INTRODUCTION

Since the first AIDS cases were described, a high prevalence of gastrointestinal alterations has been reported, especially diarrhea associated with parasitosis.

This became more evident when the appearance of a syndrome named “Slim Disease”, characterized by an intense weight loss accompanied by chronic diarrhea, prolonged fever and diffuse muscle weakness, was observed in Africa, especially in Uganda. \(^1\) Studies conducted in Zaire and Uganda have shown the presence of some pathogenic agents responsible for the “Slim Disease”, such as Isospora, Cryptosporidium, Salmonella, Shigella and Campylobacter species, amounting to a prevalence of 60 to 80\%. \(^2\) “Slim Disease” has been observed in advanced stages of HIV infection. The expression “Wasting Syndrome” was adopted in substitution by WHO in 1988 on the basis of criteria laid down by the CDC. \(^3\)

Thus, where as infections in the gastrointestinal tract play a critical role in AIDS pathogenesis and diarrheic diseases assume a prominent role, reaching a rate of up to 50% in developed countries, in developing countries there have been reports of incidence of up to 95%, as in Haiti and...
the African continent. Amongst the causes of diarrhea in developing countries, those of a parasitic origin are prominent in patients with AIDS.

Opportunistic infections caused by intestinal parasites also vary according to the geographical area and the endemic levels in each location.

The progressive decline of immunological and mucous defense mechanisms predisposes patients to early, intermediary and late gastrointestinal manifestations of HIV infection. At later stages of the disease, the alterations in non-specific defense mechanisms in the production of Ig A and the reduction in local immune cell response also progress, thus increasing the susceptibility to a number of intestinal opportunistic pathogens, among which Cryptosporidium parvum, Isospora belli and Microsporidia species are the most prominent.

After the emergence of AIDS, these parasites, until then known solely in veterinary medicine, were no longer considered as commensal organisms and are nowadays recognized as opportunistic pathogens common to these patients. Infections by these agents constitute a major secondary aggravating factor of the disease, often responsible for worsening the general health conditions, due to manifestations of diarrhea which are difficult to control, sometimes resulting in the death of the patient.

**CRYPTOSPORIDIASIS**

Cryptosporidiasis, a disease caused by an intracellular protozoan named Cryptosporidium sp, was described for the first time in 1907 by Tyzzer. This parasite was considered a commensal up to 1975, when it was identified as the cause of diarrhea in animals.

The first manifestation of cryptosporidiasis was reported by Nine et al. in 1976, and the disease became a major concern when the notification of the first 21 patients was given, 14 of whom died of chronic diarrhea caused by Cryptosporidium sp infection.

It is worth noting that outbreaks of epidemic linked to contaminated water are of extreme importance for the dissemination of this parasite such as the 1993 Milwaukee (USA) cryptosporidiosis outbreak, in which 403,000 human cases were reported, thereby becoming a relevant public health concern. After this outbreak, it was recommended that immunocompromised patients should be extremely careful with water, foodstuffs and contact with animals.

Cryptosporidiasis is distributed over all continents. In Haiti and the African continent the prevalence is 50%, while in the USA it ranges from 3 to 4%.

In Brazil, due to the continental size of the country, the rates of incidence vary with the location. In the city of São Paulo, for instance, reports have referred to levels around 12.1 to 24.44%. However, the latest epidemiological report on Brazil, dated February 1998, shows a cryptosporidiasis rate of only 3.5%.

Cryptosporidiasis in AIDS patients usually causes chronic, bulky and intermittent diarrhea, with liquid non-bloody stools, accompanied by pain and abdominal colic, and a noticeable loss of weight can be observed.

Asymptomatic cases are rarely described, occurring mostly in developing countries with patients showing milder immunodeficiency.

Extraintestinal manifestations have been clearly described in the literature, especially in the gall bladder, biliary ducts and pancreas, leading to conditions such as papillary stenosis, sclerosing cholangitis and acalculous cholecystitis. The respiratory tract can also be affected with manifestations of chronic bronchitis.

The intensity and duration of diarrhea in cryptosporidiosis cases is closely associated with the CD4+ T cell counts. This is well demonstrated in a classic study on HIV-infected patients with CD4+ cell counts higher than 180/ mm$^3$ who displayed clinical healing over a period of four weeks, while 87% of the patients presenting more severe immunosuppression, with CD4+ counts lower than 140/ mm$^3$, presented persistent and hard-to-control diarrhea.

