HIV for cells bearing the CD4 antigen, is the immunologic hallmark of AIDS. (The CD4 molecule is a surface feature of all helper T (T4) lymphocytes but is also found on the surfaces of some cells of the monocyte-macrophage series (10%–20%) and on a few B lymphocytes (<5%) and glial cells.) Cellular destruction may result directly from viral replication, or immunocytotoxic events may contribute to cell death.

In addition to a wide range of constitutional illnesses, AIDS predisposes individuals to several opportunistic parasitic infections, particularly pneumocystosis and cerebral toxoplasmosis. Other definite opportunists include human intestinal coccidia, and microsporidia have recently been shown to exhibit significant enteric pathogenicity in immunodepressed individuals (2, 3). In contrast, extracellular protozoan and helminthic infections are apparently not opportunistic in AIDS patients.

This review seeks to highlight the regional Caribbean significance of major parasitic infections implicated in AIDS. Our aim in providing this information is to encourage both laboratory diagnosti-

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cians and clinicians to become more aware of opportunistic parasites and the particular problems they cause in immunocompromised patients, and to familiarize themselves with appropriate diagnostic techniques and their clinical relevance.

SPECIFIC PARASITES

**Pneumocystis carinii**

Phylogenetically related to fungi but considered a protozoan because of its life-cycle and susceptibility to antiprotozoal drugs, *P. carinii* has a worldwide distribution in the lungs of humans and animals but usually causes no respiratory problems. Infection, through inhalation of cysts, apparently occurs early in life; some studies have shown serologic evidence of exposure by age four in more than 60% of the children tested (4). Alveolar macrophages and T<sub>H</sub> cells are thought to be important in restricting the parasite to a dormant or controlled existence in the body, and it is only when the host's immune system is "compromised" that clinical infection ensues.

*P. carinii* pneumonia is the opportunistic infection most commonly found in the United States' AIDS patients, occurring at least once in up to 80% of the victims (5). The infection results in degeneration of alveolar cells, followed by infiltration of the spaces by a foamy ground substance containing trophozoites and cysts. Oxygen transport across the alveolar-capillary space is impaired, and the patient suffers progressive dyspnea.

Diagnosis of *P. carinii* infection must be based on demonstration of organisms in lung material. The cysts measure 5–12 μm across and contain eight small sporozoites. Prior to the AIDS pandemic, the recommended diagnostic procedure was open-lung biopsy. However, less invasive procedures can be used when the presence of relatively large numbers of cysts is expected. Specifically, a combination of transbronchial biopsy and bronchoalveolar lavage is considered 100% sensitive (6). Sputum specimens are not normally acceptable for recovery of organisms. The stain of choice is methenamine silver, which stains the cyst wall. Recent success has been reported using sensitive immunofluorescent techniques, but these are not yet available commercially.

In the Caribbean, *P. carinii* pneumonitis has been encountered among AIDS patients in both Jamaica (J. F. Lindo, personal communication) and Trinidad (C. Whyte-Alleng, personal communication). Given the high recognition rate of this infection among persons with AIDS worldwide, more cases are expected in the region.

**Toxoplasma gondii**

Exposure to the coccidian *T. gondii* also occurs early in life. *T. gondii* infections are zoonotic. The infections have a cosmopolitan distribution; and while they can be transmitted transplacentally when a woman has a primary infection, they are typically transmitted to people by ingestion of oocysts in food, water, or dust contaminated with cat feces, or through ingestion of tissue cysts contained in raw or undercooked meat. Serologic testing indicates a high prevalence of infection (25%–90%) among farm animals and pets in the Caribbean (7). Similarly, a high level of exposure appears to exist among humans, with up to 57% seropositivity reported from Jamaica (8, 9), Cuba (10), the Leeward Islands, and Suriname (7). Human congenital infections in the Caribbean are associated with severe pathology (8, 11, 12) most often resulting in chorioretinitis.

Infection of normal individuals with cysts results in dissemination of tachyzoite stages to intracellular sites in the skeletal muscles and brain. These form
inactive bradyzoites, which apparently persist indefinitely in these tissues. A role for Th lymphocytes in the containment of latent T. gondii infections has been demonstrated in a mouse model (5).

