DOLORES KATZ, PHD ■ SAVITA KUMAR, MD MSPH ■ JEAN MALECKI, MD MPH ■ MICHAEL LOWDERMILK, RS ■ EMILIA H.A. KOUMANS, MD MPH ■ RICHARD HOPKINS, MD MSPH

Cyclosporiasis Associated with Imported Raspberries, Florida, 1996

At the time of the investigation reported here, Dr. Katz was an Epidemic Intelligence Service Officer with the Centers for Disease Control and Prevention (CDC), Atlanta, assigned to the state of Florida; she is currently a Regional Epidemiologist, Bureau of Epidemiology, Florida Department of Health, Miami. Drs. Kumar and Malecki and Mr. Lowdermilk are with the Palm Beach County Department of Health, Riviera Beach, Florida; Dr. Kumar is Director of the Division of Epidemiology and Disease Control; Dr. Malecki is Director of the Department; and Mr. Lowdermilk is an Environmental Specialist with the Division of Environmental Health and Engineering. At the time of this investigation, Dr. Koumans was an Epidemic Intelligence Service Officer with the Division of Parasitic Diseases, CDC, Atlanta; she is currently a Medical Epidemiologist with the Division of STD Prevention, CDC, Atlanta. Dr. Hopkins is the State Epidemiologist, Florida Department of Health, Tallahassee.

SYNOPSIS

Objectives. Until 1995, infection with *Cyclospora cayetanenis*, a parasite that causes gastroenteritis, was diagnosed in the US primarily in overseas travelers; its modes of transmission were largely unknown. In 1995, 45 cases of cyclosporiasis were diagnosed in Florida residents who had no history of recent foreign travel, but an investigation could not pinpoint a source for the parasite. In 1996, a North American outbreak of cyclosporiasis resulted in more than 1400 cases, 180 of them in Florida. The authors investigated the 1996 Florida outbreak to identify the vehicle of transmission.

Methods. The authors conducted a matched case-control study in which each of 86 laboratory-confirmed sporadic cases was matched with up to four controls. They also investigated nine clusters of cases associated with common meals and attempted to trace implicated foods to their countries of origin.

Results. In the case control study, eating raspberries was strongly associated with cyclosporiasis (matched odds ratio = 31.9; 95% confidence interval [CI] 7.4, 138.2). In the cluster investigation, raspberries were the only food common to all nine clusters of cases; a summary analysis showed a strong association between consumption of raspberries and confirmed or probable cyclosporiasis (risk ratio = 17.6; 95% CI 1.9, 188.8). Guatemala was the sole country of origin for raspberries served at six of nine events.

Conclusions. Guatemalan raspberries were the vehicle for the 1996 Florida cyclosporiasis outbreak. *Cyclospora* is a foodborne pathogen that may play a growing role in the etiology of enteric disease in this country as food markets become increasingly international.

Address correspondence to:
Dr. Katz, Dept. of Epidemiology and Public Health (R-669), Univ. of Miami School of Medicine, Box 016069, Miami FL 33101; tel. 305-243-2206; fax 305-243-3384; e-mail <dkatz@med.miami.edu>.

National and international foodborne outbreaks are a modern phenomenon, the consequence of technological developments that allow mass production and distribution of potentially contaminated food.[1] In particular, the expanding role of imported foods in the American diet creates the potential for widespread dissemination of exotic pathogens.[2,3]

Cyclospora cayetanensis, a recently identified coccidian parasite,[4,5] can cause prolonged, relapsing diarrhea.[6] Symptoms appear a median of seven days after ingestion of oocysts, which are excreted in feces in an unsporulated form and require days to weeks to sporulate and become infective[4,5]; for this reason, direct person-to-person transmission is considered unlikely. Treatment with trimethoprim-sulfamethoxazole relieves symptoms and speeds clearance of the parasite.[7]

