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Cyclospora: update on an emerging pathogen

KEY POINTS:

Cyclospora **is usually transmitted by contaminated water, but may be food-borne (eg, raspberries).**

Persons returning from or residing in endemic areas are at high risk for infection.

The diarrhea is usually self-limited but may last up to 6 weeks and be associated with profound fatigue.

Diagnosis is established by direct examination of fresh stool specimens in a laboratory with personnel experienced in identifying *Cyclospora*.

Treatment with oral trimethoprim-sulfamethoxazole is effective.

ABSTRACT: *Cyclospora cayetanensis*, an emerging pathogen with worldwide distribution, causes diarrhea in both immunocompetent and HIV-infected patients. We review the epidemiology of *Cyclospora* infection and how to diagnose and treat it.

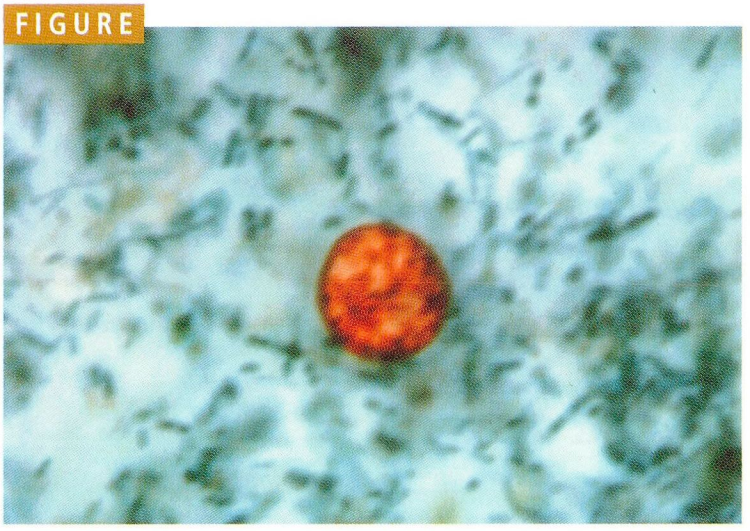
In the summer of 1996, several food-borne outbreaks of diarrheal disease caused by *Cyclospora cayetanensis* occurred in the United States and Canada and involved over 1000 persons[1,2]; this pathogen had caused only three previous outbreaks of human infection in the United States.[3] Although *Cyclospora* is not a "new" organism, it is now recognized as a cause of diarrhea and as an emerging pathogen that has invaded the food supply.[4] This article describes the diagnosis and treatment of *Cyclospora* infection.

A TYPICAL CASE

A 38-year-old housewife from northeastern Ohio presented to the outpatient clinic at the Cleveland Clinic in June 1996 with a 3-week history of nonbloody diarrhea, abdominal cramps, a 15-pound weight loss, and severe fatigue. Of note, she had consumed waffles topped with fresh raspberries over the Memorial Day weekend. Her husband, mother, father, and aunt, who also ate the raspberry-laden waffles, all developed a similar diarrheal illness. There was no history of travel outside of Ohio.

Her physical examination disclosed nothing abnormal. A modified acid-fast smear of a fresh stool specimen showed oocysts consistent with *C cayetanensis* (FIGURE). Bacterial cultures for enteric pathogens were negative, and examination of her stool revealed no other ova or parasites. Stool specimens from the patient's father and mother also contained *Cyclospora*. All the patients were treated with oral trimethoprim-sulfamethoxazole, and their symptoms resolved completely.

FIGURE



Modified acid-fast stain of stool showing *Cyclospora cayetanensis* oocyst (× 1000). The oocyst measures approximately 8 µm; in contrast, *Cryptosporidium* oocysts are half as large.

Acid-fast staining of stool samples is the gold standard for diagnosis

WHAT IS *CYCLOSPORA*?

Cyclospora is a protozoan parasite in the same suborder as four other human pathogens: *Cryptosporidium*, *Isospora*, *Toxoplasma*, and *Sarcocystis*. *Cyclospora* oocysts are 8 to 10 µm in diameter (almost twice the size of *Cryptosporidium*) and are often referred to as "*Cryptosporidium grande*." Within each oocyst are two sporocysts, each containing two sporozoites. In the past the parasite was referred to as "*Cyanobacterium*-like bodies" (CLBs).

Cyclospora was first described as an enteric pathogen of moles in 1870; the first report of an infection in man (in Papua New Guinea) was published more than 100 years later.[5] Reported cases have increased since the mid-1980s, in part because of the availability of better techniques for detecting the parasite in stool and because of increasing recognition of the parasite as a cause of diarrhea.[4]

WHO IS AT RISK FOR INFECTION?

