

## Leaf It to *Cyclospora*: A Parasite's Journey Through Oregon

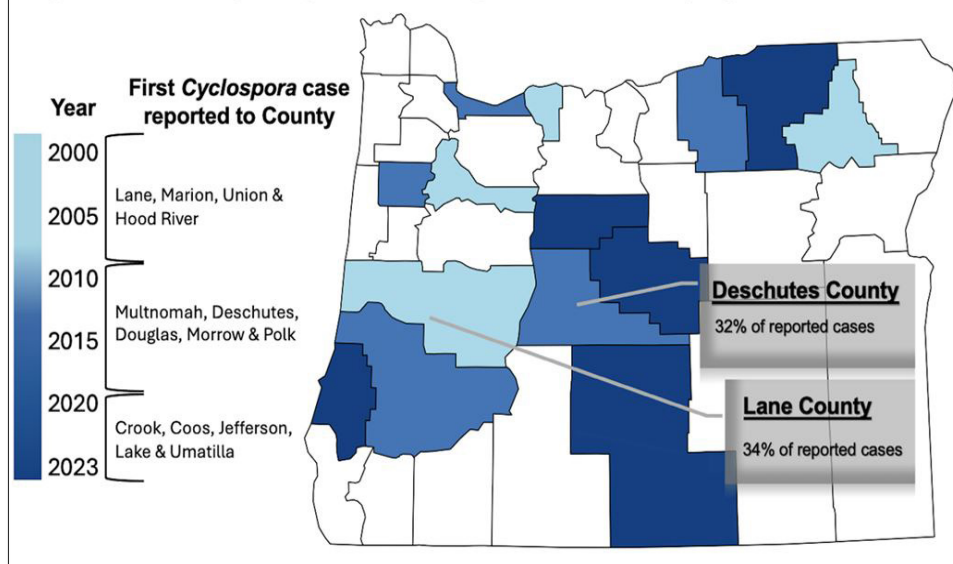
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The first cyclosporiasis cases were reported in the 1970s from travelers in geographic areas where the pathogen is endemic, most commonly in tropical and subtropical regions.<sup>1</sup> During its initial characterization, it was misidentified as “cyanobacterium-like bodies,” colloquially termed “big *Cryptosporidium*,” and was even hypothesized to be an alga based on its microscopic morphology.<sup>2,3</sup> Since then, international travel and the globalization of the food supply have increased the risk of exposure to foodborne parasites, particularly through the consumption of raw, undercooked, or improperly processed foods. In recent years, infections have increased among persons without any history of international travel. The National Institute of Allergy and Infectious Diseases has determined the organism as a Category B emerging pathogen due to its rapid increase in incidence and geographic range.<sup>4</sup> Although cases can occur year-round, national surveillance has shown increased case counts in the spring and summer within the United States.<sup>5</sup>

### *Cyclospora* diaspora

*Cyclospora cayetanensis* was formally classified in 1992 by Ynés Rosa Ortega and colleagues at the Universidad Peruana Cayetano Heredia following the first outbreak attributed to cyclosporiasis; however, the exact source of the infection remains unknown.<sup>6,7</sup> After several major multistate outbreaks linked to raspberries from Guatemala, cyclosporiasis became nationally notifiable in January 1999 and is currently reportable in 43 states.<sup>8</sup> The infectious agent is a microscopic, unicellular parasite classified as a coccidian protozoan.<sup>9</sup> Anyone can contract cyclosporiasis by ingesting sporulated oocysts that typically come from food or water contaminated with feces.<sup>9</sup> This parasite lives inside the intestinal lining—and produces oocysts that are passed in the feces.<sup>9</sup> The diameter of *Cyclospora* oocysts is 8–10 µm, approximately twice that of *Cryptosporidium*

