# Histologic Proof of Acalculous Cholecystitis Due to *Cyclospora cayetanensis*

**Fred A. Zar, Ezzat El-Bayoumi, and Margaret M. Yungbluth**
Saint Francis Hospital, Evanston, Illinois

**It is suspected that *Cyclospora cayetanensis* can infect the biliary tract in persons with human immunodeficiency virus infection, but histologic proof has never been published. We report a case of acalculous cholecystitis in a person with acquired immunodeficiency syndrome who required cholecystectomy and demonstrated *C. cayetanensis* in the gallbladder epithelium.**

*Cyclospora cayetanensis* is a coccidian parasite that clinically manifests as a profuse watery diarrhea in both immunocompetent and immunosuppressed patients [1, 2]. HIV-infected individuals may have symptoms and signs of biliary tract disease that resolve with appropriate therapy [3]. Although this is highly suggestive of direct biliary tract infection, to date there has been no histologic proof that *C. cayetanensis* can directly invade biliary epithelium. We report the first case of histologically documented *C. cayetanensis* as a cause of acalculous cholecystitis.

***Case report.*** A 35-year-old man presented to the hospital with a 10-day history of sudden onset of watery diarrhea. He was having 6 stools per day that were non–foul-smelling and without evidence of blood or pus. Five days earlier, he had noted (1) the onset of right upper quadrant pain that worsened with eating and radiated to the right subscapular region, and (2) temperatures to 38.3°C.

He had been found to be seropositive for HIV 3 years earlier and was noncompliant with antiretroviral therapy. His CD4 count 2 months earlier was 11 cells/mm$^3$. He had developed Stevens-Johnson syndrome after administration of trimethoprim-sulfamethoxazole (TMP-SMX) 3 years earlier.

On physical examination, he had a temperature of 37.4°C, blood pressure of 107/57 mm Hg, a pulse rate of 75 beats/min, and a respiratory rate of 14 breaths/min. There was no orthostasis. Examination was remarkable for pain on deep palpation of the right upper quadrant and the epigastrium without rebound, guarding, or alteration in bowel sounds. There was pain with inspiratory arrest on palpation of the right upper quadrant.

His WBC count was 4100 cells/mm$^3$; hemoglobin, 10.3 g/dL; hematocrit, 31.4%; and platelets, 129,000 platelets/mm$^3$. Electrolytes, serum creatinine, amylase, and lipase were normal. Aspartate aminotransferase level was 44 IU/L, and alanine aminotransferase level was 61 IU/L. Alkaline phosphatase level was 93 IU/L, and total bilirubin level was 0.3 mg/dL.

An ultrasound of the right upper quadrant showed thickening of the anterior portion of the gallbladder wall with no stones, pericholecystic fluid, or dilation of the bile ducts. Kinyoun stain performed on a concentrated stool specimen demonstrated acid-fast oocysts measuring 8–10 $\mu$m in diameter, typical of *C. cayetanensis.* The patient was given levofloxacin 500 mg orally once daily. Over the next 2 days, his right upper quadrant pain worsened, and a repeat ultrasound showed thickening of the entire gallbladder wall but, again, no stones or dilatation of the common bile duct. A hepatic iminodiacetic

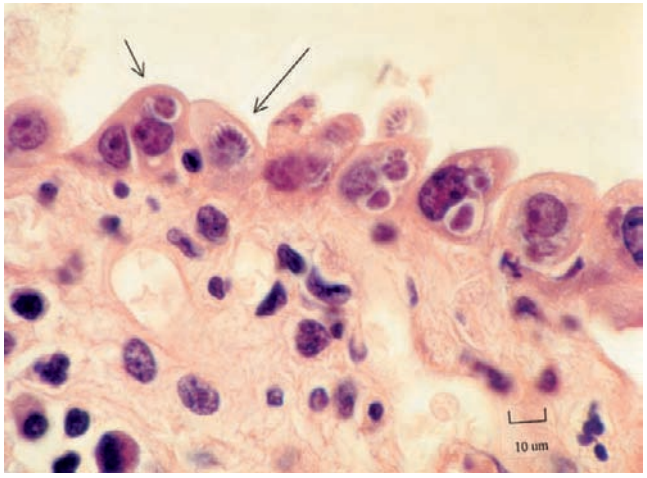


**Figure 1.** Gallbladder mucosa showing marked inflammation and edema. Surface columnar epithelial cells are infected with *Cyclospora* species at different developmental stages in the coccidian life cycle. Several epithelial cells contain large ovoid unicellular trophozoites in parasitophorous vacuoles. Two cells *(arrows)* contain meront-stage organisms with multiple crescent-shaped merozoites with pointed ends. Bar, 10 $\mu$m (hematoxylin and eosin stain; magnification, ×1000).

Received 15 May 2001; revised 31 July 2001; electronically published 8 November 2001.

