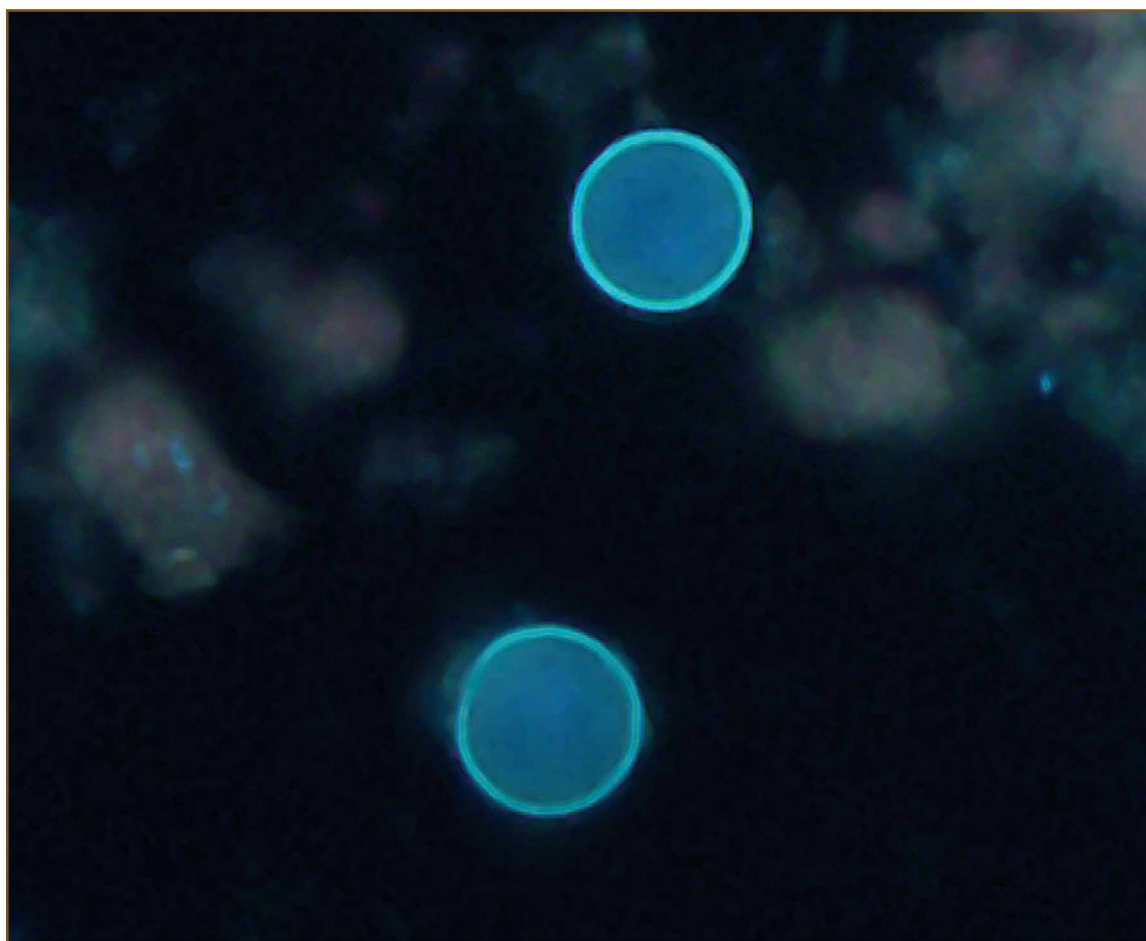


Surveillance for Laboratory-Confirmed Sporadic Cases of Cyclosporiasis — United States, 1997–2008



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

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Front cover photo: Oocysts of the parasite *Cyclospora cayentanensis* as seen by using ultraviolet (UV) fluorescence microscopy. *Cyclospora* oocysts are spherical and approximately 7.5–10 μm in diameter; they appear blue under a UV microscope (excitation filter set at 330–365 nm). More information is available at <http://www.dpd.cdc.gov/dpdx>.

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Surveillance for Laboratory-Confirmed Sporadic Cases of Cyclosporiasis — United States, 1997–2008

Rebecca L. Hall, MPH^{1,2}

Jeffrey L. Jones, MD²

Barbara L. Herwaldt, MD²

¹Atlanta Research and Education Foundation, Decatur, GA

²Division of Parasitic Diseases and Malaria, Center for Global Health, CDC

Abstract

Problem/Condition: Cyclosporiasis is an enteric disease caused by the parasite *Cyclospora cayetanensis*. Cyclosporiasis is reported most commonly in tropical and subtropical regions. In the United States, outbreaks of cyclosporiasis associated with various types of imported fresh produce have been documented and described since the mid-1990s. No molecular tools are available for linking *C. cayetanensis* cases. National data regarding laboratory-confirmed sporadic cases (i.e., cases not linked to documented outbreaks) have not been summarized previously.

Reporting Period: This summary includes laboratory-confirmed sporadic cases that occurred during 1997–2008 and were reported to CDC by 2009.

Description of System: In January 1999, cyclosporiasis became a nationally notifiable disease, and, as of 2008, it was a reportable condition in 37 states, New York City (NYC), and the District of Columbia. For 1997–2008, CDC was notified of laboratory-confirmed cases via two active surveillance systems (the *Cyclospora* Sentinel Surveillance Network and the Foodborne Diseases Active Surveillance Network), two passive systems (the National Notifiable Diseases Surveillance System and the Public Health Laboratory Information System), and informal mechanisms (e.g., electronic mail).

Results: CDC was notified of 1,110 laboratory-confirmed sporadic cases of cyclosporiasis that occurred during 1997–2008. The overall population-adjusted incidence rates ranged from a low of 0.01 cases per 100,000 persons in 1997 to a high of 0.07 in 2002. Of the 1,110 cases, 849 (76.5%) were reported by seven states: 498 (44.9%) occurred in residents of Florida (228 cases), NYC (200 cases), and elsewhere in New York state (70 cases); and >50 cases were reported by each of five other states (Connecticut, Georgia, Massachusetts, New Jersey, and Pennsylvania). Overall, the case-patients' median age was 44 years (range: 3 months–96 years); 50.5% were female, 47.2% were male, and the sex was unknown for 2.3%. A total of 372 case-patients (33.5%) had a documented history of international travel during the 2-week period before symptom onset or diagnosis, 398 (35.9%) reported no international travel, and 340 (30.6%) had an unknown travel history. Some details about the travel were available for 317 (85.2%) of the case-patients with a known history of international travel; 142 (44.8%) had traveled to Mexico (60 persons), Guatemala (44 persons), or Peru (38 persons). Among the 398 case-patients classified as having domestically acquired cases, 124 persons (31.2%) lived in Florida, and 64 persons (16.1%) lived either in NYC (49 persons) or elsewhere in New York state (15 persons). The majority (278 [69.8%]) of onset or diagnosis dates for domestically acquired cases occurred during April–August.

Interpretation: Approximately one third of cases occurred in persons with a known history of international travel who might have become infected while traveling outside the continental United States. Domestically acquired cases were concentrated in time (spring and summer) and place (eastern and southeastern states): some of these cases probably were outbreak associated but were not linked to other cases, in part because of a lack of molecular tools.

