Cyclospora cayetanensis

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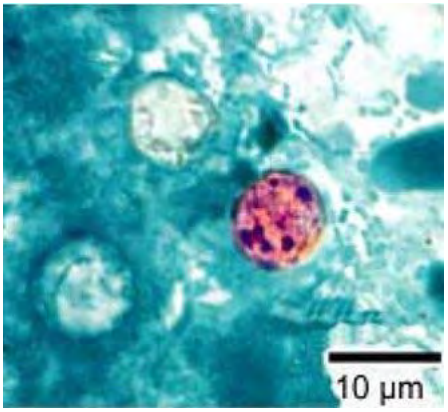
Cyclospora cayetanensis is a protozoan that causes disease in humans, and perhaps primates. It has been linked in the United States to fecally contaminated imported produce, and was virtually unknown before about 1990, but has been on the rise since. The health risk associated with the disease is usually confined to adult foreigners visiting regions where the species is endemic and acquiring the infection; consequently, *C. cayetanensis* is a cause of "traveler's diarrhea".

This species was placed in the *Cyclospora* genus because of the spherical shape of its sporocysts. The species name refers to the Cayetano Heredia University in Lima, Peru, where early epidemiological and taxonomic work was done.[1]

Cyclospora cayetanensis



Cyclospora cayetanensis oocysts

Scientific classification

Domain:	Eukaryota
(unranked):	SAR
(unranked):	Alveolata
Phylum:	Apicomplexa
Class:	Conoidasida
Subclass:	Coccidiasina
Order:	Eucoccidiorida
Suborder:	Eimeriorina
Family:	Eimeriidae
Genus:	*Cyclospora*
Species:	***C. cayetanensis***

Binomial name

Cyclospora cayetanensis

Ortega, Gilman & Sterling, 1994

Contents

History

The first published report of *Cyclospora cayetanensis* in humans appears to be by Ashford (1979), who found unidentified *Isospora*-like coccidia in the feces of three individuals in Papua, New Guinea. The photomicrographs in the paper reveal an organism morphologically identical to that we see now. Later, Narango et al. (1989) reported what may be the same organism from several Peruvians with chronic diarrhea and termed the organism *Cryptosporidium muris*-like. Other investigators thought the unsporulated oocysts appeared more similar to cyanobacteria, and the name "cyanobacterium-like body" or CLB became prevalent in the literature (occasionally, authors also used the term "coccidian-like body", or CLB). Eventually, Ortega et al. (1992) published an abstract reporting that they had sporulated and excysted the oocysts, resulting in placement of the parasite in the genus *Cyclospora*. They also created the name *Cyclospora cayetanensis* at this

time. However, since no morphologic information was presented in the abstract, *C. cayetanensis* technically became a nomen nudum (a named species without a description). Although Ortega et al. (1993) later published additional details about this coccidian, it wasn't until 1994 that a complete morphologic description was published to validate the name (Ortega et al., 1994). Thus, the correct name for this parasite is *Cyclospora cayetanensis* Ortega, Gilman, & Sterling, 1994, and the etymology of the nomen triviale is derived from Cayetano Heredia University in Lima, Peru. During this 2-year period when *C. cayetanensis* was a nomen nudum, anyone wishing to publish a complete morphologic description and change the name would have been free to do so.[1]

Characterization

Cyclospora cayetanensis is an apicomplexan, cyst-forming coccidian protozoan that causes a self-limiting diarrhea. In terms of morphology, *C. cayetanensis* has spherical oocysts that are between 7.5 and 10 micrometers in diameter that also have a 50-nanometer-thick wall with an outer threadlike coat that has been called a wrinkle by some researchers.

The only hosts for *C. cayentanensis* are humans. The protozoan lives out its lifecycle intracellularly within the host's epithelial cells and gastrointestinal tract. Infection is transmitted through the fecal-oral route, and begins when a person ingests oocysts in fecally contaminated food or water. Various chemicals in the host's gastrointestinal tract cause the oocysts to excyst and release sporozoites; generally, two are observed per oocyst. After these sporozoites invade the epithelial cells, they undergo merogony, a form of asexual reproduction that results in many daughter merozoites. These daughter cells may either infect new host cells and initiate yet another round of merogony or take on a sexual track via gametogony: Daughter merozoites become male macrogamonts—which form many microgametes—and female macrogamonts. After fertilization has occurred via male microgamete fusion with female macrogamont, the zygote matures into an oocyst and ruptures the host cell, from which point it is passed with the stool. The oocysts that are passed are not, however, immediately infectious. Sporulation can take from one to several weeks, meaning person-to-person transmission is not a likely problem. This differentiates *C. cayentanensis* from *Cryptosporidium parvum*—a closely related organism that causes a similar disease—since *C. parvum* oocysts are immediately infectious upon release from the host. [2]