Relatively little is known about the epidemiology of this pathogen, which was first identified as a cause of human illness in 1977 in Papua New Guinea.[8] Most reported cases in the Northern Hemisphere have occurred in spring and early summer.[4] Before 1995, most cases in the United States were diagnosed in travelers to developing countries[4]; some studies had identified water as a possible vehicle of transmission.[6,9,10]

1995 Florida outbreak. In June 1995, a community hospital laboratory in Boca Raton identified *Cyclospora* oocysts in the stools of seven ill Palm Beach County residents who had not recently traveled outside the US. The laboratory had begun screening for *Cyclospora* in 1992 in all stool specimens submitted for ova and parasite examination, and had diagnosed only two cases before June 1995, both in overseas travelers.

Following extensive publicity, community and state public health laboratories diagnosed cyclosporiasis in 41 other Florida residents through the end of September 1995; all but six were residents of Palm Beach County. Forty-five of the 48 patients had no known history of recent foreign travel; onset dates for these US-acquired cases ranged from May 7 through September 5. Although an investigation suggested the outbreak was foodborne and raised the possibility that consumption of raspberries imported from Guatemala or Chile was associated with *Cyclospora* infection, the evidence was inconclusive.[11]

1996 outbreak in US and Canada. A second outbreak occurred in the spring of 1996, and was traced to fresh raspberries from Guatemala.[12–14] A total of 1465 cases of cyclosporiasis were recorded by 20 states, the District of Columbia, and two Canadian provinces.[12] Florida had the second largest number of cases, after New York, and the largest number of clusters, in the 1996 outbreak.[12] Here, we describe the Florida Department of Health's investigation of the Florida cases.

Laboratory identification of cyclosporiasis in Florida. The state of Florida made cyclosporiasis a reportable condition on July 25, 1995; physicians and laboratories are required to report cases to their county health departments. Diagnosis is by identification of oocysts in stool, most commonly by use of a modified acid-fast stain,[15] but also by examination of wet mounts under phase microscopy, demonstration of autofluorescence, or, definitively, by demonstration of sporulation.[4,5] Because *Cyclospora* oocysts can be difficult to distinguish from artifacts,[16] the Florida Department of Health's case definition for cyclosporiasis requires confirmation by a reference laboratory (one with recognized expertise in *Cyclospora* identification). Since 1995, local laboratories that identify *Cyclospora* oocysts forward the slides and any available stool to the central state public health laboratory for confirmation; most slides are prepared using a modified acid-fast technique.

METHODS

We used heightened surveillance, epidemiologic studies, and extensive laboratory testing to assess the size of the outbreak, learn more about morbidity associated with cyclosporiasis, and identify the vehicle of transmission.

Surveillance. To improve the reporting of cases, Broward and Palm Beach county health departments sent "Dear Doctor" letters to local clinicians, describing the disease and the outbreak and stressing the importance of reporting. The state Bureau of Epidemiology used its weekly bulletin to county public health employees to describe the outbreak and the importance of having the state central laboratory reconfirm cases identified by local laboratories. A case report form was developed to collect basic demographic and symptom information; it was designed to be the first page of a more extensive questionnaire for cases included in the case-control study, so interviewers would not have to collect basic information twice.

To ensure that it was correctly identifying cases of cyclosporiasis, the state central laboratory sent some of its positive and negative slides to the Centers for Disease Control and Prevention (CDC) Parasitic Diseases Laboratory for re-confirmation.

A total of 1465 cases of cyclosporiasis were recorded by 20 states, the District of Columbia, and two Canadian provinces in 1996; Florida had the second largest number of cases.

Matched case control study. To identify the cause of the outbreak, we designed a case control study of sporadic cases of cyclosporiasis diagnosed during the spring and summer of 1996.

Case definition. For the case control study, a sporadic case of cyclosporiasis had to meet the following requirements: the individual reported at least one gastrointestinal symptom; *Cyclospora* infection was confirmed by a reference laboratory during the period April 1, 1996, through August 30, 1996; the individual reported no foreign travel in the two weeks before onset of illness; and the illness was not associated with a cluster of cyclosporiasis cases.