Reprints or correspondence: Dr. Fred Arthur Zar, Dept. of Medicine, Saint Francis Hospital, 355 Ridge Ave., Evanston, IL 60202 (fredzar@aol.com).

**Clinical Infectious Diseases 2001;33:e140–1**

1058-4838/2001/3312-00E3$03.00

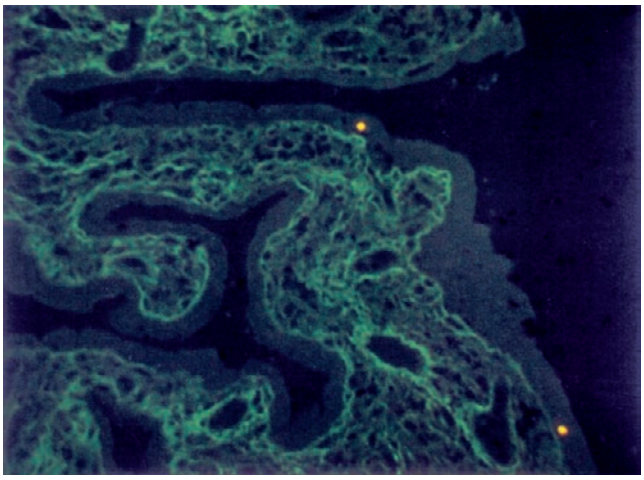

**Figure 2.** The gallbladder epithelium contains 2 *Cyclospora* oocysts. The oocyst is the only stage in *Cyclospora* development that is acid-fast; its wall binds auramine-rhodamine fluorochrome dyes and is resistant to acid-alcohol decolorization. Oocysts fluoresce orange-yellow; epithelial cells are nonstaining, and collagen in the submucosa exhibits dull-green autofluorescence (auramine-rhodamine acid-fast stain, fluorescence microscopy, ×100).

acid scan showed adequate filling of the gallbladder and the duodenum.

Because of persistent severe pain, on day 3, the patient underwent a laparoscopic cholecystectomy. The gallbladder was not distended; there were no calculi, and the mucosal surface was grossly intact. Routine histologic sections demonstrated acute and chronic cholecystitis. Similar to their histologic characteristics in the intestinal epithelium, there were numerous intracytoplasmic parasitophorous vacuoles in the gallbladder epithelium that contained *Cyclospora* trophozoite, merozoite, and schizont organisms (figure 1). Oocysts were demonstrated with auramine-rhodamine fluorochrome stain (figure 2).

The patient's symptoms resolved, and treatment was continued with a 3-week course of levofloxacin, 500 mg once daily, followed by indefinite prophylaxis with 500 mg 3 times a week. Two weeks after surgery, results of a stool examination for ova and parasites were negative.

***Discussion.*** Several opportunistic infections have been implicated as the cause of biliary disease in patients with HIV infection and immunosuppression. These organisms include cytomegalovirus, *Microsporidium, Cryptosporidium,* and *Cyclospora* species. In an earlier report, 2 patients with AIDS and *C. cayetanensis* infection had right upper quadrant abdominal pain and elevated alkaline phosphatase levels [3]. Ultrasound scans showed thickening of their gallbladders suggestive of acalculous cholecystitis. They both responded to TMP-SMX, and *C. cayetanensis* oocyst excretion ceased. Although these cases were highly suggestive of acalculous cholecystitis from *C. cayetanensis,* histologic proof was lacking. On the basis of our case, it is clear that *C. cayetanensis* should be considered as a definite cause of acalculous cholecystitis in HIV-infected immunosuppressed patients.

TMP-SMX is an effective therapy for *Cyclospora* diarrhea [2], and fluoroquinolones appear to have similar efficacy [4]. Our patient was treated with levofloxacin because of his severe allergy to TMP-SMX. Because he underwent cholecystectomy, we cannot truly assess the efficacy of this agent in *Cyclospora* cholecystitis.

## References


1. Huang P, Weber JT, Sosin DM, et al. The first reported outbreak of diarrheal illness associated with *Cyclospora* in the United States. Ann Intern Med **1995**; 123:409–14.
2. Pape WJ, Verdier RI, Boncy M, et al. *Cyclospora* infection in adults infected with HIV. Clinical manifestations, treatment and prophylaxis. Ann Intern Med **1994**; 121:654–7.
3. Sifuentes-Osornio J, Porras-Cortes G, Bendall RP, et al. *Cyclospora cayetanensis* infection in patients with and without AIDS: biliary disease as another clinical manifestation. Clin Infect Dis **1995**; 21:1092–7.
4. Verdier RI, Fitzgerald DW, Johnson WD Jr, Pape JW. Trimethoprim-salfamethoxazole compared with ciprofloxacin for treatment and prophylaxis of *Isospora belli* and *Cyclospora cayetanensis* infection in HIV-infected patients. A randomized, controlled trial. Ann Intern Med **2000**; 132:885–8.