

# Human Isosporiasis in an AIDS Patient — Report of First Case in Malaysia

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## Summary

An AIDS patient with multiple opportunistic infections (*Candida*, *Pneumocystis carinii* and *Isospora belli*) was identified at the University Hospital, Kuala Lumpur. The patient presented with profuse diarrhoea associated with lethargy, anorexia and weight loss. Routine stool examination showed *Isospora belli* oocysts. The infection responded to treatment with trimethoprim-sulfamethoxazole but relapse occurred 8 weeks later. This represents the first documented case of isosporiasis to occur in an AIDS patient in Malaysia.

**Key words:** AIDS, *Isospora belli*, Isosporiasis.

## Introduction

Human isosporiasis, caused by an enteric pathogen, *Isospora belli*, has gained worldwide recognition since the advent of the Acquired Immunodeficiency Syndrome (AIDS) epidemic. This opportunistic parasite was first described by Woodcock and Wenyon in 1915, and the first clinical description of the disease was by Gana in 1966<sup>1</sup>. The spectrum of clinical illness ranges from self-limiting enteritis to chronic diarrhoea. Severe and chronic form of the infection began to be reported with increasing frequency among AIDS patients from 1980 onwards. The highest prevalence of *I. belli* was observed in a North American institution for medically-handicapped children and in immunosuppressed patients<sup>2</sup>. The prevalence of *I. belli* in AIDS patients in developing countries has been found to fluctuate from 3% to 18%<sup>3</sup>. In these countries, the 2 most isolated opportunistic parasites have been *I. belli* and *Cryptosporidium* species.

*I. belli* infection is believed to be a specific parasite of man, though occasionally it has been isolated from stools of dogs. Transmission is believed to be by the faecal oral route, among homosexual men by sexual intercourse or anal-oral sexual contact. Like *Cryptosporidium*, *Isospora* has been considered one of the etiological agents for traveller's diarrhoea.

This report documents the first case of human isosporiasis in an AIDS patient in Malaysia.

## Case Report

The patient, a 41 year old Malaysian male, was referred to the University Hospital, Kuala Lumpur, in mid-1992 with a history of fever, cough and marked weight loss. Six months prior to being seen at the clinic, he complained of having watery diarrhoea, 8 to 10 times a day sometimes lasting for a few days in each

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week. There was no abdominal pain or blood in the stools. He had loss of appetite and loss of weight (which was approximately 15 lbs in 6 months). On physical examination, he was found to have marked weight loss, looked ill and had a low grade fever. Examination of the respiratory system did not reveal any abnormality. All other systems were normal and there was no lymphadenopathy. Fundoscopy was normal. He was diagnosed as symptomatic HIV infection with isosporiasis as the first AIDS defining illness. Initially, he was put on anti-diarrhoeal drug loperamide 2 mg (imodium) 2 to 3 tablets daily, and the diarrhoea stopped. When the stool examination revealed *Isospora* species, he was given trimethoprim 80 mg and sulfamethoxazole 400 mg (cotrimoxazole) 2 tablets every 6 hours for 2 weeks. The diarrhoea stopped after 6 days on treatment. Three weeks after the treatment for isosporiasis, he still continued to have fever and cough. Examination of sputum using both direct staining methods (modified Gomori's methenamine-silver nitrate and Periodic Acid Schiff stains) and indirect immunofluorescence test (Monofluo Kit *Pneumocystis carinii*, Diagnostic Pasteur) showed the presence of *P. carinii* cysts. He was continued on high doses of cotrimoxazole (4 tablets 6 hourly) for another 2 weeks. He also developed oral candidiasis, which was cleared with oral ketoconazole 200 mg twice daily. The CD4+ T lymphocyte counts were 102/uL and the CD4+/CD8+ ratio was 0.06. All the other biochemical tests were normal. His full blood count and haemoglobin were normal. Currently he is on prophylaxis against *P. carinii* pneumonia (PCP) with oral cotrimoxazole 2 tablets 3 times a week and the patient is on regular follow-up. He is doing well and has put on weight and is back to work.