Public Health Action: Surveillance for cases of cyclosporiasis and research to develop molecular methods for linking seemingly sporadic cases should remain U.S. public health priorities, in part to facilitate identification and investigation of outbreaks and to increase understanding of the biology of *Cyclospora* and the epidemiology of cyclosporiasis. Unidentified, uninvestigated cases and outbreaks represent missed opportunities to identify vehicles of infection, modes of contamination, and preventive measures. Travelers to known areas of endemicity should be advised that food and water precautions for *Cyclospora* are similar to those for

other enteric pathogens, except that this parasite is unlikely to be killed by routine chemical disinfection or sanitizing methods. The diagnosis of cyclosporiasis should be considered for persons with persistent or relapsing-relapsing diarrheal illness, and testing for *Cyclospora* should be requested explicitly.

Corresponding author: Rebecca L. Hall, MPH, Center for Global Health, CDC, 4770 Buford Highway N.E., MS F-22, Atlanta, GA 30341. Telephone: 770-488-7319, Fax: 770-488-7761, E-mail: bqu5@cdc.gov.

Introduction

Cyclosporiasis is an enteric disease caused by the parasite *Cyclospora cayetanensis*, a unicellular, coccidian parasite transmitted by ingestion of infective oocysts (e.g., through contaminated food or water). The most common symptom is watery diarrhea. Although humans are the only known hosts of this *Cyclospora* species, direct person-to-person transmission is unlikely; the oocysts shed in feces require days to weeks under favorable environmental conditions to become infective (1,2). The need for *Cyclospora* oocysts to survive long enough both to sporulate and subsequently to be ingested by a susceptible person suggests that the oocysts are quite hardy (1,2) and unlikely to be killed by routine chemical disinfection or sanitizing methods used for food or water (3). The incubation period averages 1 week (range: ~2–14 days). Infection responds to treatment with trimethoprim-sulfamethoxazole, but untreated persons can have prolonged illness, with remitting-relapsing symptoms, for several weeks or months (1).

Cyclosporiasis is reported most commonly in tropical and subtropical regions. In retrospect, the first cases of cyclosporiasis documented in the literature occurred in 1977 and 1978 in Papua New Guinea (4). In the mid-1980s, several cases were described in U.S. travelers returning from Haiti and Mexico (5). In the mid-1990s, *Cyclospora* emerged as a foodborne pathogen of U.S. public health concern in the context of large, multistate outbreaks in 1996 and 1997, with >1,000 outbreak-associated cases reported in both years (1,2,6,7).

In June 1998, the Council of State and Territorial Epidemiologists (CSTE) voted to add cyclosporiasis to the list of nationally notifiable conditions (NNCs), effective January 1999 (8). As of 2008, cyclosporiasis was an explicitly reportable disease (i.e., it was listed as a specific disease or as a category of diseases on reportable disease lists) in 37 states, New York City (NYC), and the District of Columbia (DC) (9,10).

CDC, in collaboration with jurisdiction public health authorities, analyzes each reported case for epidemiologic evidence of linkage to other cases to facilitate rapid identification and investigation of outbreaks. U.S. clusters of cases have been documented almost every year since 1995. Various types of imported fresh produce (e.g., raspberries and snow peas from Guatemala and mesclun lettuce and basil from Peru) have been implicated (1,2,6,7,11,12). To date, U.S. publications about the epidemiology of cyclosporiasis have focused on outbreaks (1,2,6,7,11–16). This is the first summary of national data regarding laboratory-confirmed cases of cyclosporiasis that were not linked to documented outbreaks.

Methods

Data Sources

For 1997–2008, laboratory-confirmed cases of cyclosporiasis were reported to CDC by jurisdiction health departments via multiple surveillance systems and reporting methods. These included two active surveillance systems (the *Cyclospora* Sentinel Surveillance Network and the Foodborne Diseases Active Surveillance Network), two passive systems (the National Notifiable Diseases Surveillance System and the Public Health Laboratory Information System), and informal mechanisms (e.g., electronic mail).

In February 1997 (2 years before cyclosporiasis became a NNC), CDC launched the *Cyclospora* Sentinel Surveillance Network (CSSN). The original network participants were eight of the health departments that reported outbreak-associated cases of cyclosporiasis in 1996* (6). Participating sites collect reports from selected laboratories in their jurisdictions and submit aggregate *Cyclospora* test results to CDC monthly during September–March and weekly during April–August, when heightened surveillance is conducted.

The Foodborne Diseases Active Surveillance Network (FoodNet) is the foodborne disease component of CDC's Emerging Infections Program (17). Since 1996, FoodNet has conducted laboratory-based surveillance for selected foodborne pathogens of public health importance. Surveillance for cases of *Cyclospora* infection began in 1997 in four of the five states that were in the network then: Minnesota, Oregon, and selected counties in California and Connecticut (18); Georgia began *Cyclospora* surveillance in 1998. The number of jurisdictions in the network increased each year through 2004 (18). During 2004–2008, the network included all of the counties in seven states (Connecticut, Georgia, Maryland, Minnesota, New Mexico, Oregon, and Tennessee) and selected counties in three additional states (California, Colorado, and New York state [not including NYC]). Among these 10 states, California is the only one in which cyclosporiasis had not become an explicitly reportable disease as of 2008.

The National Notifiable Diseases Surveillance System (NNDSS) was initiated in 1961, when CDC assumed responsibility for collecting and publishing data regarding NNCs (19). Electronic reporting of cases of NNCs began in 1990, with the launch of the National Electronic Telecommunications System for Surveillance (NETSS) (20).

*The original participants included Connecticut, Florida, Maryland, Massachusetts, NYC, New York state, Ohio, and South Carolina. These jurisdictions were among the 20 states that reported cases associated with the multistate outbreak in 1996; DC and two Canadian provinces also reported cases (6). The network was formed thereafter, in February 1997, in anticipation of the occurrence of outbreaks in 1997. Formal (as opposed to informal) participation in this sentinel network decreased over time. By 2008, the network consisted of Connecticut and DC.

The Public Health Laboratory Information System (PHLIS), launched in 1989, is a national surveillance system for infectious diseases, which accommodates transmission of various types of data (e.g., laboratory and epidemiologic) from and among multiple entities (e.g., hospitals, laboratories, health departments) and to CDC (21). In 1992, the reporting system was available in 41 state public health laboratories (21).

CDC also is notified of cyclosporiasis cases through informal means, such as electronic mail and telephone calls. If indicated, CDC asks the health department to complete and submit a U.S. cyclosporiasis surveillance case report form (CRF), which is available at http://www.cdc.gov/parasites/cyclosporiasis/health_professionals/index.html. The CRF solicits clinical, demographic, travel, and exposure data, including whether the case-patient attended any events at which food was served (e.g., a wedding or conference) and knew of other ill persons.

Definitions

For the purposes of these analyses, a sporadic case of *Cyclospora* infection was defined as a laboratory-confirmed case that occurred during 1997–2008, was reported to CDC by 2009, met the surveillance definition applicable at the time (Table 1), and was not linked to a documented outbreak (e.g., an event-associated cluster of cases). The exposure period was defined as the 2-week period before symptom onset or the earliest available alternative date, typically the date of diagnosis or specimen collection; a report date was used to define the exposure period for <2% of cases.

A travel-associated case was defined as a sporadic case in a U.S. resident or recent immigrant (e.g., an adopted infant) who had been outside the United States during all or part of the exposure period[†]; travel to a U.S. territory was categorized as international. A domestically acquired case was defined as a sporadic case in a U.S. resident who reported not having left the country during the exposure period.

