Cyclosporiasis Investigative Guidelines
January 2025

*REPORT WITHIN **1** WORKING DAY*

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To identify outbreaks and potential sources or sites (e.g., a food source or body of water) of ongoing transmission
2. To assess the risk of transmission to additional persons, and to prevent such transmission
3. To educate people about how to reduce their risk of infection
4. To identify additional cases
5. To characterize the epidemiology of this infection including social, environmental, and behavioral contexts for transmission
6. To identify communities and populations at elevated risk for disease or severe illness and inform equity-centered outreach.

1.2 Laboratory and Clinician Reporting Requirements

Laboratories, clinicians, and other persons providing health care are required to report positive test results and confirmed or suspect cases to the Local Public Health Authority (LPHA) by 5 p.m. of the working day following identification or diagnosis.

1.3 Local Public Health Authority Reporting and Follow-Up Responsibilities

1. Report all confirmed and presumptive (but not suspect) cases to the Oregon Public Health Division (PHD) Acute and Communicable Disease Prevention (ACDP) Section by 5 p.m. of the last working day of the week following initial clinician or lab report. Enter information into Orpheus as the investigation occurs. See §3 for case definitions.

2. Interview all confirmed and presumptive cases.
3. Identify significant contacts and educate them about the signs and symptoms of illness. Consider testing in private laboratories or offer testing at the Oregon State Public Health Laboratory (OSPHL), as appropriate. Enter all data into Orpheus by the end of the calendar week.
4. For recognized outbreaks, report to PHD by 5 p.m. of the day following identification, complete investigation in conjunction with the assigned ACDP epidemiologist, and complete the outbreak summary report within 30 day of last case onset.

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

Cyclospora cayetanensis is a coccidian protozoan. After reproducing in the human intestinal epithelium, *C. cayetanensis* coccidian oocysts (8–10 µm in diameter, twice the size of *Cryptosporidium parvum*)[1] are released in the stool of the infected host into the environment, where they sporulate (mature) into infectious oocysts days or weeks later.

Oocysts are relatively hardy in the environment, and they are chlorine-resistant. Conditions for sporulation are not fully understood and various techniques for reducing sporulation in the environment—specifically on fresh produce—are under development.[2] However, routine chemical disinfection or sanitizing methods are presumed unlikely to kill *C. cayetanensis*.[3] Boiling water for ten minutes has been shown to inactivate oocysts.[1]

C. cayetanensis was first classified by Ynés Rosa Ortega and colleagues and named for their Peruvian university, Universidad Peruana Cayetano Heredia.[4] The organism was discovered in the context of early AIDS cases, where it was seen during microscopy for *Cryptosporidium* opportunistic infections.[5]

2.2 Description of Illness

Among symptomatic persons, the most common clinical manifestation is watery diarrhea, which can be profuse and protracted, leading to weight loss. People may also experience abdominal cramps, fatigue, and myalgia (muscle pain). Diarrhea is usually self-limited after 10–24 days,but may be intermittent during this period. Immune-compromised people may experience diarrhea for months.

Asymptomatic infection has been documented, particularly in settings where cyclosporiasis is endemic.

Cyclospora infection has also been associated with immune-mediated complications including Guillain-Barré syndrome and reactive arthritis syndrome (formerly Reiter syndrome). Another clinical manifestation of *C. cayetanensis* infection in people living with HIV is biliary disease, and it has also caused acalculous cholecystitis and cholangitis in people living with AIDS.[6]

2.3 Reservoirs

While other species of *Cyclospora* have been found in primates[7] and research is exploring the potential for waterfowl as reservoirs for *Cyclospora* and other enteric pathogens,[8] humans are currently believed to be the only host of *C. cayetanensis*. Oocysts have been found in the feces of dogs and chickens, but it is not clear whether the organism is able to infect these species or to reproduce in their intestines; the oocysts could have come from something the animals ate.