### Parasitological examination

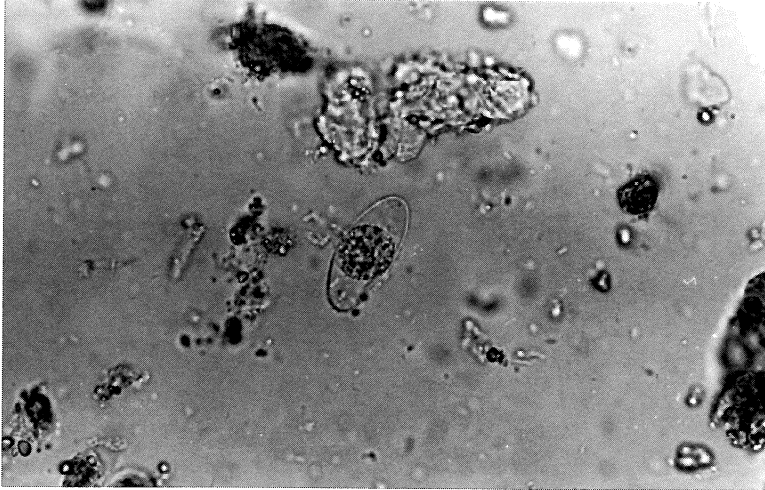
The patient's stool was collected every week for 3 weeks. Stools appeared mucoid without any trace of blood or leucocytes and was steatorrheic. The formol ether sedimentation technique was utilised. One gram of faeces was taken and added to 10 ml of 10% formalin and a suspension made. The sample was filtered through a gauze filter into a centrifuge tube. About 3 ml of ether was added to the suspension and mixed well by shaking for 1 minute. It was then placed inside the centrifuge and spun for 2 mins at a speed of 2,500 rpm. Five samples were made and the sediment was observed under 10x and 40x objectives. A drop of iodine was placed onto the specimen. Smears were also made on microscopic slides, air-dried and stained by modified Ziehl Neelson stain.

Typical ellipsoidal type oocysts, both immature and mature, measuring 20 µm to 30 µm long and 10 µm to 19 µm with a smooth double layered hyaline wall and containing 1 or 2 sporoblasts were typically identified with reduced illumination (Figs 1a, 1b, 1c). On modified Ziehl Neelson stain, the organism was acid-fast. Mature oocysts showed typical ellipsoidal shape, measuring approximately 20 µm x 19 µm with sporocysts (Fig 1d). Characteristic Charcot-Leyden crystals were also observed in the stool. The patient's stool was re-examined after 8 weeks post-treatment and the stool was found to be positive for *Isospora* oocysts.

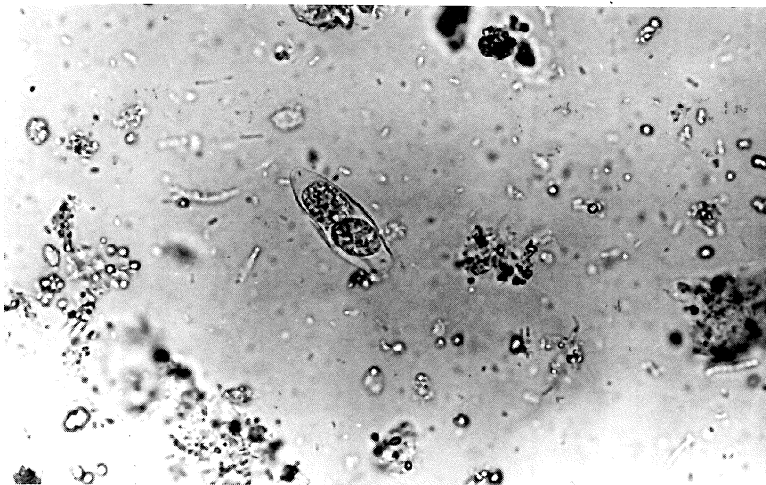
### Discussion

Coccidial infections (*Cryptosporidium* and *Isospora*) of the gastrointestinal tract cause an acute, self-limiting diarrhoeal illness in immunocompetent hosts. Chronic enteric infections with coccidial parasites have often been associated with immunodeficient states. *I. belli* has recently been recognised as an opportunistic protozoan pathogen in patients with AIDS. Isosporiasis is most common in tropical and subtropical climates and has been encountered in 15% of patients with AIDS in Haiti, less than 0.2% in AIDS patients in United States and between 3% to 18% in AIDS patients in developing countries<sup>4</sup>. The illness in an immunocompetent host is often self-limited, but serious, even fatal, diarrhoea may result. Loose stools, steatorrhea and colicky abdominal pain sometimes associated with fever and eosinophils are typical, though watery diarrhoea with severe fluid loss has been documented.

High rates of enteric protozoans are present in sexually active homosexual men, particularly those with underlying immunodeficiency states. Pitchenik *et al*<sup>5</sup>, reported 3 Haitian patients with altered immunity