Control subjects. We matched each case subject with up to four friends, relatives, or neighbors who lived in the same county, were broadly similar in age (that is, adults matched with adults, teenagers with teenagers, and children with children), and reported no gastrointestinal symptoms in the two weeks before the case subject's illness began. To identify appropriate control subjects, the interviewers first asked each case subject to provide the names and telephone numbers of well friends or relatives who did not live in the same house. If no names were provided or if the potential controls could not be interviewed, local control subjects were identified by calling telephone numbers created by adding 1 to the case subject's telephone number, subtracting 1 from the subject's number, adding 2, subtracting 2, and so on until a sufficient number of controls was obtained.

Data collection. Using a structured questionnaire, county public health department employees asked case and control subjects about consumption of raw fruits and vegetables, sources of drinking water, and exposures to soil, recreational water, and animals in the two weeks before the onset of the case subject's illness. Telephone interviews were conducted from May 23, 1995, to August 14, 1995.

Data analysis. We used Epi Info to calculate matched odds ratios (ORs) and 95% confidence intervals (CIs).[17] For variables showing significant or borderline significant associations with illness, we used SAS to conduct conditional logistic regression analyses to control for confounding among variables.[18] We defined borderline significance as a lower limit of at least 0.9 for the 95% CI.

Investigation of clusters. We used a retrospective cohort design to investigate the nine identified clusters of cyclosporiasis cases in 1996 that were associated with events at which food was served. A cluster was defined as cases of gastrointestinal illness, at least one of which was confirmed as due to *Cyclospora* infection by a reference laboratory, occurring among two or more people within one to 14 days after attendance at an event at which a meal or common food was shared. For purposes of the cluster investigation, a cluster-associated gastrointestinal illness in a person who did not submit a stool sample for testing was defined as a probable case of cyclosporiasis.

We attempted to contact all of the people who attended each event and ask them about foods consumed and subsequent symptoms. For each cluster investigation, we calculated relative risks (RRs) and Taylor series 95% CIs[19] or used Fisher's exact test[20] when applicable to assess associations with individual foods. Because most of the events involved small numbers of people and therefore had limited power to identify a vehicle of transmission, we then pooled the data from all events and performed a combined analysis. Before it was included in the combined analysis, the data from each cluster investigation was evaluated to ensure consistency of data collection and case definition. Cases were included in the combined analysis only if they were laboratory-confirmed or the case subject reported diarrhea that met one of the following definitions: (*a*) at least three loose or watery stools per day for three or more days, or (*b*) unspecified number of loose or watery stools per day for seven or more days. For the combined multivariate analysis, we used the SAS GENMOD procedure, which controls for correlation within clusters.[21]

Tracebacks. We attempted to trace the raspberries implicated in each cyclosporiasis cluster back to their countries of origin. Tracebacks were conducted by interviewing purchasers and suppliers and obtaining copies of invoices to document each step in the sales chain from grower to consumer. To compare dates of onset of illness with the timing of raspberry imports, we obtained weekly totals of Guatemalan raspberry shipments to the US from the Market News Branch of the US Department of Agriculture's Agricultural Marketing Service.