Laboratory diagnosis of cryptosporidiosis is easy to accomplish, using special staining techniques such as the Kinyoun (modified Ziehl...
Neelsen) and auramine-rhodamine methods, via the detection of reddish-stained Cryptosporidium oocysts. More sophisticated diagnostic techniques using monoclonal antibodies are already available, such as ELISA and immunofluorescence, with high sensitivity and specificity. The treatment is controversial, with rehydration via an appropriate liquid balance and the maintenance of the patient's nutritional condition being recommended. There should be careful monitoring and administration of antidiarrheic drugs when needed.

Several treatments are available but they have not shown significant clinical efficiency. Studies have been conducted with hyperimmune bovine colostrum, letrazuril and diclazuril (veterinary medicine drugs), spiramicyn and more recently azithromicyn, paromomycin, octreotide and roxithromycin.

**ISOSPORIASIS**

*Isospora belli* is a coccidium described for the first time in 1915 by Woodcock and later by Wenyon in 1923. It is found in tropical and subtropical areas and is endemic in South America, Africa and in Southern Asia, with an occurrence rate of 15% in Haiti, 0.2% in the USA and 1.8% in Brazil.

Higher rates of isosporiasis in Brazil have been reported in AIDS patients living in Santos and in São Paulo, with a prevalence of 9.9% and 6.67%, respectively. The lower prevalence of isosporiasis may be ascribed to the secondary prophylaxis for pneumocystosis through administration of sulfamethoxazole-trimethoprim during the course of AIDS, since *Isospora belli* is sensitive to this therapy.

The diarrheic condition is also noteworthy and is accompanied by fever, intestinal colic, anorexia, abdominal pain, loss of weight and peripheral eosinophilia.

Isosporiasis can also show extraintestinal dissemination features, affecting the mesenteric, periaortic, mediastinal and tracheobronchial lymph nodes. It may also be related to biliary disease, causing manifestations of acalculous cholecystitis.

*Isospora belli* differs morphologically from *Cryptosporidium* sp not only because of its intrinsic morphology (elliptical oocyst measuring 22 x 15 μm in diameter, containing two sporocysts with four sporozoites), but also for the intracellular location in the absorptive cell, while *Cryptosporidium* is restricted to the brush borders, immediately under the apical membrane of absorptive cells.

Laboratory diagnosis is carried out in the same way as for *Cryptosporidium parvum*, using the Kinyoun and auramine-rhodamine techniques, although common processes such as Faust's are often enough for the diagnosis. The special coloration thus becomes a further diagnostic element for finding the parasite.

The therapeutical recommendation for isosporiasis is the administration of sulfamethoxazole-trimethoprim for 10 days, followed by prophylaxis for a further three weeks. This leads to a reduction in the number of discharges and the recovery of body weight. In recurrent situations or in non-responding patients it is necessary to administer other drugs such as pyrimethamine, in isolation or in association with sulfadiazine, roxithromycin and metronidazole. Drugs such as tetracycline, ampicillin, nitrofurantoin, quinacrine and furazolidone have already been used but showed no therapeutic success.

**MICROSPORIDIASIS**

The third major group of intestinal pathogens to be reported are the microsporidia, which are strictly intracellular protozoa, spore-producing and with great variety of genera and species. They have widespread distribution and over 400 cases of patients with co-infection of microsporidia and HIV have been reported. The major etiologic agent is *Enterocytozoon bieneusi*.

The first description of intestinal microsporidiasis in an HIV-positive patient occurred in France. The first description of this condition in Brazil dates back to 1993, with cases having occurring in Rio de Janeiro, São Paulo and Ceará.

The world prevalence of intestinal microsporidiasis ranges between 7 and 50%. In Rio de Janeiro a recent study applying the direct
A technique for detection of microsporidian spores in the stool samples of 140 HIV-positive patients showed that the rate of prevalence of intestinal microsporidiosis was 17.86%. The fact that these cases have only recently appeared can be explained by the diagnostic difficulty, as electronic microscopy is required for confirmation of the presence of the parasite. In contrast, in the city of São Paulo only 1.3% of microsporidian spores were shown up in patients with AIDS and chronic diarrhoea via the modified trichrome staining method.

Optical microscopy methods, such as the chromotrope method, were then proposed whereby spores would appear as oval-shaped and stained pink or pale red. This technique has been improved and named Gram-chromotrope. Fecal sample smears are stained in Gram's stain, followed by a chromotrope solution.

Chronic diarrhea and/or biliary disease manifestations in HIV-infected individuals with CD4+ T cells of between 50 and 100/μL may suggest microsporidiosis. Transmission is unknown to date, but there have been reports of congenital transmission and via inhalation of airborne spores.

Regarding treatment, albendazole has been the most promising drug for handling intestinal microsporidiosis.

