Cyclospora cayetanensis

Cyclospora cayetanensis is a protozoan parasite that causes the gastrointestinal illness cyclosporiasis. Infected individuals shed a non-infectious form of the parasite in their faeces which requires an extended period of environmental exposure to develop into the infectious form. In developed countries cyclosporiasis is typically associated with international travel or consumption of imported produce.

Description of the organism

C. cayetanensis is a protozoan parasite which belongs to the phylum *Apicomplexa*, subclass *Coccidiaina* and family *Eimeriidae*. Many species of *Cyclospora* have been identified in animals. However, *C. cayetanensis* is the only species identified in humans, and appears to be restricted to this host (Arrowood 2003; Ortega and Sanchez 2010). Once sporulated, organisms of the genus *Cyclospora* have an oocyst that contains two sporocysts, and each sporocyst contains two sporozoites. *C. cayetanensis* oocysts are spherical, measuring 8–10µm in diameter, and as such are smaller than many other species of *Cyclospora* (Ortega et al. 1994; Lainson 2005; Smith 2007).

Growth and survival characteristics

C. cayetanensis can only multiply within the host. Factors that influence the survival of unsporulated and sporulated oocysts in the environment are poorly understood. Available data suggests that the viability of unsporulated oocysts is maintained for up to two months when stored at 4°C (as evidenced by sporulation occurring after storage for one week at 30°C) (Smith et al. 1997). Sathyanarayanan and Ortega (2004) and Ortega et al. (2008) have demonstrated that unsporulated *C. cayetanensis* oocysts are resistant to pesticides commonly used on farms and to sanitizers used by the food industry.

Sporulation of *Cyclospora* oocysts occurs optimally in the temperature range of 22–32°C, with 20–60% of purified oocysts sporulating within 2 weeks. The rate of sporulation slows at temperatures outside of this range (Ortega et al. 1993; Smith et al. 1997; Sathyanarayanan and Ortega 2006). A study by Sathyanarayanan and Ortega (2006) demonstrated that sporulation was prevented after 2 days at -20°C or exposure to extreme temperatures of -70 or 70°C for 15 minutes. Ortega and Liao (2006) showed that microwave heating of *C. cayetanensis* at 96°C for 45 seconds dramatically decreased the level of sporulation but did not completely inhibit sporulation.

Symptoms of disease

Cyclospora infection has a range of outcomes from no clinical symptoms of disease (asymptomatic infection) to severe diarrhoea resulting in dehydration and weight loss. Other symptoms can include anorexia, nausea, vomiting, abdominal bloating, cramping, fatigue, body aches and low-grade fever. The onset of illness is 2–14 days (average of 7 days). In untreated individuals a cycle of remitting and relapsing symptoms can occur that lasts for weeks to months. Shedding of oocysts occurs during the illness and can continue for several weeks after symptoms have abated (Arrowood 2003; Smith 2007; Hall et al. 2012). Infection with *C. cayetanensis* can lead to longer term sequelae including malabsorption, biliary disease, Reiter's syndrome (reactive arthritis) and Guillain-Barré syndrome (a peripheral nervous system disorder that causes paralysis) (Herwaldt 2000; Ortega and Sanchez 2010).

Virulence and infectivity

There are currently no animal models or *in vitro* cultivation methods to determine the infectivity of *Cyclospora* oocysts and consequently knowledge of factors that influence the virulence of *C. cayetanensis* is limited (Ortega and Sanchez 2010).