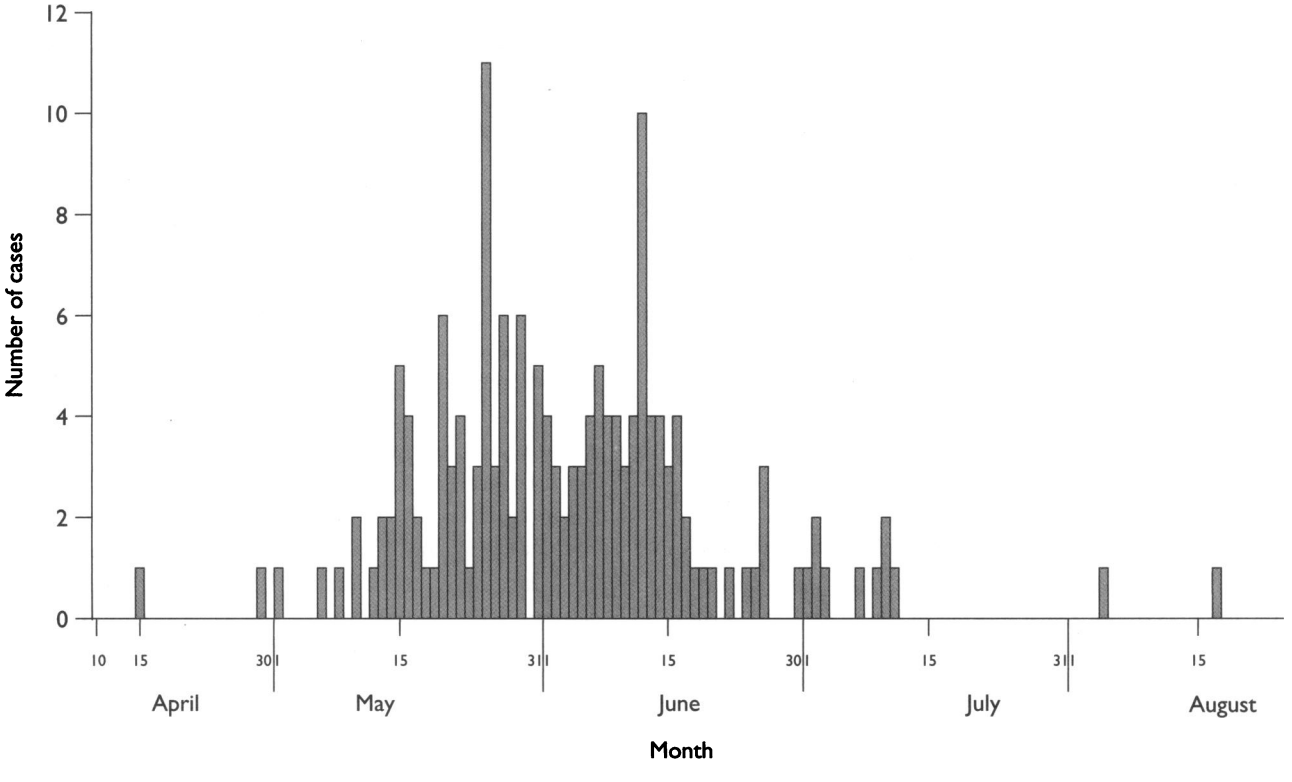
RESULTS

Surveillance findings. A total of 180 confirmed cases of cyclosporiasis were reported in 1996 in Florida residents with no history of travel outside the US in the two weeks before onset of symptoms. The state central laboratory forwarded stool specimens from 22 of these case subjects and from 36 patients whose specimens were negative to the CDC's parasitology laboratory, which confirmed the state laboratory's findings in every instance.

Onset of symptoms occurred from April 15 to August 17. The mean age of the 180 case subjects was 54.0 years (standard deviation [SD] = ±18.7 years), with a range from 10 months to 92 years; six cases occurred in children. Females accounted for 61.1% of cases. Confirmed cases were reported from 15 of Florida's 67 counties, but 74% of cases were diagnosed in residents of Palm Beach and Broward counties, which account for 17% of Florida's population.[22] The counties with the highest rates of cyclosporiasis were Palm Beach (9.6 cases per 100,000 population), which has the highest per capita income of Florida's 67 counties, and Martin (8.5 cases per 100,000 population), which has the second highest per capita income.[23] All but 17 confirmed cases were sporadic, with onset dates for sporadic cases clustered in late May and early June (Figure 1).

Diarrhea was the most common symptom, reported by all but one case subject. Loss of appetite, fatigue, and weight loss were each reported by at least 90% of case subjects (Table 1). Six case subjects were hospitalized; no deaths were reported.