Cerebral toxoplasmosis resulting from reactivation of latent infections is the most common opportunistic infection of the central nervous system in AIDS patients. HIV invasion of CD4+ glial cells is likely to result in release of viable zoites, which in turn reinvade nervous tissues. In the Caribbean, only one case of AIDS-related cranial toxoplasmosis (from Trinidad) had been reported up to 1995 (13); but approximately 30% of the AIDS cases possessing T. gondii antibodies may be expected to develop encephalitis in endemic zones (5).

The prognosis associated with Toxoplasma encephalitis is poor. One study of 67 patients (14) found a median survival period of 4 months following chemotherapy, while half of those discharged from the hospital suffered clinical relapse.

For diagnosis, serologic techniques are recommended. In an immunodeficient patient, a presumptive diagnosis of toxoplasmosis may be made if there is an elevated antibody (IgM) titer in the presence of neurologic symptoms. The indirect fluorescent antibody (IFA) technique is the most common serodiagnostic procedure currently in use, although ELISA will supersede it in the near future.

Cryptosporidium spp.

This coccidian, long known to cause diarrhea in calves and other animals, has emerged as an important diarrheal agent in AIDS cases and in malarious children of developing countries (15). Cryptosporidium is widely distributed, with a prevalence of about 2% in persons with normal immune capabilities (16). Infections are endemic in the Caribbean (17, 18), usually being found in otherwise healthy children with moderately severe diarrhea.

Cryptosporidium is typically located within a parasitophorous vacuole close to the microvillus surface of intestinal cells. Impairment of T cell function results in loss of ability to eradicate the normally self-limiting infection (19). The cholera-like symptoms manifested in immunodeficient patients are extremely difficult to treat and impossible to cure. In addition, respiratory complications associated with cryptosporidiosis have been reported in AIDS patients (20). AIDS-related cryptosporidiosis has been reported among patients in Jamaica (J. F. Lindo, personal communication) and also in Trinidad and Tobago (17).

Cryptosporidium infections are most safely detected in formalin-fixed stool or sputum following concentration. Oocysts are 4–6 μm in diameter and contain four sporozoites. Use of monoclonal antibodies (immunofluorescence) for the direct detection of cysts in fecal specimens has proven more sensitive than routine acid-fast methods that occasionally do not stain all the oocysts (21).

Isospora belli

Infections with I. belli are widespread in Africa, but well-defined endemic foci have also been identified in South America. Like Cryptosporidium, this coccidian develops within the epithelial cells of the small intestine. Infections normally result in a transient diarrhea. However, profuse diarrhea and anorexia have been described in AIDS patients (22); in such cases it is thought that impairment of T cell-mediated immunity results in reduced ability to eradicate parasite stages from the intestine.

I. belli displays a high prevalence among AIDS patients in Haiti (23) and has also been recorded in a Jamaican patient suffering from a tropical spastic paraparesis.
syndrome related to presence of the human T cell lymphotropic virus type I (HTLV-I) (author's unpublished data).

Because only small numbers of oocysts are commonly present in stools, concentration techniques are recommended for diagnosing the infection, even in AIDS patients. The oocyst of I. belli is large, about 30 μm × 12 μm, and contains a single spherical zygote. Maturation continues outside the host until the oocyst develops two sporocysts, each containing four sporozoites. It is then infective through ingestion.

**Cyclospora cayetanensis**

Similar to Cryptosporidium and Isospora, this enteric coccidian causes a self-limiting diarrheal syndrome in immunologically competent patients worldwide. The organism was first reported in 1986 as a "new intestinal pathogen" in four otherwise healthy visitors to Haiti and Mexico (24). However, four years later Cyclospora was given a potentially opportunistic status, having been detected in eight patients with diarrhea, four of whom had AIDS (25).

Infections are likely to be acquired through accidental ingestion of oocysts, possibly in water (26), or through consumption of tissue cysts in raw or undercooked meat (25).

Cyclosporiasis may be detected microscopically in fecal smears or duodenal aspirates. The spherical, unsporulated oocysts are 8–10 μm in diameter (roughly twice the diameter of Cryptosporidium oocysts but only half that of Isospora oocysts). Most stain acid-fast with Ziehl-Neelsen's stain, but some remain unstained as wrinkled spheres (27). Mature oocysts have two sporocysts, each containing two sporozoites.

