

## Cyclospora infection masquerading as coeliac disease

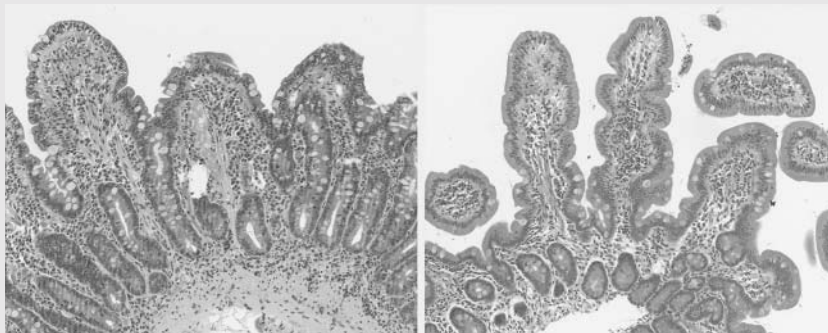
### Clinical record

A 56-year-old woman presented to her general practitioner a fortnight after a trip to Bali. She had a 2-week history of profuse loose brown stools, lethargy, weakness, nausea and some dyspeptic symptoms. The diarrhoea had initially settled with loperamide, but then recurred.

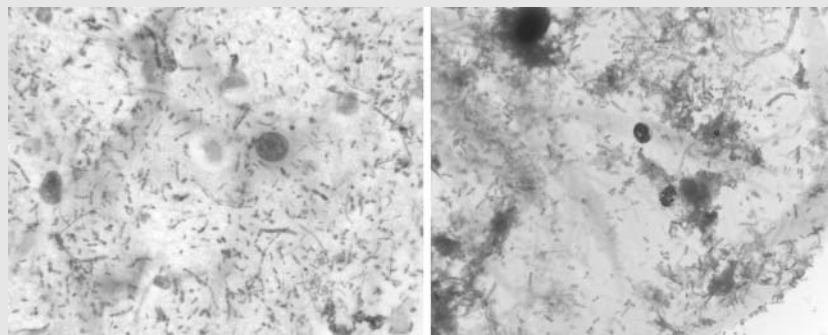
A faecal specimen was collected for microscopy, culture and testing for enteric viruses, all of which gave negative results. Routine blood tests showed mild iron deficiency with no anaemia. Serum levels of vitamin B<sub>12</sub> and folate were in the reference ranges. Serological testing for *Toxoplasma* and *Cytomegalovirus* showed no evidence of recent infection. An initial course of metronidazole for presumed *Giardia* infection was unhelpful, and she was referred for further gastroenterological evaluation.

At the time of review by the gastroenterologist, she had had persistent diarrhoea for nearly 4 weeks. Thyroid, respiratory, abdominal and cardiovascular examination gave unremarkable results. A faecal enzyme-linked immunoassay analysis for *Giardia* antigens gave negative results. Gastroscopy showed mild diffuse gastritis, and a rapid urease test for *Helicobacter pylori* was negative. The duodenum appeared normal, and small-bowel biopsy specimens were sent for disaccharidase testing and histopathological examination. No abnormalities were seen on colonoscopy. Faecal fluid was collected and sent in formalin for saline–acid fixation faecal testing.

Examination of small-bowel biopsy specimens showed moderate villous blunting with increased intraepithelial and lamina propria lymphocytes and no evidence of dysplasia or malignancy, no granulomas or parasites. The report concluded that this appearance was very suggestive of coeliac disease. (Figure 1). However, examination of the faecal specimen in saline–acid fixative revealed oocysts of *Cyclospora cayetanensis* (Figure 2).



1: Small-bowel biopsy specimens taken before and after treatment with trimethoprim–sulfamethoxazole, showing moderate villous blunting before treatment (left) and normal architecture after treatment (right) (original magnification, x50).



2: Oocysts of *Cyclospora cayetanensis* (left) and *Cryptosporidium parvum* (right), showing size difference (original magnification, x 1000).

A diagnosis was made of small intestinal villous atrophy secondary to *C. cayetanensis* infection. The patient was treated with trimethoprim–sulfamethoxazole (800 mg/160 mg twice daily for 5 days). Her symptoms resolved within days. Serological tests and a repeat small-bowel biopsy were undertaken to exclude latent coeliac disease. Serological testing was negative for antigliadin and antiendomysial antibodies, and there was no evidence of residual villous atrophy in the biopsy specimen (Figure 1). The patient remained well on follow-up after completing the course of antibiotics.

**THIS CASE OF PROTRACTED** diarrhoea in an Australian traveller initially appeared consistent with coeliac disease. Further analysis revealed infection with *Cyclospora cayetanensis*, which was successfully treated with antibiotics. The increasing number of documented outbreaks of *Cyclospora* infection,<sup>1</sup> and the need for special preparation of stool samples for their detection,<sup>2</sup> highlight the importance of a high degree of suspicion in cases of traveller’s diarrhoea.