Analyses

An aggregate database was created that incorporated case records from all of the data sources. The mechanisms used to report cases to CDC were recorded. For most reported cases, demographic data (age, sex, and state/county of residence) and one or more dates were available. Such data were used to identify, compare, and merge records that concerned the same case but that were received via different mechanisms. If case records had conflicting data (e.g., different dates), preference

was given to the data from the most detailed record (e.g., a completed CRF). Clinical data were available primarily for cases for which a CRF was submitted. At least some data regarding food consumption during the exposure period were available for 27% of cases. Food consumption data were used when cases initially were analyzed for commonalities but are not provided in this report because aggregate, incomplete, and uncontrolled data from sporadic cases spanning years and states cannot be used to generalize or hypothesize about potential vehicles of infection.

Data analyses were conducted by using SAS v 9.2 (SAS Institute, Inc.; Cary, North Carolina). Population data from the U.S. Census Bureau were used to calculate incidence rates. For each of the annual rates, the denominator comprised the aggregate populations of the jurisdictions in which cyclosporiasis was a reportable disease or under surveillance (e.g., via FoodNet), regardless of whether any sporadic cases were reported to CDC that year, and the populations of the jurisdictions that reported case(s), regardless of whether cyclosporiasis was a reportable disease. Trends were evaluated with the Cochran-Armitage test; statistical significance was defined as a two-sided p value <0.05.

Results

CDC was notified of 1,110 laboratory-confirmed cases of cyclosporiasis that occurred during 1997–2008 and fulfilled all criteria for classification as sporadic cases (Table 2; Figure 1). These cases were reported by 39 jurisdictions: 37 states, including seven in which cyclosporiasis was not an explicitly reportable disease (Tables 3 and 4); NYC; and DC. The annual number of jurisdictions that reported cases ranged from six (in 1997) to 24 (in 2007), with a median of 18 jurisdictions; during 2004–2008, >20 jurisdictions per year reported at least one case. The annual number of reported cases varied (median: 98 cases; range: 14–148); the population-adjusted incidence rates (number of cases per 100,000 persons) ranged from a low of 0.01 in 1997 to a high of 0.07 in 2002 (Table 2; Figure 1).

Of the 1,110 sporadic cases, 498 (44.9%) were in residents of Florida (228 cases), NYC (200 cases), or elsewhere in New York state (70 cases), and >50 cases were reported by each of five other states (Connecticut, Georgia, Massachusetts, New Jersey, and Pennsylvania) (Table 4). Of the 39 jurisdictions that reported at least one case, 19 (48.7%) reported a total of <10 cases.

The case-patients' median age was 44 years (range: 3 months–96 years) (Table 5); 50.5% were female, 47.2% were male, and the sex was unknown for 2.3% (Table 6). Among cases with available data, more cases were in whites

[†] In FoodNet surveillance, the question regarding international travel, which has been asked since 2004, inquires about travel "within 15 days" of the onset date, or, if onset date is unavailable, the specimen collection date.

TABLE 1. National surveillance case definitions for cyclosporiasis — 1996, 1998, and 2010*

Characteristic	1996	1998	2010†
Clinical description	An illness of variable severity caused by the protozoan <i>Cyclospora cayetanensis</i> and commonly characterized by watery diarrhea, loss of appetite, weight loss, abdominal bloating and cramping, increased flatus, nausea, fatigue, and low-grade fever. Vomiting also may be noted. Relapses and asymptomatic infections can occur.	(unchanged from 1996)	An illness of variable severity caused by the protozoan parasite <i>Cyclospora cayetanensis</i> . The 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 might be noted.
Laboratory criteria for diagnosis	Demonstration of <i>Cyclospora</i> oocysts (by morphologic criteria or by demonstration of sporulation) or <i>Cyclospora</i> DNA (by polymerase chain reaction) in stool, duodenal/jejunal aspirates, or small-bowel biopsy specimens	Detection in symptomatic or asymptomatic persons of <i>Cyclospora</i> : • oocysts in stool (by microscopic examination) or in intestinal fluid or small bowel biopsy specimens; or • demonstration of sporulation; or • DNA (by polymerase chain reaction) in stool, duodenal/jejunal aspirates, or small bowel biopsy specimens	Detection of <i>Cyclospora</i> organisms or DNA in stool, intestinal fluid/aspirate, or intestinal biopsy specimens
Case classification			
Confirmed	A case that is laboratory confirmed	A laboratory-confirmed case that is associated with: • at least one of the symptoms described above (i.e., confirmed, symptomatic); or • none of the above symptoms (i.e., confirmed, asymptomatic)	A case that meets the clinical description and at least one of the criteria for laboratory confirmation as described above
Probable‡	A clinically compatible case that is linked epidemiologically to a confirmed case		A case that meets the clinical description and that is linked epidemiologically to a confirmed case

Source: Adapted from CDC. Case definitions for infectious conditions under public health surveillance. Available at http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/index.htm.

*The case definitions were developed in collaboration with epidemiologists at CDC and the Council of State and Territorial Epidemiologists (CSTE). On CDC's web site, they are referred to as the 1996, 1998, and 2010 definitions. In June 1998, CSTE voted to add cyclosporiasis to the list of nationally notifiable conditions, effective January 1999.

†In June 2009, CSTE approved a revised case definition, which was implemented in January 2010.

‡The probable category is not applicable for the sporadic cases included in this surveillance summary, all of which were laboratory-confirmed cases not linked to known outbreaks. However, the case counts for outbreaks include probable and confirmed cases, even for outbreaks during the period when the 1998 definition was applicable.

and non-Hispanics than in persons of other races and ethnicities (Table 6). Overall, 372 case-patients (33.5%) had a documented history of international travel during at least part of the 2-week exposure period, 398 (35.9%) reported that they had not traveled internationally during this period, and 340 (30.6%) had an unknown travel history. The proportion whose travel history was unknown (e.g., because the case-patient was lost-to-follow-up) varied among jurisdictions (Tables 3 and 4). The annual number of reported cases that were classified as domestically acquired increased significantly ($p<0.001$), whereas the number of travel-associated cases did not ($p=0.1$).

Travel-Associated Cases

For the 372 case-patients whose cases were classified as travel associated, 317 case records (85.2%) included the country/region or type of travel; 35 case-patients had traveled to multiple countries (Table 7). Among the 357 country visits for which the geographic region was known, 255 (71.4%) were in the Western Hemisphere, particularly in Central America ($n = 79$), Mexico ($n = 60$), the Caribbean ($n = 57$), or South America ($n = 53$); 102 visits (28.6%) were in the Eastern Hemisphere, particularly, in Asia ($n = 78$). The destinations encompassed all continents except Antarctica. Country-level destinations have been listed in descending order by frequency and compared with overall U.S. travel statistics for the same countries during similar periods (Table 7).