**GIARDIASIS AND AMEBIASIS**

The protozoans *Giardia lamblia* and *Entamoeba histolytica* are important causes of acute diarrhea in homosexual males, even for those that are not HIV-positive. Together with *Campylobacter, Salmonella, Shigella* and *Yersinia* they cause high frequencies of enteritis, colitis and proctitis.

Statistical data found in the literature are rather divergent, but the incidence of these protozoans amongst the homosexual populations of large cities, such as New York, Los Angeles, San Francisco and Toronto is quite high.

The prevalence of *Entamoeba histolytica* in HIV-negative homosexual patients in the USA ranges between 21 and 32%, and is around 12% in the United Kingdom.

A study performed in Los Angeles with 100 HIV-positive patients, mostly homosexuals, showed a prevalence rate of 55% for giardiasis and 3% for amoebiasis.

In France, studies focused upon the prevalence of intestinal parasitosis showed a high frequency of protozoan species in AIDS patients, and the rates of *Giardia lamblia* and *Entamoeba histolytica* were 5.8% and 2%, respectively.

Previous studies demonstrated that giardiasis incidence does not differ amongst HIV-positive and negative patient populations.

Infection with *Giardia lamblia* and HIV amongst homosexual males is correlated with enteritis or enterocolitis, but no histological study of the colonic mucosa has yet been carried out.

In Brazil, examination of 771 fecal samples from AIDS patients living in São Paulo, performed under the program for the control and prevention of AIDS, have shown rates of 5.18% and 8.49% of amebiasis and giardiasis, respectively. In a recent study in the city of São Paulo analyzing patients with more severe immunodeficiency, *E. histolytica* was not observed but *G. lamblia* cysts were seen in about 27% of the examined patients.

Despite this high prevalence, classical protozoa such as *Giardia Lamblia* and *Entamoeba histolytica* are less frequent as causes of severe illnesses in HIV-infected patients, when compared with *Microsporidia, Isospora belli* and *Cryptosporidium parvum* and they are not considered as opportunistic infections in AIDS.

Amebiasis may present with invasive characteristics, but this has rarely been reported in the literature.

More recently, in Recife, a study was conducted to evaluate invasive amebiasis in AIDS patients. Seventy four patients were examined, out of which 54 had diarrhea but *Entamoeba histolytica* was found in only one patient (1.3%) and practically an absence of invasive amoebiasis.

**STRONGYLOIDIASIS**

Among the helminths in association with AIDS, there is no doubt that the most important pathogen is *Strongyloides stercoralis*, which was
first described in 1876 by Normand, after necropsy of patients with diarrhea in from Cochin-China, then an autonomous region of China.67

This geohelminth presents its major effects in immunodepressed patients, leading to the dissemination of the infection. This occurs in transplanted patients, individuals presenting malnutrition and patients submitted to prolonged use of corticosteroids, suffering from leukemia, lymphomas or AIDS.68,69

Despite the possibility of dissemination of this helminth in HIV-positive patients, only 14 cases had been reported by 1994 in the international literature.70

A case of massive infection by *Strongyloides stercoralis* in AIDS patients in São Paulo was recently reported, presenting the nematode even in sputum samples.71

The clinical syndrome of disseminated strongyloidiasis is characterized by gastrointestinal signs and symptoms, such as nausea, vomiting, meteorism, anorexia and diarrhea, alternating with periods of intestinal constipation and secondary infections. Respiratory symptoms such as dyspnea, hemoptysis, coughing, or manifestations of asthma and even extensive pneumonia, may be observed. At the same time, the patient can present fever, cachexia and loss of weight.72,73

In immunosuppressed patients, self-infestation is speeded up and a large number of larvae are released, causing the dissemination of the infection.74

In Brazil, the prevalence of strongyloidiasis in HIV-positive patients is around 4 to 15%, in comparison with 1.4% in the general population.15,17,69

Laboratory diagnosis is based upon the Baerman-Moraes or Rugai-Mattos-Brisola methods, presenting as their basic principle the thermo and hydrotropism of *Strongyloides stercoralis* larvae seen in stool samples.67

*Strongyloides stercoralis* larvae may also be detected in aspirated duodenal material, sputum, broncho-alveolar lavage, cervicovaginal cytology, cerebrospinal fluid and gastric cytology.74

Generally, the search for *Strongyloides stercoralis*, even in isolated samples, shows a positivity of 30% in immunocompromised individuals with AIDS. When three or more samples are taken, this positivity reaches levels as high as 80%.67

Thiabendazole is considered the drug of choice for treating strongyloidiasis, in immunosuppressed individuals. The rates of eradication by this anti-helminth drug can reach levels as high as 90%.57,68,72 Other chemotherapy agents that may be used include albendazole and cambendazole.