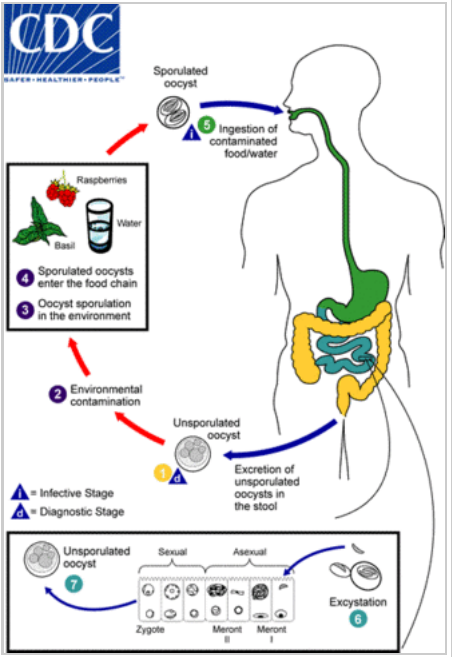
Symptoms

C. cayentanensis causes gastroenteritis, with the extent of the illness varying based on age, condition of the host, and size of the infectious dose. Symptoms include "watery diarrhea, loss of appetite, weight loss, abdominal bloating and cramping, increased flatulence, nausea, fatigue, and low-grade fever", though this can be augmented in more severe cases by vomiting, substantial weight loss, excessive diarrhea, and muscle aches. Typically, patients with a persistent watery diarrhea lasting over several days may be suspected of harboring the disease, especially if they have traveled to a region where the protozoan is endemic. The incubation period in the host is typically around a week, and illness can last six weeks before self-limiting. Unless treated, illness may relapse. The more severe forms of the disease can occur in immunocompromised patients, such as those with AIDS.[3]

Risk factors

Persons living or traveling in the poorly developed areas, tropics and subtropics may be at an increased risk of acquiring *C. cayetanensis* as there are identified as endemic areas. Additionally, in some regions infections

tend to me more prevalent at certain times of the year, typically most frequently in late spring and summer. In addition, this time of year correlates with increased import of fruits and vegetables into the US from the more southern neighbors.[1] Consuming food or water while visiting developing countries is a well-documented way of developing traveler's diarrhea. Travelers are often warned against such actions, but over 70 percent of selected produce consumed in the United States is imported from developing countries, making "traveler's diarrhea" possible without international travel.[4] It should be noted that since the oocysts are shed in the feces of infected persons and then have to mature in the environment 2–14 days before it can become infectious, it is unlikely to get an infection directly from an infected person, such as a restaurant worker who did not wash their hands fully after using the toilet [5]



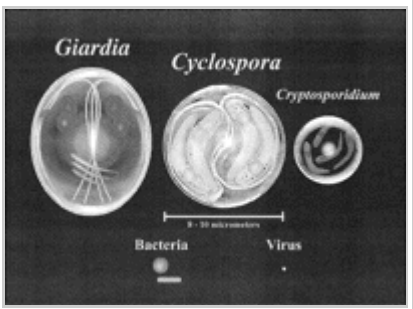
Picture showing the lifecycle

Recognition

Due to its small size, intracellular habitat, and inability to properly take up many histological stains, diagnosis of *C. cayetanensis* can be very difficult. Four methods have thus far been established for positive diagnosis of the protozoan: microscopic detection in stool samples of oocysts; recovering oocysts in intestinal fluid/small bowel biopsy specimens; demonstration of oocyst sporulation; and amplification by polymerase chain reaction (PCR) of *C. cayetanensis* DNA. Since detection is so hard, one negative result should not discount the possibility of *C. cayetanensis*: tests involving fresh stool samples over the next few days should also be considered.