TABLE 2. Number,* percentage,[†] and incidence of reported laboratory-confirmed sporadic cases of cyclosporiasis, by year of symptom onset or diagnosis and by international travel history — United States, 1997–2008

Year	Travel associated		Domestically acquired		Unknown travel history		Total No.	Incidence rate [§]
	No.	(%)	No.	(%)	No.	(%)		
1997	5	(35.7)	5	(35.7)	4	(28.6)	14	0.01
1998	18	(35.3)	7	(13.7)	26	(51.0)	51	0.05
1999	17	(31.5)	12	(22.2)	25	(46.3)	54	0.04
2000	34	(54.0)	12	(19.0)	17	(27.0)	63	0.03
2001	26	(26.0)	35	(35.0)	39	(39.0)	100	0.05
2002	36	(24.3)	49	(33.1)	63	(42.6)	148	0.07
2003	47	(56.0)	28	(33.3)	9	(10.7)	84	0.04
2004	46	(47.9)	34	(35.4)	16	(16.7)	96	0.04
2005	36	(24.5)	56	(38.1)	55	(37.4)	147	0.06
2006	38	(32.8)	33	(28.4)	45	(38.8)	116	0.05
2007	37	(37.0)	39	(39.0)	24	(24.0)	100	0.04
2008 [¶]	32	(23.4)	88 [¶]	(64.2)	17	(12.4)	137 [¶]	0.06
Total	372		398		340		1,110	

Sources: Population estimates are from the Population Division, U.S. Census Bureau. State population estimates: annual time series, July 1, 1990 to July 1, 1999 (ST-99-3), available at <http://www.census.gov/popest/archives>. Annual estimates of the resident population for the United States, regions, states, and Puerto Rico: April 1, 2000 to July 1, 2009 (NST-EST2009-01), available at <http://www.census.gov/popest/states>. County population estimates and demographic components of population change: annual time series, July 1, 1990 to July 1, 1999 (CO-99-8), available at <http://www.census.gov/popest/archives>. Annual estimates of the resident population for counties: April 1, 2000 to July 1, 2009 (CO-EST2009-01), available at <http://www.census.gov/popest/counties>.

* N = 1,110.

[†] Percentages (per year) might not total 100% (not shown) because of rounding.

[§] Per 100,000 population on the basis of U.S. population estimates.

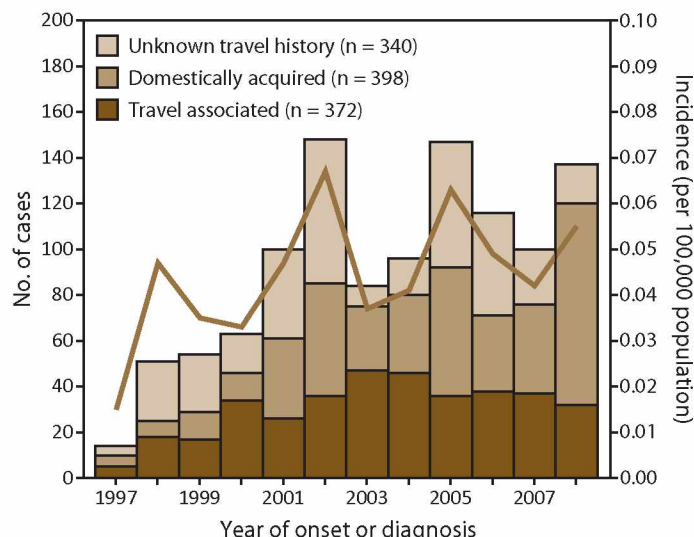
[¶] In 2008, Florida reported 61 (44.5%) of the 137 total cases, including 52 (59.1%) of the 88 domestically acquired cases. Among these 61 cases, 37 (60.7%) had symptom onset or diagnosis dates in May or June. Overall, for the 12-year surveillance period, Florida accounted for 228 (20.5%) of the 1,110 total cases, including 124 (31.2%) of the 398 domestically acquired cases. The 61 cases Florida reported in 2008 constituted the highest number reported by any jurisdiction during any year of the surveillance period; the next highest was 34 cases, which was the number Florida reported in 2002.

The 372 travel-associated cases were reported by 32 jurisdictions (30 states, NYC, and DC) (Tables 3 and 4). Among the 10 jurisdictions that reported ≥ 10 cases, only one (California) is not eastern or southeastern. NYC and Florida reported the most cases per jurisdiction (76 and 48 cases, respectively). The cases occurred in all 12 months, with the majority (240 [64.5%]) of onset or diagnosis dates during April–July (Figure 2).

Domestically Acquired Cases

By definition, the 398 case-patients classified as having domestically acquired cases had not been outside the United States during the 2-week exposure period. However, not all of them necessarily were exposed where they lived (Figure 3): 82 case-patients (20.6%) reported a history of interstate or inter-jurisdictional travel, five (1.3%) reported intrastate travel, and six (1.5%) reported both types of domestic travel. Overall, the 398 case-patients lived in a total of 28 jurisdictions (26 states, NYC, and DC); 124 case-patients (31.2%) lived in Florida, and 64 (16.1%) lived either in NYC (49 persons) or elsewhere in New York state (15 persons) (Tables 3 and 4). In total, 152

FIGURE 1. Number* and incidence of reported laboratory-confirmed sporadic cases of cyclosporiasis, by year of symptom onset or diagnosis and by international travel history — United States, 1997–2008



Sources: Population estimates are from the Population Division, U.S. Census Bureau. State population estimates: annual time series, July 1, 1990 to July 1, 1999 (ST-99-3), available at <http://www.census.gov/popest/archives>. Annual estimates of the resident population for the United States, regions, states, and Puerto Rico: April 1, 2000 to July 1, 2009 (NST-EST2009-01), available at <http://www.census.gov/popest/states>. County population estimates and demographic components of population change: annual time series, July 1, 1990 to July 1, 1999 (CO-99-8), available at <http://www.census.gov/popest/archives>. Annual estimates of the resident population for counties: April 1, 2000 to July 1, 2009 (CO-EST2009-01), available at <http://www.census.gov/popest/counties>.

* N = 1,110.

case-patients (38.2%) either lived in Florida (124 persons) or had traveled there (28 persons). Of the 124 reported domestically acquired sporadic cases in residents of Florida, 61 (49.2%) comprised an unexplained temporal-spatial cluster of cases in the spring of 2008 (Table 2); no common event or vehicle of infection of infection was documented. Overall, among the nine jurisdictions that reported at least 10 domestically acquired cases, only one (Illinois) is not eastern or southeastern. The cases occurred in all 12 months, with the majority (278 [69.8%]) of onset or diagnosis dates during April–August, particularly during May–July (Figure 2).

Clinical Aspects and Intervals to Diagnosis and Reporting

Clinical data were available for 184 case-patients (16.6%), two of whom reportedly were asymptomatic. Overall, diarrhea was the most common symptom (158 of 162 [97.5%]). Other reported symptoms included abdominal cramps (97 of 118 [82.2%]); fatigue (82 of 109 [75.2%]); weight loss (84 of 116 [72.4%]), with a median loss of 4.5 kilograms (range: 1.1–11.8 kg; n = 65); nausea (81 of 117 [69.2%]); anorexia (67 of 103

TABLE 3. Number* and percentage† of reported laboratory-confirmed sporadic cases of cyclosporiasis, by state/area of residence* and international travel history — United States, 1997–2008