Figure 1. First *Cyclospora* case reported in County by Year, 2005-2023



*parvum*.<sup>9</sup> The oocysts have to sporulate after maturing over days to weeks in the environment in order to become infective; direct person-to-person spread is unlikely and in fact has not been documented.<sup>9</sup> Although some cases may be asymptomatic, the most common symptom of infection is watery non-bloody diarrhea; with frequent, and sometimes explosive stool.<sup>10</sup> Other common symptoms include loss of appetite and weight, stomach pain or cramps, nausea, prolonged fatigue, increased flatus, vomiting, low-grade fever, myalgia and other nonspecific symptoms.<sup>10</sup> Without treatment, symptoms can persist for several weeks to a month or longer and may follow a relapsing-remitting pattern.<sup>10</sup>

Transmission dynamics of *Cyclospora* in endemic regions remains inadequately characterized, primarily due to limitations in the sensitivity and specificity of current environmental detection methods.<sup>11</sup> Humans are the only known host.<sup>12</sup> In the United States, cyclosporiasis outbreaks have been linked to a variety of fresh produce, including raspberries, basil, cilantro, snow peas, and mesclun and

romaine lettuce.<sup>9</sup> The largest outbreak in the U.S. was in 2020: 14 states in the Midwest saw a total of 701 confirmed cases with 38 hospitalizations (but no deaths) attributed to the consumption of bagged salad.<sup>9</sup> Two outbreaks of *Cyclospora* infection have been investigated in Oregon. In 2005, four confirmed and 24 presumptive cases cropped up among members of a large group of medical relief workers who had traveled to Guatemala; despite an investigation, the source remains unknown. In 2021, Deschutes County had an outbreak with six confirmed cases that met the definition and no international travel. Health officials investigated a local restaurant as the potential source but were unable to identify the exact cause. This incident was notable as it marked the first time such an outbreak was detected in Oregon without any connection to international travel.

### Diagnosis dialogue

Diagnosis of *Cyclospora* infection is challenging; providers must request specific testing for parasites. The use of polymerase chain reaction panels and specific DNA probes is becoming more common. Stool culture does not identify parasitic infec-

tions—cyclosporiasis, cryptosporidiosis or giardiasis. If one is thinking a parasitic infection, an appropriate test must be specified. Culture-independent diagnostic tests (CIDTs) such as BioFire and Nano-sphere can test for multiple gastrointestinal pathogens and have increasingly been used for diagnostics across the U.S.<sup>13</sup> Since 2021, 77% of reported cyclosporiasis cases in Oregon have been diagnosed using a CIDT.

Compared to bacterial enteric pathogens, such as *Salmonella*, *Shigella*, Shiga toxin-producing *E. coli*, or *Campylobacter*, public health has less experience using genetic sequencing data to detect disease clusters. With *Cyclospora*, genotyping is the main tool to detect clusters. The Centers for Disease Control and Prevention (CDC) reports these genetically identified clusters weekly during peak season, May–September. Genotyping helps local epidemiologists prioritize cases for follow-up and suggests cases that likely share a common source of infection. The Oregon State Public Health Laboratory (OSPHL) does not have the capacity to sequence *Cyclospora*, so we rely on CDC for this work. This requires that positive specimens be sent to OSPHL for forwarding to CDC. In practice, we generally request specimens only when we see a cluster or know that the patient did not travel internationally during their exposure period. These efforts are important to contribute to the genetic library of data for understanding *Cyclospora* transmission and spread within the United States. We applaud Oregon labs that contribute to this work.

## The Oregon Experience

Oregon records but a handful of cyclosporiasis cases each year. More than half (63%) have been female, ranging in age from 13 to 86 years (median, 49). Geographically, cases first appeared in Lane, Union and Hood River County, but since 2010 have been seen in Central Oregon and Portland Metro regions—most likely following the pattern of laboratories adopting CIDTs. No Oregon cases have been hospitalized or died from their illness. *Figure 1* shows how case reports of this pathogen have emerged over time and geographically across Oregon, and the counties that have the highest percentage of reported cases. *Figure 2* compares Oregon to U.S. incidence rates by year from 2005 to 2020. Oregon cyclosporiasis rates of aligned with those of the U.S. until 2012. While Oregon has seen slight increases in cases per 100,000 persons per year, the national rates have skyrocketed. Hypotheses for increased rates are still being considered.<sup>11</sup>