Our understanding of C. cayetanensis infections is still incomplete, but increased awareness coupled with careful microscopic diagnosis should provide additional information about their epidemiologic and clinical aspects.

**Histoplasma capsulatum**

*H. capsulatum* is a fungus with moderate levels of endemicity in the Caribbean and other parts of the Americas (28, 29). Spores are typically found in soil containing the composted manure of birds (including fowl) and bats, which are among its wide array of natural animal hosts. Humans are usually infected by inhaling the spores. Benign pulmonary infections are sometimes seen among speleologists (28, 30), hence the common name "cave disease." However, disseminated histoplasmosis (which in some respects resembles visceral leishmaniasis) is known to be associated with host immune defense deficiency. Cutaneous infections have been reported in 11 of 18 AIDS patients attending the General Hospital in Port of Spain, Trinidad and Tobago (31).

Diagnosis of disseminated Histoplasma infection may be made by examining a patient's sputum, excised lymph glands, ulcer base, bone marrow, or peripheral blood. Fungal cells appear within large mononuclear cells (occasionally polymorphs) in the buffy coat as oval masses measuring 2–3 × 3–4 μm.

**Cryptococcus neoformans**

Cryptococcosis is also a fungal infection. It involves a primary focus in the lung with a characteristic spread to the meninges and viscera that is greatly accelerated in immunodeficient hosts. Its distribution is worldwide, with many animal reservoirs.

*C. neoformans* grows quickly in accumulations of pigeon droppings, and inhalation of spores is probably the usual route of human infection. Patients nor-
mally seek medical care as a result of blurred vision or mental disturbances. Disseminated infection was first reported in an AIDS patient in Trinidad and Tobago (23), but additional AIDS-related infections have emerged in Puerto Rico (32).

A diagnosis of cryptococcosis is strongly suggested by a finding of yeast cells in a preparation of sputum, pus, or cerebrospinal fluid stained with India ink. The cells range from 15 μm to 45 μm in diameter and contain a single mass of centrally located protoplasm 5–15 μm across. Culture on glucose agar or Sabouraud's medium will distinguish nonpathogenic forms.

**Strongyloides stercoralis**

*S. stercoralis* is a small nematode that produces a chronic, usually subclinical, enteric infection in humans. Although disseminated strongyloidiasis was originally included in the U. S. Centers for Disease Control and Prevention's classification of AIDS-related infections in 1986, such infection is no longer listed as an index diagnosis for AIDS.

Difficulties associated with detection of strongyloidiasis, even in compromised hosts, have resulted in confusion regarding the disease's relevance in HIV-infected patients. Several independent studies have indicated that agar plate culture detects *S. stercoralis* infections with significantly higher sensitivity (87%–100%) than other parasitologic methods (33). The most convenient and widely used immunodiagnostic technique for detecting strongyloidiasis in non-AIDS patients is ELISA (34). A modification involving preincubation of sera with filarial antigen recently produced a sensitivity of 85%–100% and a specificity of 97% in a Jamaican population (35).

Only a few well-documented cases of AIDS with disseminated strongyloidiasis have been reported, and there is an apparent lack of epidemiologic association between the two diseases (36, 37). Among other things, work on Martinique found no association between *S. stercoralis* infections and AIDS (38). In contrast, a strong epidemiologic association has been reported for severe strongyloidiasis and potentially immunosuppressive HTLV-I infections in Jamaica (39).

Eosinophils and IgE antibodies appear to be important in the regulation of strongyloidiasis (39, 40), but their activity is in turn regulated by lymphokines produced by T cells that are presumably vulnerable to HIV. Even so, it appears that disseminated *S. stercoralis* infection is unlikely to feature prominently in AIDS.

**Sarcoptes scabiei**

The itch mite, *S. scabiei*, has a cosmopolitan distribution with discrete strains parasitizing humans and domestic animals. Adult mites excavate serpiginous burrows in the upper epidermis, and a delayed (type IV) hypersensitivity reaction to dead mites and their feces causes intense itching. Scratching may result in bleeding and scab formation, and secondary bacterial infection often follows. The disease is diagnosed by finding adult mites or their eggs, usually at the distal parts of fresh burrows in the skin. Edermal scrapings may be cleared by adding a few drops of 20% aqueous potassium hydroxide prior to microscopic examination.