Except for PCR amplification, once a sample with suspected oocysts has been recovered, standard tests are followed to identify *C. cayetanensis*. These tests include phase contrast microscopy to check for the spherical oocysts described earlier, modified acid-fast staining to check for variable staining (from pale to red), and autofluorescence with UV lights. Obtaining these oocysts is usually the challenge, though recent studies show easier methods of obtaining them. In a recent study on different techniques used in fecal exams to identify oocysts, centrifuging a sample of feces in a sucrose solution and then transferring a small amount to a slide was found to be remarkably effective—both in oocysts found and relative ease of labor—in detecting *C. cayetanensis* oocysts: indeed, the paper concluded the positive samples obtained were around 84%.[6]

C. cayetanensis has been confused with other protozoan infections in the past, most commonly being misidentified as *Cryptosporidium parvum*. Several differences can be noted between the two, however, to ensure proper diagnosis. These differences include: size difference—*C. parvum* is smaller; differing results from modified acid-fast staining—*C. parvum* has consistent red staining, whereas *C. cayetanensis* shows variable staining; and autofluorescence under UV light—*C. cayetanensis* exhibits this, whereas *C. parvum* does not.



Comparing eggs with Cyclospora: Giardia-Cyclospora-Cryptosporidium-bacterium-virus

Treatment

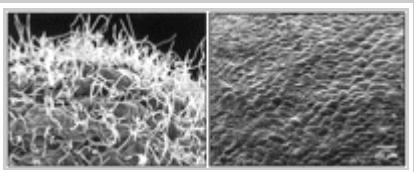
Most people who have healthy immune systems will recover without treatment. If not treated, the illness may last for a few days to a month or longer. Symptoms may seem to go away and then return one or more times (relapse). Anti-diarrheal medicine

may help reduce diarrhea, but consult with a health care provider before the medicine is taken. People who are in poor health or who have weakened immune systems may be at higher risk for severe or prolonged illness.[7] To date, the most effective drug for the treatment of the protozoan is a seven-day course of oral trimethoprim-sulfamethoxazole (TMP-SMX). Effects of the drug include a significant decrease in the duration of oocyst excretion, cessation of diarrhea, and stool samples negative for oocysts within two to three days.[7] TMP-SMX is classified as a Category C during pregnancy, meaning potential adverse effects (such as teratogenic or embryocidal or other) could results and should only be given if the potential benefit significantly justifies the risk. The drug should be avoided near-term as there are high potentials for hyperbilirubinemia and kernicterus in newborns. Additionally, TMP-SMX can be excreted in breast milk, which is compatible in healthy, full-term newborns, but should be avoided in premature, ill, stressed, jaundice infants.[8] No highly alternative antibiotic regimen has been discovered yet for patients who possess a sulfa-allergy.[9]

Prevention

No vaccine against this pathogen is available.[10] Since infection occurs via fecally contaminated food and water in endemic environments, several simple solutions have been suggested for the prevention of *C. cayetanensis* infections. The simplest is to warn travelers not to visit regions where the protozoan is endemic (in general, tropical and subtropical regions where sanitation is poor, such as Peru, Brazil, and Haiti), especially when the season is best for spreading: Travelers also should be aware that treatment of water or food with chlorine or iodine is unlikely to kill Cyclospora oocysts.[11] Additionally, better health practices in the originating agricultural setting—such as making sure produce watering systems are not pulling water that has access to human feces Additionally, using filtering systems such as a 1 micron absolute carbon filtration system will reduce the presence of *Cyclospora*, drastically decreasing the incidence of the spread of this parasite.[5] The odds of becoming infected with *Cyclospora*, and many other foodborne pathogens, can be greatly diminished by thoroughly washing fruits and vegetables in clean water prior to consumption. However, it should be noted that simply washing foods does not remove 100% of the oocysts present.[1]

Cyclospora and raspberries



Surface of raspberry in comparison to blackberry.

There was a study done testing stool specimens of raspberry farm workers, showing a higher incidence of *Cyclospora* oocysts in their specimen compared to other people in the area.[12] This could be due to the fact that *Cyclospora* are highly resistant to disinfectants commonly used by workers for hygiene purposes, and for food and water processing. This resistance is probably heightened by higher binding affinities to certain fresh produce. Fine, hair like projections on raspberries help facilitate the entrapment of the sticky oocysts to their surfaces compared to that of other fruits, such as blackberries. Refer to image. Contrast between the surface of a raspberry (left) and a blackberry (right), as viewed by scanning electron microscopy. Note the uneven surface of the raspberry, complete with crevices and hairs.[13]