Histories for 68 (96%) of Or-

gon's confirmed cases included travel: predominantly to Guatemala (47%) or Mexico (44%), but also to El Salvador, Peru, China, Malaysia, Thailand, Laos, or Costa Rica. The first domestically acquired Oregon case was reported in 2017, followed by a second within the same year. Both cases' source of infection was unknown even after extensive public-health interrogation to identify possible risks. Since 2017, six (15%) of the reported cases were apparently domestically acquired. Four of these were part of an outbreak in 2021 associated with a restaurant; but after a detailed outbreak questionnaire administered to employees and cases, collection of stool specimens from employees, and a thorough environmental investigation, the source of infection was never found.

## Endemic Burden

There is a concern that *Cyclospora* will become endemic in the U.S. due to the sharp rise (a 101% increase) of reported domestically acquired cases in the last year, with cases reported from more than 40 States.<sup>9</sup> CDC has reported 8,070 domestically acquired cyclosporiasis cases from 2019 through 2023.<sup>14</sup>

In 2019, the U.S. Food and Drug Administration (FDA) created a *Cyclospora* Task Force in response to the increased burden of foodborne cyclosporiasis in the U.S.<sup>15</sup> The task force will focus on three main areas: improving prevention, enhancing response activities and filling knowledge gaps.<sup>15</sup> During February–June 2023, FDA also developed a screening assay for detection of *Cyclospora* within produce, soil, and surface agricultural water.<sup>15</sup>

Detecting *C. cayetanensis* from produce, environmental samples, and stool is difficult due to generally low levels of oocysts. Chemicals used for food or water treatment, like pesticides and antimicrobials, have little to no effect on sporulation and survival of *C. cayetanensis*.<sup>16</sup> Continued challenges with testing, diagnosis, and prevention, along with increased importation of fresh produce and failures to mitigate the disease, raise concerns of a shift to endemicity in the U.S.

## Clinician Role and prevention:

Cyclosporiasis should be considered in the differential diagnosis for persons who present with prolonged or remitting-relapsing diarrheal illness, and specific testing for *Cyclospora* must generally be requested. The treatment of choice for cyclosporiasis is a combination of trimethoprim at 160 mg and sulfamethoxazole at 800 mg taken twice daily for 7–10 days in immunocompetent adults; for children aged 2 months to 18 years, the recommended dose is 8 to 10 mg of trimethoprim and 40 to 50 mg of sulfamethoxazole per kilogram

of body weight per day, divided into two doses, while immunocompromised individuals may require an extended duration of treatment.<sup>17</sup>

As recommended by FDA, they should be advised to wash produce thoroughly before ingesting to reduce risk of infection.<sup>9</sup> Travelers to cyclosporiasis-endemic areas should be advised that food and water precautions are similar to those for other intestinal pathogens; however, the parasite is unlikely to be killed by standard chemical disinfectants, and no vaccine is available to prevent cyclosporiasis.

Cyclosporiasis is reportable in Oregon: suspected and confirmed cases should be reported to the appropriate Oregon local public health authority (LPHA) within one working day. If your information systems are unable to report electronically (via electronic laboratory or case report), you can enter reports manually into our secure, confidential '[Online Morbidity Report](#)' portal. Reports can also be made directly to your LPHA by fax or telephone.