*C. cayetanensis* is a protozoan which was first recognised as a human intestinal parasite in the early 1990s.<sup>3</sup> In 1994, Butcher et al described the first case in an Australian traveller of explosive diarrhoea caused by a large acid-fast spherical organism that had only recently been classified as a member of the genus *Cyclospora*.<sup>4</sup> Since then, reports of outbreaks of *Cyclospora* infection have increased,<sup>1</sup> presumably due to greater awareness of this parasite. Outbreaks have been reported from many parts of the world, including

North, Central and South America, Europe, South East Asia, India, South Africa, and the Caribbean Islands.<sup>5,6</sup>

The mode of transmission is thought to be faecal–oral, or via ingestion of contaminated water. The mechanism by which the protozoan causes villous atrophy is not well understood, but organisms have been found at the site of inflammatory changes. Like *Cryptosporidium* spp. (which are morphologically similar [Figure 2]), *Cyclospora* spp. cause nausea, profuse diarrhoea and weight loss, as well as profound fatigue. Abdominal pain and bloating can manifest as “indigestion” or “heartburn”. If untreated, symptoms last for 6 weeks to 3 months (longer in the immunocompromised), and can be mistaken for irritable-bowel syndrome. The treatment of choice is trimethoprim–sulfamethoxazole, with ongoing prophylaxis for patients with AIDS.<sup>7</sup>

Clinicians need to be aware that the histopathological appearance of the small intestine in *C. cayetanensis* infection

**Lessons from practice**

- *Cyclospora cayetanensis* was relatively recently recognised as an intestinal parasite that causes protracted diarrhoea.
- Beware of histological and clinical overlap with other conditions, including coeliac disease, cryptosporidiosis and irritable-bowel syndrome.
- *Cyclospora* organisms can be difficult to detect: faecal specimens need to be transported in a saline–acid fixative, and examination for *Cyclospora* needs to be specifically requested.
- Treatment is a 7–10-day course of trimethoprim–sulfamethoxazole.

is similar to that in coeliac disease. Other causes of small-intestine villous atrophy include viral enteritis, giardiasis, and cows' milk allergy. Hence, diagnosis of coeliac disease should not be based purely on the finding of villous atrophy. Investigations that we used to test the diagnosis in this patient included a highly specific immunoassay for giardia antigens, as well as testing for antiendomysial and antigliadin antibodies to disprove coeliac disease definitively. However, the clinical history (particularly onset and duration of illness) needs to be considered before requesting these tests. In the setting of recent travel or a community outbreak, a high index of suspicion for infectious causes of villous blunting is warranted.

Despite the increasing knowledge about the genus *Cyclospora*, many infections are missed, as the parasite can be difficult to detect in human faecal samples. Clinicians need to be aware that acid-fast staining is required, and that this requires preservation of the faecal specimen in formalin.<sup>3</sup> It is also important to realise that *Cyclospora* oocysts are usually shed in low numbers, even when the patient is very ill. In addition, faecal specimens sent to pathology laboratories for examination for ova and parasites are commonly not examined for *Cyclospora* spp. Hence, *Cyclospora* testing must be specifically requested.<sup>2</sup>

Finally, laboratory investigators need to be aware that *Cyclospora* cysts are morphologically similar to cysts of *Cryptosporidium parvum*. The most obvious difference is size, as *Cyclospora* cysts are larger (8–10 µm) than *Cryptosporidium* cysts (4–6 µm) (Figure 2). It is important to differentiate the two, as *Cyclospora* infection can be treated with antibiotic therapy, whereas management of *Cryptosporidium* infection is largely supportive.<sup>5</sup> Dialogue between the clinician and pathologist can help to avoid confounding diagnoses. Newer techniques, such as polymerase chain reaction (PCR) testing for parasite DNA, are currently being developed, but are expensive and may not be available in a routine laboratory.

**Vidyut Pingé-Suttor,\* Chris Douglas†  
Antony Wettstein‡**

\*Registrar, St Vincent's Hospital, Victoria Street, Darlinghurst, NSW 2010 and Conjoint Associate Lecturer, University of NSW, Sydney, NSW

†Pathologist, Histopath Specialist Pathologists, Sydney, NSW

‡Gastroenterologist, St Vincent's Clinic, Sydney, NSW  
vidyutpinge@hotmail.com

*Competing interests:* None identified.

1. Herwaldt BL. *Cyclospora cayetanensis*: a review, focusing on the outbreaks of cyclosporiasis in the 1990s. *Clin Infect Dis* 2000; 31: 1040-1057.
2. Wurtz R. *Cyclospora*: A newly identified intestinal pathogen of humans. *Clin Infect Dis* 1994; 18: 620-623.
3. Ortega YR, Sterling CR, Gilman RH, et al. *Cyclospora* species — a new protozoan pathogen of humans. *N Engl J Med* 1993; 328: 1308-1312.
4. Butcher AR, Lumb R, Coulter E, Nielsen DJ. Coccidian/Cyanobacterium-Like Body associated diarrhoea in an Australian traveler returning from overseas. *Pathology* 1994; 26: 59-61.
5. Collins PA, Wright MS. Emerging intestinal protozoa: a diagnostic dilemma. *Clin Lab Sci* 1997; 10: 273-278.
6. Ortega YR, Sterling CR, Gilman RH. *Cyclospora cayetanensis*. *Adv Parasitol* 1998; 40: 399-418.
7. Katz DE, Taylor DN. Parasitic infections of the gastrointestinal tract. *Gastroenterol Clin North Am* 2001; 30: 797-815.

(Received 30 Sep 2003, accepted 18 Dec 2003)

□