Cyclospora appears to be most common in tropical and subtropical regions of the world,[1] and sporulation of the oocysts depends on ambient temperature.[9] *C. cayetanensis* is currently considered endemic in Central and South America, parts of the Middle East and North Africa, the Indian subcontinent, and Southeast Asia.[6] Notable prevalence has been observed in Bangladesh, Brazil, Chile, China, Cuba, Dominican Republic, Egypt, Guatemala, Haiti, India, Indonesia, Jordan, Mexico, Morocco, Nepal, Nigeria, Pakistan, Peru, the U.S. territory of Puerto Rico, Romania, Saudi Arabia, Tanzania, Thailand, Türkiye (formerly Turkey), Venezuela, Vietnam, and Zimbabwe.[5]

It is expected that the geographical range of *Cyclospora* and other enteric protozoa will be altered with the changing climate.[10]

2.4 Sources and Routes of Transmission

Transmission of *C. cayetanensis* is environmentally mediated fecal-oral. Sporulated oocysts are ingested either through drinking contaminated water or consuming contaminated uncooked fruits and vegetables. Unlike *Giardia* and other parasites with irregular shedding patterns, *C. cayetanensis* is believed to be released continuously at low levels in stool.[9] Notably, *C. cayetanensis* oocysts in freshly excreted stool are not immediately infectious; they require days to weeks outside the host at temperatures of 22–32°C to sporulate and become infectious. As a result, person-to-person transmission is unlikely.

In the United States, outbreaks of cyclosporiasis associated with various types of imported fresh produce have been recognized and investigated almost every year since 1995.[5] Bagged salad greens have been associated

with multiple outbreaks.[11] Other outbreaks have been attributed to raspberries, basil and other fresh herbs, mesclun/spring mix (assorted baby greens), and snow peas. Large outbreaks have been associated with prepared produce items, such as prepackaged salads[12] and vegetable trays.[13]

In 2018, *Cyclospora* was identified on U.S.-grown produce (cilantro) for the first time,[14] but no outbreaks have been definitively traced to U.S.-grown produce.[9] One outbreak showed a possible link to contamination of pesto sauce by a U.S.-based food handler.[2]

Instances of a domestic sewer backup, ingestion of water from a salt aquarium, and drinking water storage facilities at a hospital suggest that waterborne transmission of *Cyclospora* is possible in the U.S.[5,15] *Cyclospora* has been found in drinking water in many locations in the world, and an outbreak of cyclosporiasis in Nepal was attributed to drinking water.[5] *Cyclospora* has also been found in wastewater and environmental water, though there is no definitive evidence of this causing disease in the U.S..[5]

C. cayetanensis has been found in soil, and cyclosporiasis incidence is highly associated with fecally contaminated soil in areas where sanitary toilet facilities are limited.[6] There may be an association between *Cyclospora* infection and contact with livestock.[16] There is limited scientific literature about detection of *C. cayetanensis* in soil or water.[17]

Many aspects of the biology of *C. cayetanensis* and the epidemiology of cyclosporiasis are poorly understood,[18] and it is often difficult to identify the mode of transmission due to the characteristics of the organism (it takes several days to sporulate) and the nature of raw produce consumption (ingredients are often mixed together, oocysts may have been on garnishes that went unnoticed by consumers, produce has a short shelf life).

Advances in clinical diagnosis may have contributed to the rise in reported cyclosporiasis cases,[9] but it is also believed that increased incidence is driven by the growth in international travel, globalization of food systems, and changing dietary habits.[2]

Genetically linking cases of cyclosporiasis has historically been difficult, but new laboratory technologies are showing promise.[11]

2.5 Risk Dynamics

Any person can be infected with *Cyclospora.* Some populations may be at elevated risk of contact with water or food contaminated with sporulated *Cyclospora* oocysts because of their living or working conditions.

Cyclospora has also been associated with diarrhea in travelers to Asia, Central and South America, and Africa.[1] Therefore, people who travel to these regions are at elevated risk. A person's travel behaviors and destinations could be influenced by their wealth (leisure travel) or their cultural heritage (personal or historical connections in an area). In endemic areas, low socioeconomic status and neighborhood poverty are correlated with infection.[6] Accordingly, people who travel to or from these communities to the U.S. may be at increased risk.

Additionally, since most outbreaks are associated with uncooked produce, people with a high amount of unwashed and raw, unpeeled, or lightly cooked fruits and vegetables in their diet could be at elevated risk—particularly if they are consuming produce that has been imported from outside the U.S. or ready-to-eat produce items such as salad kits.