Although *Cyclospora* infections have been documented worldwide, most of our epidemiologic knowledge comes from studies in Nepal, Haiti, and Peru, where it is endemic.[6–9] Cyclosporiasis appears to be seasonal, with peak incidence during the rainy seasons (from April to June in Peru and May to September in Nepal).[7,10] Although all age groups can acquire the disease, the highest attack rates occur among children older than 18 months.[11] There is no apparent immunity to infection, and reinfection can occur at all ages.[12]

Cyclospora is an increasingly recognized cause of traveler's diarrhea, causing up to 11% to 20% of cases of diarrhea in studies of expatriates in Nepal.[6,10,11] Documentation of infection acquired in the United States is also increasing. The earliest recorded outbreak of diarrheal disease associated with *Cyclospora* in the United States occurred in 21 resident physicians in a Chicago hospital in 1990 and was epidemiologically linked to a contaminated water supply.[3] Subsequently, more than 1000 confirmed cases in the United States and Canada were reported to the Centers for Disease Control and Prevention in the summer of 1996.[1,2]

HOW IS *CYCLOSPORA* TRANSMITTED?

Cyclospora oocysts are excreted unsporulated in the stool and require a period of time before they become infective; therefore, direct transmission from an infected patient to another person is unlikely. The infective dose necessary to cause disease in man is unknown.

Cyclospora infection occurs most commonly via contaminated water.[3,4,13] *Cyclospora*, like *Cryptosporidium*, is resistant to chlorination and is not readily detected by methods that are currently used to assure the safety of drinking water. There is also epidemiologic evidence of transmission by contaminated food. In the multistate *Cyclospora* outbreak of 1996, raspberries grown in Guatemala were served at the events related to clusters of *Cyclospora* illness.[1,2]

Further studies are underway to identify which populations are at highest risk for *Cyclospora* infection and to delineate further the modes of transmission of this emerging pathogen.

CLINICAL FEATURES OF CYCLOSPORIASIS

Infection by *C cayetanensis* can be asymptomatic, cause a self-limited diarrhea, or cause chronic diarrhea. *Cyclospora* has an incubation period of 2 to 10 days (median 7 days).[4] The diarrhea is usually watery and nonbloody, clinically indistinguishable from other types of noninvasive or secretory infectious diarrhea. There are often accompanying abdominal cramps, and patients may report a rapid loss of weight. The clinical picture may sometimes be dominated by severe fatigue and, at times, fever, anorexia, and chills.[4,14] These nonspecific symptoms often lead to delay in diagnosis while the practitioner pursues other possible causes of fatigue. There are no specific findings on physical examination. A more chronic clinical course with biliary disease has been described in patients with HIV infection.[15]

Upper endoscopic studies of the small bowel in patients with cyclosporiasis have shown erythema of the distal duodenum, and duodenal biopsies have shown a loss of brush border and changes consistent with epithelial injury, blunting and severe partial atrophy of villi, crypt hyperplasia, and both acute and chronic inflammation in the lamina propria.[12]

DIAGNOSING CYCLOSPORIASIS

The diagnosis of cyclosporiasis is made by direct examination of stool samples. In a study of HIV-infected patients, Pape and coworkers[8] compared the sensitivities of various staining techniques commonly used for the laboratory diagnosis of *C cayetanensis* infection, using the modified acid-fast stain as the gold standard. The wet-mount technique had a sensitivity of 75%, safranin O staining had a sensitivity of 30%, and auramine rhodamine staining had a sensitivity of 23%. Physicians should notify the laboratory when *Cyclospora* is suspected, so that a combination of a wet-mount study and a modified acid-fast staining study will be performed.

Under modified acid-fast staining the organism varies from dark red to transparent (FIGURE). Of note, the diagnostic yield correlates with the experience of the laboratory personnel—the false-negative rate is high in laboratories where technicians are not specifically trained to look for this pathogen. Methods based on the polymerase chain reaction are being developed and have a reported sensitivity of 62% and specificity of 100%.[16]

TREATMENT

Trimethoprim-sulfamethoxazole is the only drug that has shown efficacy so far against *C cayetanensis*. Two prospective trials have documented the efficacy of this oral preparation (160 mg of trimethoprim and 800 mg of sulfamethoxazole twice daily for 7 days) in treating cyclosporiasis.[8,17] ■

Give trimethoprim 160 mg and sulfamethoxazole 800 mg twice daily for 7 days

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