State/Area*	Travel associated		Domestically acquired		Unknown travel history		Total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Alabama [§]	1	(0.3)	0		0		1	(0.1)
Alaska	1	(0.3)	0		0		1	(0.1)
Arizona [§]	0		1	(0.3)	0		1	(0.1)
Arkansas [¶]	0		0		0		0	
California [§]	14	(3.8)	3	(0.8)	0		17	(1.6)
Colorado	7	(1.9)	9	(2.3)	10	(2.9)	26	(2.3)
Connecticut	27	(7.3)	32	(8.0)	5	(1.5)	64	(5.9)
Delaware	0		1	(0.3)	1	(0.3)	2	(0.2)
District of Columbia	26	(7.0)	9	(2.3)	4	(1.2)	39	(2.8)
Florida	48	(12.9)	124	(31.2)	56	(16.5)	228	(20.8)
Georgia	26	(7.0)	38	(9.5)	50	(14.7)	114	(10.4)
Hawaii [¶]	0		0		0		0	
Idaho**	0		0		0		0	
Illinois	9	(2.4)	13	(3.3)	2	(0.6)	24	(2.2)
Indiana	2	(0.5)	1	(0.3)	0		3	(0.3)
Iowa	2	(0.5)	0		3	(0.9)	5	(0.5)
Kansas	0		0		1	(0.3)	1	(0.1)
Kentucky**	0		0		0		0	
Louisiana [¶]	0		0		0		0	
Maine [§]	0		1	(0.3)	0		1	(0.1)
Maryland	6	(1.6)	7	(1.8)	3	(0.9)	16	(1.5)
Massachusetts	26	(7.0)	31	(7.8)	3	(0.9)	60	(5.4)
Michigan	2	(0.5)	4	(1.0)	7	(2.1)	13	(1.2)
Minnesota	2	(0.5)	1	(0.3)	3	(0.9)	6	(0.6)
Mississippi**	0		0		0		0	
Missouri	0		1	(0.3)	2	(0.6)	3	(0.3)
Montana**	0		0		0		0	
Nebraska [§]	0		1	(0.3)	1	(0.3)	2	(0.2)
Nevada**	0		0		0		0	
New Hampshire	0		0		1	(0.3)	1	(0.09)
New Jersey	27	(7.3)	12	(3.0)	22	(6.5)	61	(5.5)
New Mexico	7	(1.9)	1	(0.3)	0		8	(0.7)
New York state ^{††}	10	(2.7)	15	(3.8)	45	(13.2)	70	(6.4)
New York City	76	(20.4)	49	(12.3)	75	(22.1)	200	(18.0)
North Carolina	2	(0.5)	3	(0.8)	5	(1.5)	10	(0.9)
North Dakota**	0		0		0		0	
Ohio	2	(0.5)	0		1	(0.3)	3	(0.3)
Oklahoma [¶]	0		0		0		0	
Oregon	4	(1.1)	0		0		4	(0.4)
Pennsylvania [§]	16	(4.3)	22	(5.5)	14	(4.1)	52	(4.8)
Rhode Island	1	(0.3)	0		0		1	(0.09)
South Carolina	2	(0.5)	0		10	(2.9)	12	(1.1)
South Dakota	1	(0.3)	0		0		1	(0.09)
Tennessee	6	(1.6)	3	(0.8)	3	(0.9)	12	(1.1)
Texas	3	(0.8)	4	(1.0)	6	(1.8)	13	(1.2)
Utah [¶]	0		0		0		0	
Vermont [§]	2	(0.5)	0		1	(0.3)	3	(0.3)
Virginia	5	(1.3)	7	(1.8)	1	(0.3)	13	(1.2)
Washington	5	(1.3)	2	(0.5)	5	(1.5)	12	(1.1)
West Virginia [¶]	0		0		0		0	
Wisconsin	4	(1.1)	3	(0.8)	0		7	(0.6)
Wyoming [¶]	0		0		0		0	
Total	372	(99.9)	398	(100.7)	340	(100.3)	1,110	(100.6)

* CDC was notified of a total of 1,110 sporadic cases by 37 states and two independent jurisdictions (New York City [NYC] and the District of Columbia) via multiple surveillance systems and reporting methods; no U.S. territories reported sporadic cases. All 50 states are listed regardless of whether they reported any sporadic cases. See footnotes below regarding whether cyclosporiasis was an "explicitly reportable disease" in particular jurisdictions during all or part of the period of interest (1997–2008)—i.e., whether cyclosporiasis was "listed as a specific disease or as a category of diseases on reportable disease lists" (10). See text for the states/areas in the *Cyclospora* Sentinel Surveillance Network and for those in the Foodborne Diseases Active Surveillance Network (FoodNet).

† Percentages might not total 100% because of rounding.

§ Not an explicitly reportable disease in this state, but sporadic cases were reported to CDC.

¶ An explicitly reportable disease in this state, but no sporadic cases were reported to CDC.

** Not an explicitly reportable disease in this state, and no sporadic cases were reported to CDC.

†† New York state exclusive of NYC.

TABLE 4. Number* and percentage† of reported laboratory-confirmed sporadic cases of cyclosporiasis, by state/area of residence and international travel history — United States, 39 jurisdictions, 1997–2008

State/Area (No. of yrs) [§]	Travel associated	Domestically acquired	Unknown travel history	Total	
	No.	No.	No.	No.	(%)
Florida (11)	48	124	56	228	(20.8)
New York City (11)	76	49	75	200	(18.0)
Georgia (10)	26	38	50	114	(10.4)
New York state (11) [¶]	10	15	45	70	(6.4)
Connecticut (11)	27	32	5	64	(5.9)
New Jersey (8)	27	12	22	61	(5.5)
Massachusetts (9)	26	31	3	60	(5.4)
Pennsylvania (7)**	16	22	14	52	(4.8)
District of Columbia (10)	26	9	4	39	(2.8)
Colorado (10)	7	9	10	26	(2.3)
Illinois (9)	9	13	2	24	(2.2)
California (7)**	14	3	0	17	(1.6)
Maryland (8)	6	7	3	16	(1.5)
Virginia (7)	5	7	1	13	(1.2)
Texas (6)	3	4	6	13	(1.2)
Michigan (8)	2	4	7	13	(1.2)
Tennessee (5)	6	3	3	12	(1.1)
Washington (5)	5	2	5	12	(1.1)
South Carolina (6)	2	0	10	12	(1.1)
North Carolina (5)	2	3	5	10	(0.9)
New Mexico (5)	7	1	0	8	(0.7)
Wisconsin (6)	4	3	0	7	(0.6)
Minnesota (3)	2	1	3	6	(0.6)
Iowa (3)	2	0	3	5	(0.5)
Oregon (2)	4	0	0	4	(0.4)
Indiana (2)	2	1	0	3	(0.3)
Missouri (2)	0	1	2	3	(0.3)
Ohio (3)	2	0	1	3	(0.3)
Vermont (3)**	2	0	1	3	(0.3)
Delaware (2)	0	1	1	2	(0.2)
Nebraska (2)**	0	1	1	2	(0.2)
Arizona (1)**	0	1	0	1	(0.1)
Maine (1)**	0	1	0	1	(0.1)
Alabama (1)**	1	0	0	1	(0.1)
Alaska (1)	1	0	0	1	(0.1)
Rhode Island (1)	1	0	0	1	(0.1)
South Dakota (1)	1	0	0	1	(0.1)
Kansas (1)	0	0	1	1	(0.1)
New Hampshire (1)	0	0	1	1	(0.1)
Total	372	398	340	1,110	(100.6)

* CDC was notified of 1,110 sporadic cases by 37 states and two independent jurisdictions (New York City [NYC] and the District of Columbia) via multiple surveillance systems and reporting methods. The 39 jurisdictions that reported sporadic cases are listed in descending order of the number of reported cases; the secondary and tertiary sorts were the numbers of domestically acquired and travel-associated cases, respectively. See Table 3, including footnotes, for additional details and perspective.

† Percentage does not total 100% because of rounding. In Table 3, percentages also are provided for the various categories of cases (travel associated, domestically acquired, and unknown travel history).