In temperate climates, incidence is higher during the warm season; in the U.S. cases are highest in May, June, and July. However, seasonal variation is different in different parts of the world, usually reflecting warm or rainy seasons.[16]

People HIV or HIV/tuberculosis coinfection may be vulnerable to more severe disease.[1,19]

Reported U.S. cyclosporiasis has primarily occurred among adults, with relatively few cases among children and older adults. It is unknown, however, if this distribution reflects lower rates of exposure (e.g., due to diet), infection, illness, diagnosis, or reporting of cases in these groups.[3]I In endemic areas, children are at risk of more severe disease, but symptoms seem to be less common as people age—suggesting that frequent exposure reduces the likelihood of illness. In endemic areas, people may start to experience symptoms again as they reach old age.[2]

People who encounter contaminated water are at increased risk of cyclosporiasis. This could include agricultural workers (exposed to irrigation water) and people who spend time in areas with less stringent food handling or wastewater management practices, including situations where drinking water is drawn from surface water sources. People can also be exposed by recreating in water.

2.6 Incubation Period

The incubation period for cyclosporiasis ranges from 2 to 14 or more days, with an average of 7 days.

2.7 Period of Communicability

Not applicable. Person-to-person transmission of *Cyclospora* seems unlikely.

2.8 Treatment

A 7–10-day course of oral trimethoprim-sulfamethoxazole has been shown to cure about 90% of cases. Ciprofloxacin is less effective but may be used for infected people allergic to sulfa drugs.[1] Laboratory diagnosis is important before beginning treatment, since treatment of *Cyclospora* differs from that of some other protozoa that cause similar symptoms.[10]

Patients with HIV may require higher dosages and longer treatment, and this may also be the case for patients with compromised immune systems.[10] All patients should be supported to maintain hydration and electrolyte balance during treatment. People who go untreated may experience prolonged, remitting, and relapsing symptoms.[1]

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

3.1 Confirmed Case

A confirmed case is defined as a person who meets the clinical description of cyclosporiasis and one of the criteria for laboratory confirmation:

1) The clinical description is illness of variable severity where most common symptom is watery diarrhea. Other common symptoms include loss of appetite, weight loss, abdominal cramps/bloating, nausea, body aches, and fatigue. Vomiting and low-grade fever also may be noted.

AND

2) Laboratory confirmation is:
   - detection of *Cyclospora* organisms, **OR**
   - DNA in stool, intestinal fluid/aspirate, **OR**
   - intestinal biopsy specimens.

3.2 Presumptive Case Definition

A presumptive case is defined as a person with a diarrheal illness (often watery) including loss of appetite, weight loss, abdominal cramps/bloating **AND** is epidemiologically linked to a confirmed case.

3.3 Services Available at the Oregon State Public Health Laboratories (OSPHL)

OSPHL does not perform microscopy for *Cyclospora*.

OSPHL can perform PCR testing for *Cyclospora* using BioFire. Testing must be approved by ACDP Epidemiologists prior to specimen submission.

Collect fresh stool and place in Cary Blair transport media. Mix well. Complete specimen acceptance criteria are available on the OSPHL Lab Test Menu at www.healthoregon.org/labtests. All specimens must be properly packaged for transport and be accompanied by the Virology/Immunology Test Request Form (Form #42).

Molecular testing or genotyping of stool specimens is available at the CDC in certain situations after consultation with and approval from ACDP.

3.4 *Cyclospora* Laboratory Testing

Samples can be examined by light microscopy, in wet mount (enhanced by ultraviolet fluorescence) or in stained smears (using a modified acid-fast stain or modified safranin technique). Molecular tests, such as polymerase chain reaction (PCR), are increasingly being used to detect deoxyribonucleic acid (DNA) in stool samples and are commercially available.[1] *C. cayetanensis* is not tested in standard ova and parasite (O&P) clinical diagnostic panels, nor in all gastrointestinal PCR panels.[3] Therefore, clinicians must request a *C. cayetanensis*-specific investigation, such as targeted microscopy or PCR for diagnosis. The most sensitive method for clinical *Cyclospora* detection is quantitative real-time PCR (qPCR). This format is employed by the BioFire® FilmArray® Gastrointestinal (GI) Panel, which allows clinicians to test for *C. cayetanensis* as part of a routine syndromic workup.[9]

4. ROUTINE CASE INVESTIGATION

Routine case investigation should include the documentation of case demographic, laboratory, and clinical data. Personal information should be collected based on people's self-reported identities and should include "REAL-D" and "SOGI" information.

Interview the case (or primary caregivers) and any additional persons who may be able to provide pertinent information. Use professional interpretation services rather than relying on family members or community interlocutors unless there is mutual consent between the case and the lay interpreter that they will feel more comfortable communicating without a professional intermediary.