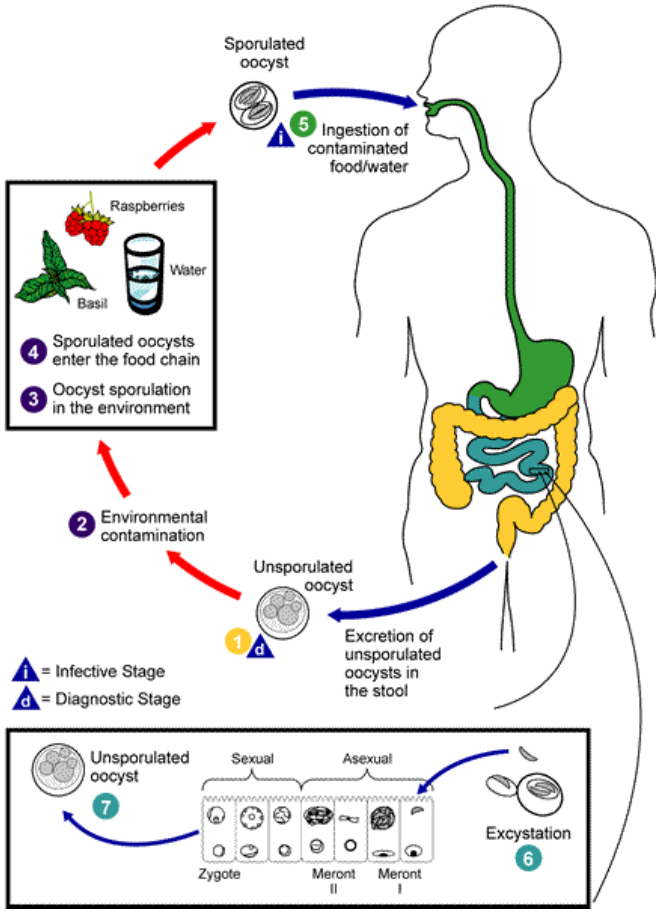
C. cayetanensis oocysts are unsporulated and non-infective when shed in the faeces, and it is thought that a prolonged period outside the host is required for the oocysts to sporulate and become infectious. Factors that affect the sporulation process of *C. cayetanensis* are not well characterised, however, ambient temperature and the presence of higher concentrations of atmospheric oxygen appear to be involved (Smith 2007).

Cyclospora spp. appear to have a higher binding affinity for particular types of fresh produce. For example the fine hair-like projections on the surface of raspberries are thought to facilitate the attachment of “sticky” *Cyclospora* oocysts. The adhesins responsible for this strong attachment are unknown (Ortega and Sanchez 2010).

Mode of transmission

C. cayetanensis is transmitted via the faecal-oral route by consumption of contaminated food or water. Direct person-to-person transmission is unlikely as the oocysts shed from individuals are not infectious and require extended periods of time outside the host to sporulate (Ortega and Sanchez 2010; Hall et al. 2012).

Figure 1: Life cycle of *C. cayetanensis* (CDC-DPDx 2009)



(1) When shed in the faeces, *C. cayetanensis* oocysts are unsporulated and non-infective.

(2) Oocysts contaminate the environment.

(3) Oocysts sporulate in the environment and develop sporocysts and sporozoites. The sporulated oocysts are the infectious form of *C. cayetanensis*.

(4) Fresh produce and water can serve as vehicles for transmission.

(5) The sporulated oocysts are ingested (in contaminated food or water).

(6) The oocysts excyst, releasing sporozoites in the gastrointestinal tract. The sporozoites infect the epithelial cells lining the small intestine, in particular the jejunum. Once inside the intestinal cell, sporozoites multiply asexually and produce type I meronts which in turn form type II meronts. The type II meronts infect other intestinal cells and initiate sexual multiplication by producing either microgametocytes or macrogametocytes. The microgametocytes fertilize the macrogametocytes, leading to the production of a zygote.

(7) The zygotes differentiate into unsporulated oocysts, which are released into the lumen of the intestine and shed in the faeces.

(Smith 2007; CDC-DPDx 2009; Ortega and Sanchez 2010)

Incidence of illness and outbreak data

C. cayetanensis has been reported worldwide, however, it is more common in tropical and sub-tropical environments and in many developing countries, particularly in parts of South America, the Caribbean and Asia. The incidence of *C. cayetanensis* is seasonal, with cases most commonly occurring in spring and summer (Ortega and Sanchez 2010; Chacin-Bonilla 2010; Hall et al. 2012).

Infection with *C. cayetanensis* is not a notifiable disease in Australia or New Zealand and hence very little data is available. In the United States (US) the notification rate for cyclosporiasis in 2010 was 0.07 cases per 100,000 population, which was an increase on the 2009 rate of 0.05 cases per 100,000 population (CDC 2012).

Outbreaks of *C. cayetanensis* have largely been associated with fresh produce (refer to Table 1).

Table 1: Selected major foodborne outbreaks associated with *C. cayetanensis* (>50 cases and/or ≥1 fatality)

Year	No. cases	Food	Country	Comments	Reference
2010	314	Fresh produce (cantaloupe, chives & lettuce)	Cruise ship (multiple countries)	Food taken on board the cruise ship from south east Asian destinations	(Gibbs et al. 2013)
2005	142	Fresh basil	Canada	Fresh basil imported from Mexico, contamination possibly from human handling or irrigation water	(Milord et al. 2012)
2004	96	Fresh snow peas	US	Snow peas imported from Guatemala, all from the same batch	(CDC 2004)
2000	54	Raspberry filling of a wedding cake	US	Frozen unwashed raspberries were thawed and mixed into the cream filling of the cake. Raspberries were imported from Guatemala	(Ho et al. 2002)
1997	93	Mesclun lettuce	US	Lettuce thought to be imported from Peru	(Herwaldt 2000)
1996	1465	Raspberries	US and Canada	Raspberries imported from Guatemala. Berries were picked and sorted by hand, well water was used for washing	(Herwaldt et al. 1997)