§ The number of years that the jurisdiction reported sporadic cases is provided in parentheses; the maximum possible number would be 12.

¶ New York state exclusive of NYC.

** Not an explicitly reportable disease in this state, but sporadic cases were reported to CDC.

[65.0%]); fever (42 of 97 [43.3%]), with a median temperature of 100.3°F (37.9°C) (range: 99.0–103.5°F [37.2–39.7°C]; n = 20); and vomiting (31 of 102 [30.4%]). Among the 16 case-patients with available data, the median duration of illness was 17.5 days (range: 10–30 days). Eleven case-patients (6.7% of 165) reported having been hospitalized; their median age was 47 years (range: 9–88 years). No deaths were reported.

TABLE 5. Number and percentage of reported laboratory-confirmed sporadic cases of cyclosporiasis, by age group and international travel history — United States, 1997–2008

Age group (yrs)	Travel associated		Domestically acquired		Unknown travel history		Total
	No.	(%)	No.	(%)	No.	(%)	
0–9	23	(47.9)	11	(22.9)	14	(29.2)	48
10–19	33	(54.1)	15	(24.6)	13	(21.3)	61
20–29	52	(33.5)	44	(28.4)	59	(38.1)	155
30–39	61	(33.9)	66	(36.7)	53	(29.4)	180
40–49	67	(31.6)	77	(36.3)	68	(32.1)	212
50–59	73	(35.8)	76	(37.3)	55	(27.0)	204
60–69	39	(27.3)	64	(44.8)	40	(28.0)	143
70–79	14	(21.5)	32	(49.2)	19	(29.2)	65
≥80	1	(6.3)	13	(81.3)	2	(12.5)	16
Total	363		398		323		1,084*

* Age group unknown or missing for 26 cases.

Both the onset date and the diagnosis date were available for 452 cases (40.7%); the median interval from onset to diagnosis was 13 days (range: 0–375 days; 25–75% interquartile range [IQR]: 9–19 days) (Table 8). Among the 194 cases (17.5%) with available data, the median interval from diagnosis to notification was 28 days (range: 0–367 days; IQR: 17–59 days). Overall, CDC received a total of 2,134 case reports regarding the 1,110 cases (Table 9); information was obtained via NNDSS for the majority of cases (955 [86.0%]).

Discussion

For 1997–2008, a total of 1,110 laboratory-confirmed cases of cyclosporiasis reported to CDC were classified as sporadic because they were not linked to documented outbreaks. Approximately 3,000 outbreak-associated cases were reported for the same period (1,2,7,11–16; CDC, unpublished data, 2011), which does not include 1996, the year of the first documented large (with >1,000 reported cases) multistate outbreak (1,2,6). Although the annual reported numbers of both outbreak-associated cases and sporadic cases fluctuated, the number of sporadic cases varied less markedly (range: 0–1,448 for outbreak-associated cases compared with 14–148 for sporadic cases).

Overall, approximately one third (33.5%) of the reported sporadic cases occurred in persons with a known history of international travel who might have become infected outside the United States (Figure 1). Because the majority of the case-patients with available data had been in the United States at least 1 day during the 2-week exposure period, the country in which they became infected could not be established definitively, nor could the precise location or mode of transmission.

Guatemala and Peru together accounted for 82 (23%) of the country visits by case-patients but only ~1% of the destinations

TABLE 6. Number* and percentage† of reported laboratory-confirmed sporadic cases of cyclosporiasis, by selected demographic group and international travel history — United States, 1997–2008

Characteristic	Travel associated		Domestically acquired		Unknown travel history		Total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Sex								
Male	171	(46.0)	192	(48.2)	161	(47.4)	524	(47.2)
Female	190	(51.1)	205	(51.5)	166	(48.8)	561	(50.5)
Unknown/Missing	11	(3.0)	1	(0.3)	13	(3.8)	25	(2.3)
Total	372	(100.1)	398	(100.0)	340	(100.0)	1,110	(100.0)
Race								
AI/AN	2	(0.5)	3	(0.8)	1	(0.3)	6	(0.5)
A/PI	10	(2.7)	4	(1.0)	5	(1.5)	19	(1.7)
Black	4	(1.1)	13	(3.3)	15	(4.4)	32	(2.9)
White	185	(49.7)	279	(70.1)	142	(41.8)	606	(54.6)
Other	8	(2.2)	7	(1.8)	8	(2.4)	23	(2.1)
Unknown/Missing	163	(43.8)	92	(23.1)	169	(49.7)	424	(38.2)
Total	372	(100.0)	398	(100.1)	340	(100.1)	1,110	(100.0)
Ethnicity								
Hispanic	39	(10.5)	23	(5.8)	22	(6.5)	84	(7.6)
Non-Hispanic	149	(40.1)	231	(58.0)	126	(37.1)	506	(45.6)
Unknown/Missing	184	(49.5)	144	(36.2)	192	(56.5)	520	(46.8)
Total	372	(100.1)	398	(100.0)	340	(100.1)	1,110	(100.0)

Abbreviations: AI/AN = American Indian/Alaska Native and A/PI = Asian/Pacific Islander.

* N = 1,110.

† Percentages might not total 100% because of rounding.

for U.S. travelers in general (Table 7). Fresh produce from these two countries and Mexico (the most frequent destination both for case-patients and overall) have been linked to outbreaks in North America; indigenous cases also have been described in these countries (1,2,22–24). Several case-patients reported having traveled to Puerto Rico; the first described outbreak of cyclosporiasis in Puerto Rico occurred in 2008 in a rural community and was thought to be waterborne (25). Collection of detailed travel data (including destinations and durations of travel) might serve the dual functions of identifying cases potentially acquired outside the continental United States and of identifying additional foci of endemicity (26).

Another one third (35.9%) of the reported sporadic cases were classified as domestically acquired. These cases, like the travel-associated sporadic cases, as well as the documented U.S. outbreak-associated cases (CDC, unpublished data, 2011), occurred year-round, with the highest case counts during spring and summer months. Although the temporal distribution of cases diagnosed in the United States could reflect in part seasonal differences in considering and testing for *Cyclospora*, the distribution largely mirrors the to-date unexplained seasonality of infection in some of the source countries of imported produce items implicated in outbreak investigations (1,2,6,7,11,12).

The geographic distribution of the cases, like the temporal distribution, was both broad and concentrated: 28 jurisdictions (26 states, NYC, and DC) notified CDC of domestically acquired cases, whereas the majority of the reported cases were

TABLE 7. International destinations for U.S. travel-associated laboratory-confirmed sporadic cases of cyclosporiasis, 1997–2008, and estimated percentages of U.S. outbound travel accounted for by these destinations*

Destination*	Sporadic case-patients*†			U.S. outbound travel data§	
	Country visits		Also traveled elsewhere†	Estimated % of all travel	Period with available data
	No.	(%)			
Mexico	60	(16.6)	6	31.5	1997–2008
Guatemala	44	(12.2)	4	0.5	2001–2003
Peru	38	(10.5)	6	0.5	1996–2004
Dominican Republic	20	(5.5)	2	1.8	2001–2004
China	19	(5.3)	2	1.5	1997–2008
Indonesia	14	(3.9)	1	0.2	1996–2004
El Salvador	12	(3.3)	2	0.5	2001–2004
Haiti	11	(3.0)	1	§	§
Bahamas	9	(2.5)	0	1.8	1996–2004
India	8	(2.2)	3	1.0	1997–2008
Costa Rica	7	(1.9)	2	0.8	2001–2004
Honduras	7	(1.9)	3	§	§
Nicaragua	7	(1.9)	1	§	§
Puerto Rico*	7	(1.9)	0	¶	¶
Thailand	6	(1.7)	5	0.7	1997–2008
Other**	92	(25.5)		¶	¶
Total	361	(99.8)		¶	¶

* Among the 372 case-patients with travel-associated cases, some information about the destination (or type) of travel was known for 317 (85.2%). These 317 case-patients had a total of 361 country visits during the 2-week exposure period. For the purposes of these analyses, visits to the Commonwealth of Puerto Rico were considered travel outside the United States. With the exception of the Other category, the destinations are listed in descending order, by the number of country visits; the percentage does not total 100 because of rounding.