In *Strongyloides stercoralis* hyperinfection cases, treatment with thiabendazole may be used for prolonged periods, followed by maintenance doses. Often, eradication is difficult.70,71 Another option in these cases is the administration of ivermectin, a drug used for onchocerciasis, with healing rates around 94%.70,75,76 This drug is not yet available in Brazil.

**OTHER PARASITES**

Other helminths such as *Ascaris lumbricoides* (3.52%), *Trichiuris trichiura* (4.14%), *Ancylostomidae* (2.69%), *Enterobius vermicularis* (0.21%), *Schistosoma mansoni* (1.66%), *Taenia sp* (0.21%) and *Hymenolepis nana* (10.41%) have shown lesser frequency and importance in AIDS patients.15

Several other intestinal parasitoses may lead to aggravation and/or dissemination of the course of AIDS. Protozoa such as *Cyclospora sp* and *Blastocystis hominis* have arisen, which may also cause major diarrhea manifestations.

*Blastocystis hominis* is a potentially pathogenic parasite, more predominant in male homosexuals than in other population groups, and its occurrence is not higher in individuals suffering from digestive disturbances.77 It has been isolated in human feces with a frequency ranging from 1 to 60% in individuals from different parts of the world and exposure to contaminated water contributes to the increase of this parasitosis.78

The association of *Blastocystis hominis* with immunodepression has been well-documented, chiefly in diabetic and leukemic patients.79,80 In AIDS, *Blastocystis hominis* leads to chronic diarrhea manifestations; six cases in Bahia (Brazil)
were recently reported with parasite eradication in the stool samples after specific treatment.\textsuperscript{81,82} 

Blastocystis infection is common in immunocompromised hosts and it may be diagnosed through conventional techniques such as the Lutz and Faust methods. There are reports in the literature that show trichrome stains and Ficol concentrations as alternatives for finding this parasite.\textsuperscript{84} 

There is some controversy about the appropriateness of treating this enteroparasitosis. When treatment is chosen, metronidazole is used.\textsuperscript{85} 

Cyclospora \textit{cayatenensis} was initially isolated in 1870 by Eimer. The first report on its association with AIDS dates back to March 1989, in a male patient with chronic diarrhea.\textsuperscript{86} 

Studies on the prevalence of cyclosporiasis show very low rates, not higher than 1% in developed countries.\textsuperscript{86,87} 

Outbreaks of cyclosporiasis due to the consumption of raspberries imported from Guatemala occurred recently: 1465 cases were reported from 20 states of the USA.\textsuperscript{88} Other outbreaks were reported in Virginia (USA), due to contamination of fresh basil, causing gastrointestinal disease.\textsuperscript{89} 

The diagnosis of infection by \textit{Cyclospora cayatenensis} is based upon the detection of oocysts in fecal samples, via optical microscopy. \textit{Cyclospora cayatenensis} differs from Cryptosporidium in its large size.\textsuperscript{30} Due to the morphological similarities and lack of knowledge on how to differentiate between these two species, diagnosis of cyclosporiasis is seldom accomplished.\textsuperscript{33} It is essential to determine the sporulation of Cyclospora, which may be done using 2.5% potassium dichromate. 

The low frequency of this protozoan may once again be explained by the use of sulfamethoxazole-trimethoprim administration as a prophylactic treatment against \textit{Pneumocystis carinii} in AIDS patients presenting CD4+ cell counts lower than 200/\text{mm}^3.\textsuperscript{91,92} 

**CONCLUSION**

It can be noted that parasitosis presents a very significant interface with AIDS, and this has been the object of studies by many authors. Investigations on the etiology of diarrhea in HIV-infected patients indicate parasitosis as the cause in up to 40% of patients.
44. Forthall D, Guest SS. Isospora belli enteritis in three homosexual men.


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Sources of funding: Not declared
Conflict of interest: Not declared
Last received: 19 March 1999
Accepted: 7 April 1999
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RESUMO

OBJETIVO: Relatar a importância das parasitoses intestinais em pacientes com AIDS, mostrando dados relevantes na literatura médica, com enfoque em especial, abordando a epidemiologia, diagnóstico e tratamento das enteroparasitoses, principalmente da criptosporidíase, isosporíase, microsporidíase e estrongiloidíase. TIPO DE ESTUDO: Revisão narrativa.

PALAVRAS-CHAVE: HIV. AIDS. Parasitoses.