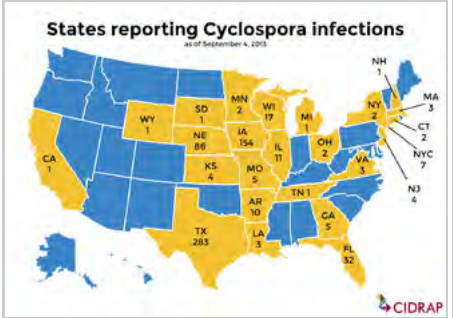
2013 United States outbreak

At least 285 people in 11 states have been affected as of July 26, 2013. The exact cause of the outbreak has not yet been identified according to the U.S. Centers for Disease Control and Prevention (CDC). The majority of cases are located in the Midwest, with 138 reported cases in Iowa and 70 in Nebraska. The other states affected

are: Texas, Florida, Georgia, Wisconsin, Connecticut, Illinois, Kansas, Minnesota, New Jersey, and Ohio.

As of July 29, 2013, the CDC reported 373 people in 15 states have been affected by the outbreak. So far, 21 patients from three states have been hospitalized, but no deaths have been reported. No food source has been identified yet, but health officials in Iowa—the state reporting the most cases—have said they suspect imported vegetables.[14]

On July 30, 2013, the Nebraska Department of Health & Human Services and the Iowa Department of Health announced that a restaurant chain's prepackaged salad was the disease vector for the parasite.[15] However, the CDC and the U.S. Food and Drug Administration (FDA) are still assessing information from other states to see if the findings apply to illnesses there.[16]



Map of states reporting *Cyclospora* infections as of August 19, 2013 from CIDRAP

In an August 1, 2013, update, the CDC reported 397 cases, while and Iowa and Texas added another 22 more. This pushed the unofficial count to over 400 cases. Additionally, Louisiana reported its first case, bringing the total number of states affected to 16.[17]

On August 3, 2013, CNN reported that the outbreak was traced to prepackaged salad served at Olive Garden and Red Lobster restaurants that was manufactured by Taylor Farms de Mexico.

On August 15, 2013, the CDC reported nine more Cyclospora infections, raising its case count to 548. The number of affected states remained at 19, but the CDC said that not all cases are confirmed to be linked to an outbreak in Iowa and Nebraska traced to a contaminated salad mix from Mexico.[18]

On August 19, 2013, the CDC reported 10 more Cyclospora cases, raising the unofficial count to over 600. Tennessee also reported its first case, bringing the number of states affect to 20. The CDC still cautions that it is not clear whether cases in all of the states are related to outbreaks in Iowa and Nebraska.[19]

On August 27, 2013, the origination still remained a mystery. The FDA says it found no food safety violations at the Taylor Farms de Mexico salad plant in Mexico that was linked to some of the illnesses.[20]

2015 Texas outbreak

In an FDA statement the CDC is quoted, "there is currently (in July 2015) another ongoing outbreak of cyclosporiasis in the United States in which both the Texas Department of State Health Services and the Wisconsin Department of Health Services and the Wisconsin Department of Agriculture, Trade and Consumer Protection have identified cilantro from the Mexican state of Puebla as a suspect vehicle with respect to separate illness clusters." Last year, Texas had 200 cases, some of which were associated with cilantro from the Puebla region.[21]

2016 Texas outbreak

Health officials say more than a dozen cases of cyclosporiasis have been confirmed in North Texas' four major counties and that the source is likely contaminated food. The Texas Department of State Health Services said Wednesday the parasite was found in Dallas, Tarrant, Collin and Denton counties and that the origin may be

linked to a fresh produce item.

County officials told NBC 5 there have been four cases recorded in Dallas County, three in Collin County, four in Denton County and seven in Tarrant County. The Denton County cases and at least four of the Tarrant County cases had recently traveled out of the country—calling into question the point of origin.

Across the state, there are currently 66 confirmed cases of cyclosporiasis—though the sources of infection haven't been confirmed. For most people, the symptoms are serious. "But for those who are very young and those who are older, or those who have a suppressed immune system, this illness can cause major problems," said Dr. Khang Tran, chief medical officer at The Medical Center of Plano. In recent years, 2012-2015, cyclospora outbreaks were associated with fresh cilantro imported from Puebla, Mexico. Since the summer of 2015, the Food and Drug Administration has instituted ban on imports from that region between from April through August.