*S. scabiei* infections appear to be exacerbated in persons whose immunity is compromised by any means, but a generalized dermatitis, characterized by extensive scaling and crusting, has been reported in patients with HTLV-I seropositivity and adult T cell leukemia (ATL) (41), and also in patients with AIDS (42, 43). Cases of severe scabies infection and HIV have been recognized in Jamaica (L. LaGrenade, personal communication). A strong association between infective der-
matitis and HTLV-I has also been reported from Jamaica (44) in cases having increased CD4:CD8 ratios with elevated total CD4 counts.

*Leishmania* spp.

Visceral leishmaniasis is endemic in Central and South America. The responsible organisms live in mononuclear phagocytes of the host and are detected through microscopic observation as Leishman-Donovan bodies (amastigotes) in affected tissues. ELISA provides sensitive immunodiagnosis, but problems with specificity still exist in areas where other hemoflagellate infections occur.

Elimination of the infection requires activation of T lymphocytes and macrophages. It is therefore not surprising that opportunistic leishmanial infections of this type have been recognized in HIV-positive patients in Europe and South America (45). In the Caribbean, however, only historical reports exist of symptoms associated with "leishmaniose viscerale" in non-AIDS patients from Guadeloupe and Martinique (45, 46).

Cutaneous leishmanial infections, besides being endemic in Central and South America, are also endemic in the Dominican Republic, French Antilles, and Trinidad (45). A case of disseminated cutaneous leishmaniasis (probably caused by *L. braziliensis*) has been reported in a Brazilian AIDS patient (45), and it seems likely that the combination of T cell and macrophage dysfunction seen in HIV-associated visceral infections is also important in cutaneous infections. Due to their low level of endemicity in the Caribbean islands, however, leishmanial infections are unlikely to pose a major risk to AIDS patients in the region.

*Trypanosoma cruzi*

There is serologic evidence of exposure to *T. cruzi* in Jamaica, Curacao, and Trinidadd, but this has not been clinically correlated (47). On the other hand, *T. cruzi* is associated with significant morbidity and mortality in Central and South America, where infections have been associated with acute CNS symptoms in AIDS patients. Impairment of the primary role played by activated macrophages in stemming infection, particularly in the acute phase, is likely to be crucial here.

**DISCUSSION**

In the Caribbean, as elsewhere, AIDS-related opportunistic parasites are restricted to those species that can exploit the specific immune defect associated with AIDS and are thus able to proliferate and cause problems. Within this context, HIV-infected individuals are susceptible to parasites that fall roughly into two categories: immune-regulated "endogenous" parasites such as *P. carinii*, *T. gondii*, and possibly *S. stercoralis*; and intracellular species, particularly those that invade macrophages and whose elimination requires T cells or T cell-macrophage cooperation, such as enteric coccidia, some hemoflagellates, and fungi such as *Cryptococcus neoformans* and *Histoplasma capsulatum*.

There are comparatively few published reports of AIDS-related parasitic infections in the Caribbean, but with increased awareness of opportunistic organisms more cases are likely to be diagnosed in the future. It should also be noted that there is a comparatively low prevalence in the Caribbean islands of potentially opportunistic hemoflagellates such as *Leishmania* spp. and *Trypanosoma cruzi*.

Undoubtedly, the most troublesome opportunistic parasites are the endogenous ones. They are likely to be encountered early in life, adding parasitologic concerns to the other reasons why avoidance of exposure to HIV is paramount. In the case of HIV-infected individuals
with depressed CD4 counts, health management programs often incorporate prophylaxis for *Pneumocystis carinii* pneumonia—since nearly all AIDS patients are expected to have an episode of it if they survive long enough. Chemoprophylaxis involving pyrimethamine-sulfadoxine, trimethoprim-sulfamethoxazole, or inhaled pentamidine has been used with considerable success in the United States (48).

As the AIDS pandemic progresses without prospect for a vaccine in the foreseeable future, much less a cure, the incidence of primarily endogenous opportunistic infections is likely to feature more prominently among AIDS patients in the Caribbean region.

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**REFERENCES**


33. Conway DJ, Lindo JF, Robinson RD, Bundy DAP. New options to diagnose and control Strongyloides stercoralis [Submitted for publication].
46. Courmes E, Escudie A, Fauran P, Monnerville A. Premier cas autochtone de
Regional Disaster Documentation Center

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