† Among the 317 case-patients, 35 (11.0%) traveled to multiple countries.

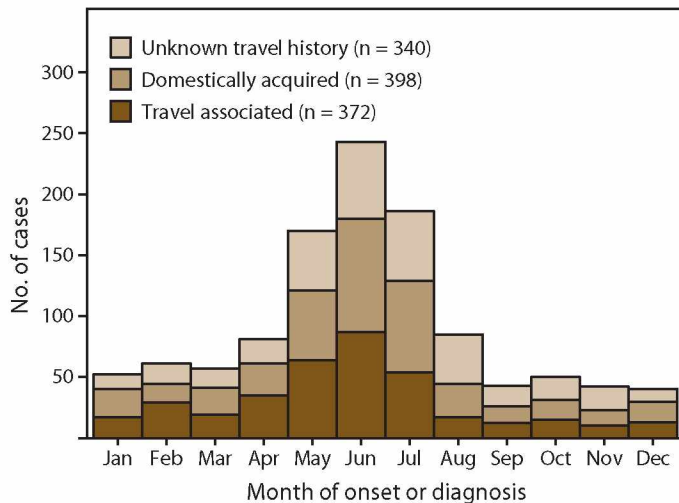
§ U.S. outbound travel estimates are based on data from the U.S. Department of Commerce, International Trade Administration, Office of Travel and Tourism Industries. U.S. resident travel abroad historical visitation estimates for U.S. outbound 1996–2006 (one or more nights) published in July 2007 (available at <http://www.tinet.ita.doc.gov/view/f-2006-11-001/index.html>) and U.S. resident travel abroad 1999–2008 revised historical outbound visitation (one or more nights) published in September 2009 (available at http://www.tinet.ita.doc.gov/outreachpages/download_data_table/2008_US_Travel_Abroad.pdf). Travel estimates were unavailable if the sample size for a particular country/year was <400 respondents (for 2005–2008) or <100 (for 1996–2004). The country-specific percentages were calculated by dividing the average of the available annual travel estimates for that country by the average of the annual totals for U.S. outbound travel for the same period.

¶ Not applicable.

** Each of the specified destinations (or types) of travel in this category was associated with fewer than six case-patients. The destinations include 40 countries not listed in the Table. Only region-level data were available for 13 country visits (e.g., Europe or Africa), and only the type of travel was reported for four case-patients (i.e., three Peace Corps volunteers and one person who took a cruise), each of whom was counted as having one country visit. Overall, 255 (71.4%) of the 357 visits with at least region-level data were in the Western Hemisphere, including Central America (n = 79), Mexico (n = 60), the Caribbean (n = 57), South America (n = 53), Canada (n = 5), and Bermuda (n = 1). The other 102 visits (28.6%) were in the Eastern Hemisphere, including Asia (n = 78), Europe (n = 11), Africa (n = 11), and Australia/New Zealand (n = 2).

in residents of major cities and surrounding metropolitan areas in Florida, New York, and several other eastern or southeastern states (Figure 3). This seeming geographic focality might reflect in part more frequent recognition and reporting of cases in particular eastern and southeastern jurisdictions, which also reported the majority of the travel-associated cases. The extent to which the focality also reflects a higher overall occurrence of cases is unknown, although some states, most notably Florida (1,2,6,14,15), have figured prominently in outbreaks

FIGURE 2. Number* of reported laboratory-confirmed sporadic cases of cyclosporiasis, by month of symptom onset or diagnosis† and by international travel history — United States, 1997–2008

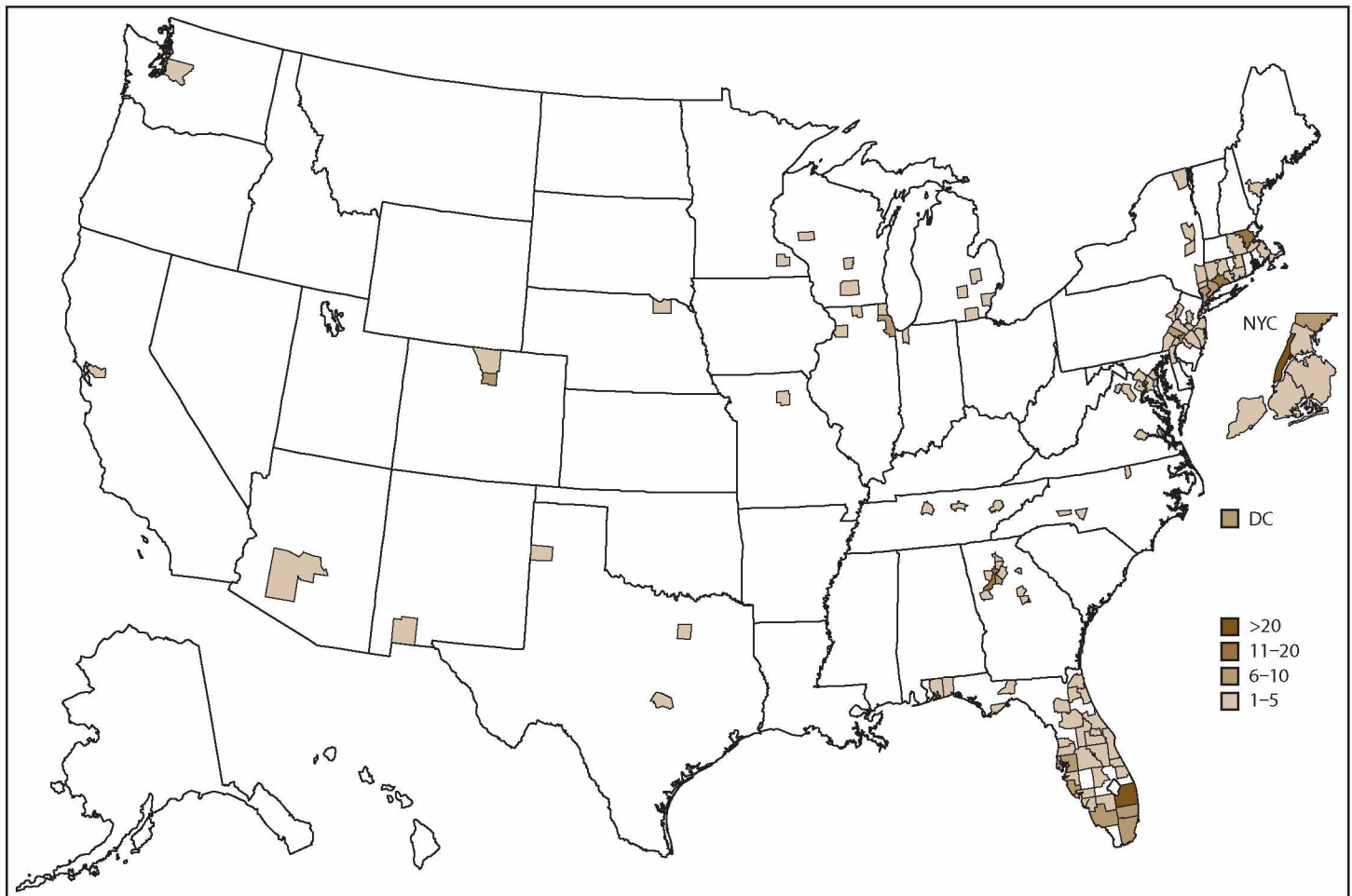


*N = 1,110.