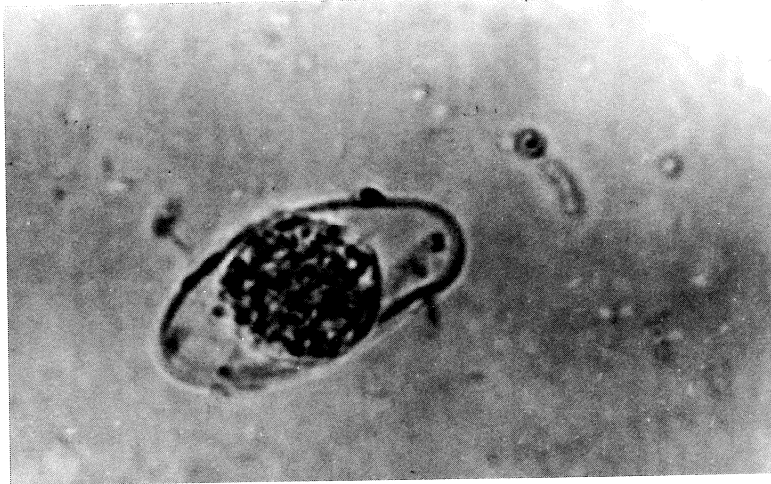


**Fig 1a: Immature oocyst of *Isospora belli* with zygote x 100.**



**Fig 1b: Immature oocyst of *Isospora belli* with 2 sporoblasts x 100.**

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**Fig 1c:** Immature oocyst of *Isospora belli* showing one sporoblast - Iodine stain x 400.



**Fig 1d:** Immature oocyst of *Isospora belli* showing one sporoblast - Acid fast stain x 400.

and chronic isosporiasis. Forthal and Guest<sup>6</sup> reported *I. belli* enteritis occurring in 3 homosexual men, one of whom had concomitant *Cryptosporidium* infections. The 3 patients had lymphopenia and 2 had profound reversals of T cell helper-suppressor ratios. In this case report, a similar situation, i.e., reversal in the T cell ratio, was observed.

DeHovitz *et al*<sup>7</sup>, found chronic diarrhoea of more than 2 months duration as the main presenting symptom in 110 AIDS patients with isosporiasis and cryptosporidiosis. Fifteen or 11% of the AIDS patients had only isosporiasis, while 80 patients (61%) had both *I. belli* and *Cryptosporidium*. All the 15 patients with isosporiasis had weight loss of at least 10% during the 2 months before diagnosis of the disorder. Other opportunistic infections developed in 9 of these patients (60%). *I. belli* infection was the first opportunistic infection diagnosed in all the 9 patients. Twelve of the patients with isosporiasis were tested for HTLV-III and were found to be seropositive, and these included the 6 patients who had isosporiasis as their sole opportunistic infection. The average duration of diarrhoea was  $5.8 \pm 4.8$  months (range, 2 to 18). All 15 patients had diffuse, crampy abdominal pain and nausea. Fever and vomiting were less common, occurring in 5 and 3 patients respectively. Seven of the 15 patients required hospitalisation because of dehydration. In this Malaysian case, the patient presented with the same signs and symptoms and isosporiasis is the first AIDS defining illness. Subsequently, he also developed 2 other opportunistic infections viz oral candidiasis and *P. carinii* pneumonia. How he may have acquired the isosporiasis infection can only be speculated, but there is increasing evidence to prove that, like amoebiasis and giardiasis, this infection may be transmitted sexually with the homosexual community.

Isosporiasis responds promptly to treatment with oral trimethoprim (160 mg) and sulfamethoxazole (800 mg), given 4 times a day for 10 days and then twice a day for 3 weeks<sup>8</sup>. Symptomatic isosporiasis recurred in 50% of the patients within 8 weeks of completing therapy. The same group later suggested that isosporiasis in AIDS patients can be treated effectively with a 10 day course of trimethoprim-sulfamethoxazole and that recurrent disease can subsequently be prevented by an ongoing prophylaxis with either trimethoprim-sulfamethoxazole or sulfadoxine-pyrimethamine. In this case, the patient was treated with the same dosage of cotrimoxazole, but for 14 days, and for *P. carinii* infection he was given a higher dosage for 2 weeks. Typical oocysts were absent in the stool after treatment, suggesting efficacy, but when the stool was re-examined after 8 weeks oocysts were found, indicating relapse.

The advent of AIDS has brought into the limelight infections with *I. belli* and *Cryptosporidium*, 2 newly recognised enteric pathogens. These parasites have been associated with severe, persistent enteritis in AIDS patients. A higher index of suspicion is essential to make a diagnosis of isosporiasis in an HIV-infected individual with a history of watery diarrhoea, crampy abdominal pain, weight loss, anorexia, malaise and flatulence. The diarrhoea and abdominal pain are often exacerbated by eating. The physical examination usually reveals only signs of dehydration. The faeces is usually mucoid, which is occasionally tinged with blood with the presence of leucocytes. The presence of Charcot-Leyden crystals in stool, lactose intolerance, fat malabsorption, non-specific radiographic abnormalities such as prominent mucosal folds, thickening of the intestinal wall and disordered motility are characteristic. Stool examination to observe protozoans is mandatory to differentiate cryptosporidiosis from isosporiasis as they are both clinically indistinguishable. Information on the prevalence of isosporiasis in AIDS patients in Malaysia and the regions of the ASEAN countries is scarce and under this condition proper epidemiological and clinical studies need to be carried out to determine the ecologic profile of pathogens usually encountered in AIDS patients and to determine the true prevalence of isosporiasis.

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