Occurrence in food

C. cayetanensis has been identified in international surveys of fresh produce. Dixon et al. (2013) detected *Cyclospora* spp. in 1.7 % of packaged leafy greens purchased from grocery stores in Canada (n=544). In a study of herbs in Vietnam, 10.4% of basil (n=96), 11.6% of coriander (n=86) and 7.7% of marjoram samples (n=26) were positive for *Cyclospora* spp. oocysts (Tram et al. 2010). Ortega et al. (1997) detected *C. cayetanensis* oocysts in 1.7% of vegetables sampled from markets in Peru (n=172). In Nepal *Cyclospora* spp. have been detected in drinking water and on cabbage and lettuce (Sherchand et al. 1999).

As *C. cayetanensis* infections have only been observed in humans (Ortega and Sanchez 2010), there does not appear to be an animal reservoir. It is likely that the most significant transmission occurs where sewage, or water contaminated by human faeces, has been applied to horticultural crops (Dawson 2005). This could occur via the use of contaminated water for the application of pesticides, sprinkling contaminated water on horticultural produce to maintain freshness, or washing the produce in contaminated water drawn from ponds, lakes or rivers. Contaminated hands of food handlers, baskets and containers in markets could also lead to contaminated produce (Sherchand et al. 1999; Ortega and Sanchez 2010; Tram et al. 2010).

Host factors that influence disease

People of all ages are susceptible to *C. cayetanensis* infection. Young children, the elderly and immunocompromised individuals develop more severe clinical symptoms. In endemic areas, the severity of symptoms and duration of infection tends to decrease after repeated infections, suggesting possible immunity in older children and adults (Ortega and Sanchez 2010).

Dose response

The number of *C. cayetanensis* oocysts required to cause infection is not known, however, it is presumed to be low (possibly as low as 10 oocysts) on the basis of data from outbreak investigations (Smith 2007; RTI International 2009).

Recommended reading and useful links

FDA (2012) Bad bug book: Foodborne pathogenic microorganisms and natural toxins handbook, 2nd ed, US Food and Drug Administration, Silver Spring, p. 127–129. http://www.fda.gov/Food/FoodborneIllnessContaminants/CausesOfIllnessBadBugBook/ucm2006773.htm

Ortega YR, Sanchez R (2010) Update on *Cyclospora cayetanensis*, a food-borne and waterborne parasite. *Clinical Microbiology Reviews* 23(1):218-234

Smith HV (2007) *Cyclospora.* Ch 10 In: Simjee S (ed) Foodborne Diseases. Humana Press, Totowa, p. 277-301

References

Arrowood MJ (2003) *Cyclospora cayetanensis*. Ch 29 In: Miliotis MD, Bier JW (eds) International Handbook of Foodborne Pathogens. Marcel Dekker, New York, p. 503–510

CDC (2004) Outbreak of cyclosporiasis associated with snow peas - Pennsylvania, 2004. Morbidity and Mortality Weekly Report 53(37):876–878

CDC-DPDx (2009) Laboratory identification of parasites of public health concern - Parasites & health.
http://dpd.cdc.gov/dpdx/HTML/Para_Health.htm. Accessed 23 December 2010

CDC (2012) Summary of notifiable diseases - United States, 2010. Morbidity and Mortality Weekly Report 59(53):1–111

Chacin-Bonilla L (2010) Epidemiology of *Cyclospora cayetanensis*: A review focusing in endemic areas. Acta Tropica 115(3):181–193

Dawson D (2005) Foodborne protozoan parasites. International Journal of Food Microbiology 103(2):207–227

Dixon B, Parrington L, Cook A, Pollari F, Farber J (2013) Detection of *Cyclospora, Cryptosporidium,* and *Giardia* in ready-to-eat packaged leafy greens in Ontario, Canada. Journal of Food Protection 76(2):307–313

Gibbs RA, Nanyonjo R, Pingault NM, Combs BG, Mazzucchelli T, Armstrong P, Tarling G, Dowse GK (2013) An outbreak of *Cyclospora* infection on a cruise ship. Epidemiology and Infection 141:508–516