† The month of report was used for 14 cases.

in multiple years, linked to vehicles from various sources. The occurrence in Florida of an unexplained temporal-spatial cluster of cases in the spring of 2008 (Table 2) underscores the difficulties associated with attempts to document linkage among non-event-associated cases, without the benefits of molecular tools or of sufficient numbers of cases and resources to conduct definitive case-control studies. Many of the documented outbreaks during 1997–2008 affected multiple states, either because of multistate distribution of the implicated produce item or because persons from multiple states attended an event (e.g., a conference); the event-associated clusters have not been limited to eastern and southeastern states. However, generalizing from particular years, states, and outbreaks is complicated by the nonuniform importation, distribution, and consumption of contaminated produce, as well as by the many unknowns regarding such factors and the epidemiology of cyclosporiasis in general (e.g., the incidence of and risk factors for infection in the United States and elsewhere).

FIGURE 3. Number* of domestically acquired laboratory-confirmed sporadic cases of cyclosporiasis, by county of residence — United States, 1997–2008



*N = 390. County of residence was unknown or missing for eight case-patients.

TABLE 8. Intervals from symptom onset to diagnosis and from diagnosis to first notification of CDC of laboratory-confirmed sporadic cases of cyclosporiasis — United States, 1997–2008

Description of interval and selection criteria	No.*	Median (days)	Range (days)	25%–75% Interquartile range (days)
Interval from symptom onset to diagnosis				
All cases with available data	452	13	0–375	9–19
Interval from diagnosis to first notification of CDC				
All cases with available data	194	28	0–367	17–59
Surveillance system/reporting method†				
NNDSS	129	34	1–367	21–80
Electronic mail	33	17	0–69	9–31
CSSN	20	20	1–71	14–24
Telephone/Facsimile	9	19	3–62	14–25
PHLIS	3	22	8–34	8–34

Abbreviations: NNDSS = National Notifiable Diseases Surveillance System, CSSN = *Cyclospora* Sentinel Surveillance Network, and PHLIS = Public Health Laboratory Information System.

* Number of cases for which the dates/intervals of interest were available. Data for cases reported solely via the Foodborne Diseases Active Surveillance Network (FoodNet) are not included.

† In descending order, by number of cases with available data.

TABLE 9. Number* and percentage of reported laboratory-confirmed sporadic cases of cyclosporiasis, by the surveillance systems and reporting methods through which CDC obtained information — United States, 1997–2008

System/method, stratified by type	No.	(%)†
Active		
<i>Cyclospora</i> Sentinel Surveillance Network	179	(16.1)
Foodborne Diseases Active Surveillance Network (FoodNet)	255	(23.0)
Passive		
National Notifiable Diseases Surveillance System	955	(86.0)
Public Health Laboratory Information System	299	(26.9)
Electronic mail	258	(23.2)
Other passive mechanism§	188	(16.9)

*N = 1,110. CDC received at least some information about these cases via a total of 2,134 case reports. CDC often receives information about individual cases via multiple mechanisms, depending in part on the technologic capacity, surveillance network membership, and general reporting policies/procedures of the health department, as well as the amount and type of information provided via various systems/methods.

† Denominator is all 1,110 cases.

§ A telephone call or facsimile (e.g., of a case report form or a line list) from a health department.

The reported sporadic cases of cyclosporiasis have a bell-shaped age distribution, with relatively few cases in the very young and very old (Table 5). In contrast, for giardiasis and cryptosporidiosis, two enteric parasitic diseases that occur quite commonly in the United States, reported cases have a skewed or bimodal age distribution, with the highest proportion occurring among children aged 1–9 years (27,28). The paucity of reported cases of cyclosporiasis among infants and young children is suggestive of an exposure that is more common among adults, which likely applies to the types of fresh produce implicated to date in U.S. outbreak investigations.

The median interval from symptom onset to diagnosis was 13 days (Table 8); this includes the time required to decide to seek care, to be evaluated by a clinician, and to provide and test stool for *Cyclospora*. Although the median interval from diagnosis to notification of CDC was 28 days, CDC typically did not have information regarding when cases were reported to health departments. Most laboratories do not perform diagnostic testing for *Cyclospora* without an explicit, billable request for such testing (29); this parasite usually is not detected by a routine examination for ova and parasites. CDC tests specimens that are sent via state public health laboratories for *C. cayetanensis*. CDC also provides reference diagnostic support through DPDx, a telediagnosis system (available at <http://www.dpd.cdc.gov/dpdx>) initiated in 1998 that enables laboratory and clinical staff to submit images (e.g., of suspect *Cyclospora* oocysts) electronically for rapid diagnosis of parasitic diseases. The available clinical data regarding the case-patients' symptoms (e.g., magnitude of weight loss), duration of illness, and hospitalization rate underscore the importance of prompt diagnosis and treatment of this potentially severe infection, as well as the need for preventive measures.

Limitations

Surveillance for cyclosporiasis, like that for other notifiable conditions, is dependent on the completeness and accuracy of the available data. In this context, the findings presented in this report are subject to at least five limitations. First, in general, not all cases of cyclosporiasis are diagnosed and reported (30), cyclosporiasis is not reportable in all jurisdictions, and notifying CDC is voluntary. Second, even for reported cases, the details provided to CDC might be incomplete. For example, the travel history was unknown for approximately one third of the reported sporadic cases (30.6%), and details about the destination and duration of travel were incomplete for many of the cases for which some travel data were reported. Third, reporting might be delayed, which reduces the likelihood of identifying epidemiologic commonalities among cases. The relatively long incubation period for cyclosporiasis (median: 1 week) contributes to delays in detecting, reporting, and investigating cases. Fourth, the lack of molecular tools for linking cases compounds the implications of incomplete and delayed reporting. Finally, the trend analyses regarding the annual number and incidence of cases during the 12-year surveillance period should be interpreted with caution. The optimal denominators to use to calculate incidence rates are unclear, a robust baseline period is not available, and the actual (true) total number of domestically acquired cases in a given year is unknown.

Conclusion

Health-care providers should consider the diagnosis of *Cyclospora* infection for persons with persistent or relapsing-diarrheal illness, regardless of the season or U.S. region; explicitly request testing for this parasite; and report identified cases to local public health authorities, who, in turn, are encouraged to notify CDC. Vigilant surveillance and innovative research to develop molecular methods for linking seemingly sporadic cases should remain U.S. public health priorities. Unidentified, uninvestigated cases and outbreaks represent missed opportunities to identify vehicles of infection or modes of contamination and to implement evidence-based, targeted, prevention and control measures. Additional information about cyclosporiasis is available at <http://www.cdc.gov/parasites/cyclosporiasis>.

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