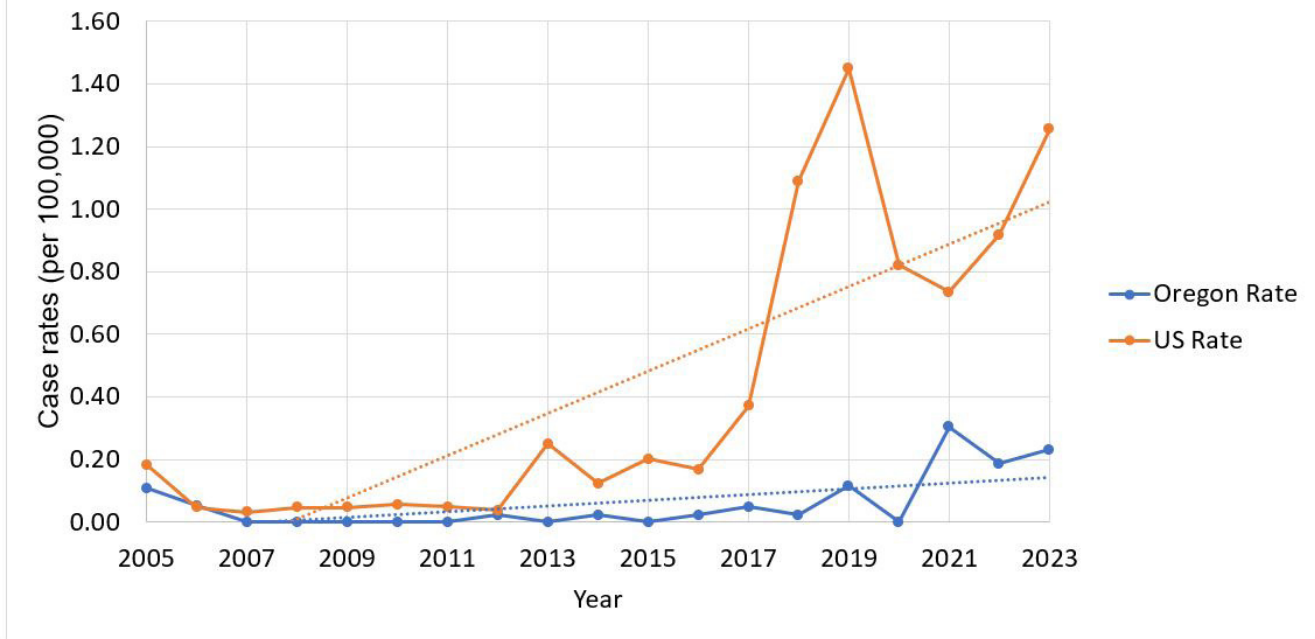
## For More Information:

- OHA information on *Cyclospora*: [www.oregon.gov/oha/PH/DISEASES/CONDITIONS/DISEASESAZ/Pages/cyclosporiasis.aspx](http://www.oregon.gov/oha/PH/DISEASES/CONDITIONS/DISEASESAZ/Pages/cyclosporiasis.aspx)
- Oregon outbreak investigation webpages: [www.oregon.gov/oha/PH/DiseasesConditions/CommunicableDisease/Outbreaks/Pages/index.aspx](http://www.oregon.gov/oha/PH/DiseasesConditions/CommunicableDisease/Outbreaks/Pages/index.aspx)
- Oregon restrictions on school and day-care attendance, food handling and patient care: [www.oregon.gov/oha/PH/DiseasesConditions/CommunicableDisease/ReportingCommunicableDisease/Pages/rules.aspx](http://www.oregon.gov/oha/PH/DiseasesConditions/CommunicableDisease/ReportingCommunicableDisease/Pages/rules.aspx)
- FDA: [www.fda.gov/food/food-borne-pathogens/cyclospora](http://www.fda.gov/food/food-borne-pathogens/cyclospora)
- CDC: [www.cdc.gov/parasites/cyclosporiasis/index.html](http://www.cdc.gov/parasites/cyclosporiasis/index.html)
- Historic CDC Outbreak Data (2000–2017): [www.cdc.gov/parasites/cyclosporiasis/outbreaks/foodborneoutbreaks.html](http://www.cdc.gov/parasites/cyclosporiasis/outbreaks/foodborneoutbreaks.html)

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**Figure 2. Cyclosporiasis case rates in Oregon vs nationwide, 2005-2023**



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