Cyclosporiasis Case Counts and Incidence Rates in Texas, 2001-2015 [22]

Year	Case Count	Incidence Rate
2015	316	
2014*	200	0.7
2013*	351	1.3
2012*	44	0.2
2011*	14	0.1
2010	9	0.0
2009	10	0.0
2008	6	0.0
2007	2	0.0
2006	1	0.0
2005	1	0.0
2004	4	0.0
2003	1	0.0
2002	1	0.0
2001	0	0.0

IR=incidence rate per 100,000
* incidence rates are bases on projected census data obtained from the DSHS Center for Health Statistics.

U.S. foodborne outbreaks of cyclosporiasis—2000–2014

Foodborne outbreaks of cyclosporiasis have been reported in the United States since the mid-1990s and have been linked to various types of imported fresh produce, including raspberries, basil, snow peas, mesclun lettuce, and cilantro; no commercially frozen produce has been implicated to date. U.S. foodborne outbreaks of cyclosporiasis that occurred before 2000 were summarized (http://www.cdc.gov/parasites/cyclosporiasis/publications.html) previously, as were the major documented outbreaks in 2013 (http://www.cdc.gov/parasites

/cyclosporiasis/outbreaks/investigation-2013.html) and 2014 (http://www.cdc.gov/parasites/cyclosporiasis/outbreaks/2014/index.html). Foodborne outbreaks during the 15-year period of 2000–2014 are summarized in table. The table provides information about 31 reported foodborne outbreaks of cyclosporiasis that occurred in the United States during 2000–2014; the total case count was 1,562. No outbreaks were reported in 2003, 2007, or 2010. Overall, a median of two outbreaks were reported per year, with a median of 20 cases per outbreak (range, 3 to 582 cases). Although the outbreaks occurred during 8 different months (December through July), the peak months were May, June, and July. As indicated in the table, a food vehicle of infection was identified for 15 of the 31 outbreaks.

Summary of U.S. foodborne outbreaks of cyclosporiasis, 2000–2014 [23]

Year(s)*	Month(s)*	Jurisdiction(s)*	No. of cases†	Food vehicle and source, if identified‡
2000	May	Georgia	19	Raspberries and/or blackberries (suspected)
2000	June	Pennsylvania	54	Raspberries
2001	January–February	Florida	39	
2001	January	New York City	3	
2001–02	December–January	Vermont	22	Raspberries (likely)
2002	April–May	Massachusetts	8	
2002	June	New York	14	
2004	February	Texas	38	
2004	February	Illinois	57	Basil (likely)
2004	May	Tennessee	12	
2004	May–June	Pennsylvania	96	Snow peas from Guatemala
2005	March–May	Florida	582 ¶	Basil from Peru
2005	May	South Carolina	6	
2005	April	Massachusetts	58	
2005	May	Massachusetts	16	
2005	June	Connecticut	30	Basil (suspected)
2006	June	Minnesota	14	
2006	June	New York	20	
2006	July	Georgia	3	
2008	March	Wisconsin	4	Sugar snap peas (likely)
2008	July	California	45 ¶	Raspberries and/or blackberries (likely)
2009	June	District of Columbia	34	
2011	June	Florida	12	
2011	July	Georgia	100	
2012	June–July	Texas	16	
2013**	June	Iowa and Nebraska	161	Bagged salad mix from Mexico
2013**	June–July	Texas	38	Cilantro from Mexico
2013	July	Wisconsin	8	Berry salad (suspected)
2014	June	Michigan	14	
2014††	June–July	Texas	26	Cilantro from Mexico

2014	July	South Carolina	13	

* The entries in the first three columns refer to the known or likely year(s), month(s), and jurisdiction(s) in which the exposure(s) to Cyclospora occurred.
** For additional details, see summary information about the outbreak investigations in 2013 (http://www.cdc.gov/parasites/cyclosporiasis/outbreaks/investigation-2013.html). For the purposes of this table, the exposure month(s) and case counts are limited to those explicitly linked in the investigations to the food item specified in the last column.
† The case counts include laboratory-confirmed and probable cases of cyclosporiasis. By definition, each outbreak included at least two linked cases, at least one of which was laboratory confirmed.
‡ A food vehicle is specified only if a single ingredient or commodity was identified in an outbreak investigation.
¶ Cases that occurred in Canadian travelers to the United States were not included.
†† For additional perspective, see summary information about outbreak investigations in 2014 (http://www.cdc.gov/parasites/cyclosporiasis/outbreaks/2014/index.html). For the purposes of this table, the exposure months and the case count for the outbreak in Texas are limited to those explicitly linked in the investigations to the food item specified in the last column.

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