Figure 1. Onset dates of confirmed sporadic cyclosporiasis cases, Florida, April–August 1996



This outbreak demonstrates the usefulness of epidemiologic methods in identifying vehicles of transmission when laboratory data are unavailable.

Table 1. Symptoms reported by 180 Florida residents with laboratory-confirmed *Cyclospora* infections, April 1996–August 1996

Symptom[a]	n	Reported the symptom	
		Number	Percent
Diarrhea[b]	180	179	99.4
Loss of appetite	171	158	92.4
Fatigue	176	161	91.5
Weight loss[c]	173	155	89.6
Abdominal pain or cramps	174	122	70.1
Nausea	178	125	70.2
Fever[d]	160	68	42.5
Vomiting	175	53	30.3

[a]Interviewers specifically asked about the symptoms shown in the Table. In addition, the following symptoms were volunteered by two or more respondents: bloating and/or gas or both (n = 36); headache (13); chills and/or sweating (14); body aches (4); dizziness (5).

[b]The median number of stools per day was 7.0 (range 1 to 48; n = 168). The median duration of diarrhea was 12 days (range 1 to 120; n = 172). One person reported bloody stools.

[c]The median weight loss was 6.5 pounds among 78 people who reported the amount of weight loss.

[d]The median highest temperature was 37.8° C (range 37.2° to 39.4°) among the 34 people who reported their highest temperature.

Matched case control study. When data collection ended on August 14, 86 sporadic case subjects had been matched with 150 control subjects. The age distributions of case and control subjects were similar: 4.7% (4/86) of case subjects and 3.3% (5/150) of control subjects were younger than 18 years of age; 33.7% of case subjects and 33.3% of control subjects were ages 18 to 49 years; and 61.6% of case subjects and 63.3% of control subjects were ages 50 years and older. In both groups the majority were female: 60.5% of case subjects and 71.3% of controls (P = 0.09 for the difference in sex distribution between cases and controls). Case and control subjects were from six counties; 82.6% were from Palm Beach and Broward counties.

Control subjects included 80 friends and associates of case subjects (53.3% of control subjects) and 70 people identified by systematic phone dialing (46.7% of control subjects). The two groups of control subjects had similar age and sex distributions. Mean ages were 54.8 years (SD = +18.1 years) for friend/associate controls and 54.7 years (SD = ±18.3 years) for phone-dialed controls. In both groups the majority were female: 56 (70.0%) of friend/acquaintance controls and 51 (72.9%) of phone-dialed controls.

In preliminary analyses (not shown), we found similar associations between exposures and illness for the two types of control subjects: in both groups, berries were most strongly associated with illness, and raspberries showed the strongest association. To improve the precision of the odds ratio (OR) estimates, we combined all control subjects; the results that follow are for the combined groups.

Table 2 shows univariate matched ORs for exposures with significant or borderline significant associations with *Cyclospora* infection and the proportions of subjects exposed. Consumption of fresh berries was strongly associated with illness. Raspberry consumption was most strongly associated with infection, with an OR of 42.9 (95% CI 11.2, 365.0). Approximately two-thirds of case subjects reported eating raspberries in the two weeks before their symptoms began, while 86% reported eating strawberries; only 34% of case subjects reported eating blueberries and only 22% reported eating blackberries. Consumption of oranges and spinach were associated with lower risk of illness.

In conditional logistic regression analysis (Table 3), only raspberries and strawberries were significantly associated with illness; raspberries' association with infection (OR = 31.9; 95% CI 7.4, 138.2) was approximately seven times that of strawberries (OR = 4.7; 95% CI 1.6, 13.6). Although oranges remained negatively associated with infection (OR = 0.04; 95% CI 0.01, 0.23), their inclusion

Table 2. Exposures associated with *Cyclospora* infection in the case control study: results of univariate matched analysis