Hall RL, Jones JL, Hurd S, Smith G, Mahon BE, Herwaldt BL (2012) Population-based active surveillance for *Cyclospora* infection - United States, Foodborne Diseases Active Surveillance Network (FoodNet), 1997-2009. Clinical Infectious Diseases 54(Suppl 5):S411–S417

Herwaldt BL (2000) *Cyclospora cayetanensis:* A review, focusing on the outbreaks of cyclosporiasis in the 1990s. Clinical Infectious Diseases 31:1040–1057

Herwaldt BL, Ackers ML, Cyclospora Working Group (1997) An outbreak in 1996 of cyclosporiasis associated with imported raspberries. New England Journal of Medicine 336:1548–1556

Ho AY, Lopez AS, Eberhart MG, Levenson R, Finkel BS, da Silva AJ, Roberts JM, Orlandi PAJ, Johnson CC, Herwaldt BL (2002) Outbreak of cyclosporiasis associated with imported raspberries, Phildelphia, Pennsylvania, 2000. Emerging Infectious Diseases 8(8):783–788

Lainson R (2005) The genus *Cyclospora* (Apicomplexa: Eimeriidae), with a description of *Cyclospora schneideri* n.sp. in the snake *Anilius scytale scytale* (Aniliidae) from Amazonian Brazil - A review. Memórias do Instituto Oswaldo Cruz 100(2):103–110

Milord F, Lampron-Goulet E, St-Amour M, Levac E, Ramsay D (2012) *Cyclospora cayetanensis:* A description of clinical aspects of an outbreak in Quebec, Canada. Epidemiology and Infection 140:626–632

Ortega YR, Liao J (2006) Microwave inactivation of *Cyclospora cayetanensis* sporulation and viability of *Cryptosporidium parvum* oocysts. Journal of Food Protection 69(8):1957–1960

Ortega YR, Sanchez R (2010) Update on *Cyclospora cayetanensis*, a food-borne and waterborne parasite. Clinical Microbiology Reviews 23(1):218–234

Ortega YR, Gilman RH, Sterling CR (1994) A new coccidian parasite (Apicomplexa: Eimeriidae) from humans. Journal of Parasitology 80(4):625–629

Ortega YR, Mann A, Torres MP, Cama V (2008) Efficacy of gaseous chlorine dioxide as a sanitizer against *Cryptosporidium parvum, Cyclospora cayetanensis,* and *Encephalitozoon intestinalis*. Journal of Food Protection 71(12):2410–2414

Ortega YR, Sterling CR, Gilman RH, Cama VA, Diaz F (1993) Cyclospora species - A new protozoan pathogen of humans. New England Journal of Medicine 328(18):1308–1312

Ortega YR, Roxas CR, Gilman RH, Miller NJ, Cabrera L, Taquiri C, Sterling CR (1997) Isolation of *Cryptosporidium parvum* and *Cyclospora cayetanensis* from vegetables collected in markets of an endemic region in Peru. American Journal of Tropical Medicine and Hygiene 57(6):683–686

RTI International (2009) Fresh produce risk ranking tool summary: Identification of priority pathogen-commodity combinations for quantitative microbial risk assessment. http://foodrisk.org/default/assets/File/Produce_RRT_report_RTI.pdf. Accessed 14 November 2012

Sathyanarayanan L, Ortega Y (2004) Effects of pesticides on sporulation of *Cyclospora cayetanensis* and viability of *Cryptosporidium parvum*. Journal of Food Protection 67(5):1044–1049

Sathyanarayanan L, Ortega Y (2006) Effects of temperature and different food matrices on *Cyclospora cayetanensis* oocyst sporulation. Journal of Parasitology 92(2):218–222

Sherchand JB, Cross JH, Jimba M, Sherchand S, Shrestha MP (1999) Study of *Cyclospora cayetanensis* in health care facilities, sewage water and green leafy vegetables in Nepal. The Southeast Asian Journal of Tropical Medicine and Public Health 30(1):58–63

Smith HV (2007) *Cyclospora*. Ch 10 In: Simjee S (ed) Foodborne Diseases. Humana Press, Totowa, p. 277–301

Smith HV, Paton CA, Mtambo MMA, Girdwood RWA (1997) Sporulation of *Cyclospora* sp. oocysts. Applied and Environmental Microbiology 63(4):1631–1632

Tram NT, Hoang LMN, Cam PD, Chung PT, Fyfe MW, Issac-Renton JL, Ong CSL (2010) *Cyclospora* spp. in herbs and water samples collected from markets and farms in Hanoi, Vietnam. Tropical Medicine and International Health 13(11):1415–1420

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