4.1 Identify Source of Infection

Ask about possible exposures in the 1–14 days before onset, and be sure to obtain:

1. Name, diagnosis, and phone number of any acquaintances or household members with a similar illness. (N.b.: any person meeting the presumptive case definition should be reported and investigated in the same manner as a confirmed case)
2. Information for the Cyclosporiasis National Hypothesis Generating Questionnaire v3.4,[20] which addresses potential exposures including:
   - Travel outside the United States, particularly tropical or semitropical regions
   - Eating berries, fresh herbs, lettuce, and other produce, particularly imported products
   - Consuming unboiled drinking water, particularly during travel
3. Other high-risk exposures as detailed in the Cryptosporidiosis case-report form or in the Orpheus Risks tab

4.2 Identify Potentially Exposed Persons

Person-to-person transmission is unlikely; focus on others exposed to the suspected source of infection who also have a similar diarrheal illness. Consider meal companions or other congregate settings with similarly ill persons. If others are identified, consider starting an outbreak investigation.

5. CONTROLLING FURTHER SPREAD

5.1 Education

Given the unlikelihood of person-to-person transmission, consumers should be educated about the general benefit of hygienic food preparation practices, such as washing and refrigerating produce. Therefore, control should focus preventing the introduction of oocysts to sites of food production and preparation; see §5.5.

1. Cases should be educated about proper hand hygiene particularly after using the toilet and before preparing food.
2. People who travel to risk areas (endemic regions, tropical and semitropical areas) should be advised about the potential for exposure and advised to drink only boiled water (chlorine or iodine treatment is not effective) and eat only cooked hot foods or produce (fruits and vegetables) that they peel themselves.
3. As a general rule, fresh produce should be washed and refrigerated.

4. People with diarrhea should avoid swimming pools.
5. Contact precautions should be used for diapered or incontinent persons.
6. Persons should try to avoid swallowing recreational water, especially when traveling in risk areas.

5.2 Isolation and Work or Child Care Restrictions

As a general rule, persons should not work as food handlers or attend child care while they have diarrhea. See OAR 414-310-0550 for exclusion criteria from certified child care facilities. Per OAR 333-175-0051**,** a person may not work in food service for 24 hours after symptoms of vomiting or diarrhea have ended.

5.3 Case Follow-up

Generally not indicated.

5.4 Protection of Contacts

1. Contacts (including those sharing potential exposures) with symptoms compatible with cyclosporiasis should be referred to a health care provider for evaluation.
2. Contacts are generally at low risk for acquiring infection from a case since oocysts excreted in the stool are not infectious.

5.5 Environmental Measures

Because person-to-person transmission of *Cyclospora* is unlikely, control emphasis should therefore be placed on limiting introduction of oocysts into the environment and onto produce, where they can sporulate. Food growers and handlers should wash hands regularly, wear gloves when possible, and abstain from work if experiencing diarrhea. The Food and Drug Administration has released recommendations for agricultural settings to reduce contamination of produce[21] and many techniques are being explored to reduce contamination of berries, which have been implicated repeatedly in outbreaks of cyclosporiasis.[22] Managing waste water and runoff from areas where humans defecate are other important mechanisms for minimizing the spread of *Cyclospora* and other enteric protozoa.[10]

6. MANAGING SPECIAL SITUATIONS

6.1 Case Attends a Childcare Facility

If the case is a child, determine whether they should be excluded (see §5.2). If the facility includes diapered children, interview the operator and inspect attendance records to identify additional cases among other children or staff during the preceding month.

Instruct the facility operator and staff about proper food handling and hand washing after diaper-changing, and the importance of keeping diaper-changing areas away from food preparation areas.

6.2 Contaminated Swimming Pools and Recreational Water Facilities

Some amount of feces in pools (“accidents”) is unavoidable but does pose a risk to other bathers. The risk from formed stools (which are most likely to be detected) is much lower than the risk from loose matter from a toddler with an infection. Fecal accidents should be managed using general guidelines for dealing with “stool-in-pool” events.

Review the CDC’s recreational water illness outbreak response and healthy swimming guidelines,[23,24] and consult with ACDP staff in any situation in which a presumed or confirmed case is linked to any recreational water site.

6.3 Reported Incidence is Significantly Higher than Usual

If the number of reported cases in your county is higher than usual for the time of year or for a particular group (age, gender, race, ethnicity, etc.), or you note possible epidemiological connections, consider the possibility of common-source outbreaks. Review the temporal, geographic, and demographic clues that you have. Remember to account for seasonal patterns; cyclosporiasis season begins in late spring.

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UPDATE LOG

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