Source of exposure	Odds ratio	95% CI	Percent of case subjects exposed	Percent of control subjects exposed
Food				
Raspberries	42.9	11.2, 365.0	65.1	6.8
Blueberries	8.0	2.9, 27.0	34.1	11.5
Blackberries	6.5	2.1, 26.6	22.4	7.4
Strawberries	6.2	2.9, 15.5	86.0	51.7
Pineapple	2.7	1.3, 5.7	33.7	20.1
Bananas	2.0	0.9, 4.8	87.2	77.9
Radishes	2.0	0.9, 4.7	19.0	12.9
Lemons	1.9	1.0, 3.9	50.0	41.6
Romaine lettuce	1.7	0.9, 3.2	50.0	40.3
Red grapes	1.6	0.9, 3.0	38.8	29.7
Oranges	0.53	0.03, 1.0	27.9	40.3
Spinach	0.55	0.2, 1.2	15.5	24.3
Other				
Swimming in a pool	2.3	1.0, 6.0	22.6	14.0
Outdoor gardening	1.9	0.9, 4.1	37.6	28.8
Water from a cooler	1.8	0.9, 3.8	28.0	20.1
Male sex	1.8	0.9, 3.4	39.5	28.7

CI = confidence interval

in the analysis only increased the strength of the associations with raspberries and strawberries and did not change the relative strengths of the associations; we excluded them from the final analyses.

Assuming that raspberries were the vehicle for the 1996 cyclosporiasis outbreak, the proportion of sporadic infections acquired in Florida that could be attributed to raspberry consumption can be calculated using the formula

$$\frac{P_e(RR\text{-}1) + 1}{P_e(RR\text{-}1)}$$

where RR, the risk ratio, is estimated from the logistic regression OR and P_e, the proportion of the population exposed, is estimated from the proportion of exposed control subjects.[24] Based on this calculation, 67.8% of the 163 sporadic cases of cyclosporiasis acquired in Florida in 1996 could be attributed to raspberry consumption.

Cluster investigations. Nine clusters of cyclosporiasis cases were identified in Florida in 1996, eight associated with meals in private residences and one with a catered event at a museum.[12] Ninety-nine (92.5%) of 107 attendees at these meals were interviewed. Seventeen confirmed and 43 probable cases were identified. Confirmed

Table 3. Results of conditional logistic regression analysis of exposures associated with *Cyclospora* infection in the case control study

Source of exposure	Odds ratio	95% CI	Percent of case subjects exposed	Percent of control subjects exposed
Raspberries	31.9	7.4, 138.2	65.1	6.8
Strawberries	4.7	1.6, 13.6	85.7	51.7

Table 4. Cyclosporiasis clusters associated with nine shared meals, Florida, 1996

Date of meal	Number attending	Number interviewed	Number of cases		Fresh fruit item served	Attack rate among those exposed		Attack rate among those not exposed		P value[a]
			Probable	Confirmed		Number	Percent	Number	Percent	
May 5	16	12	7	1	Salad of raspberries, strawberries, blackberries, red grapes	8/8	100.0	0/4	0	0.002
May 12	6	6	1	2	Yogurt topped with raspberries[b]	4/4	100.0	0/2	0	0.07
May 12	6	6	2	3	Salad of raspberries, strawberries, blackberries, blueberries, other non-berry fruits	5/5	100.0	0/1	0	0.17
May 21	7	6	0	2	Salad of raspberries, strawberries, other non-berry fruits[c]	2/4	50.0	0/1	0	0.60
May 29	11	9	2	3	Raspberry-blueberry salad	5/8	62.5	0/1	0	0.44
June 1	44	43	22	1	Platter of raspberries, strawberries, blueberries	20/27	74.1	1/11	9.1	—[d]
June 8	11	11	6	3	Yogurt topped with raspberries, strawberries	9/9	100.0	0/2	0	0.018
June 14	3	3	2	1	Raspberries	3/3	100.0	0/0	0	Undefined
June 14	3	3	1	1	Raspberries	2/2	100.0	0/1	0	0.33

NOTE: Eight meals were served at private residences; one (June 1) was a catered banquet at a museum.

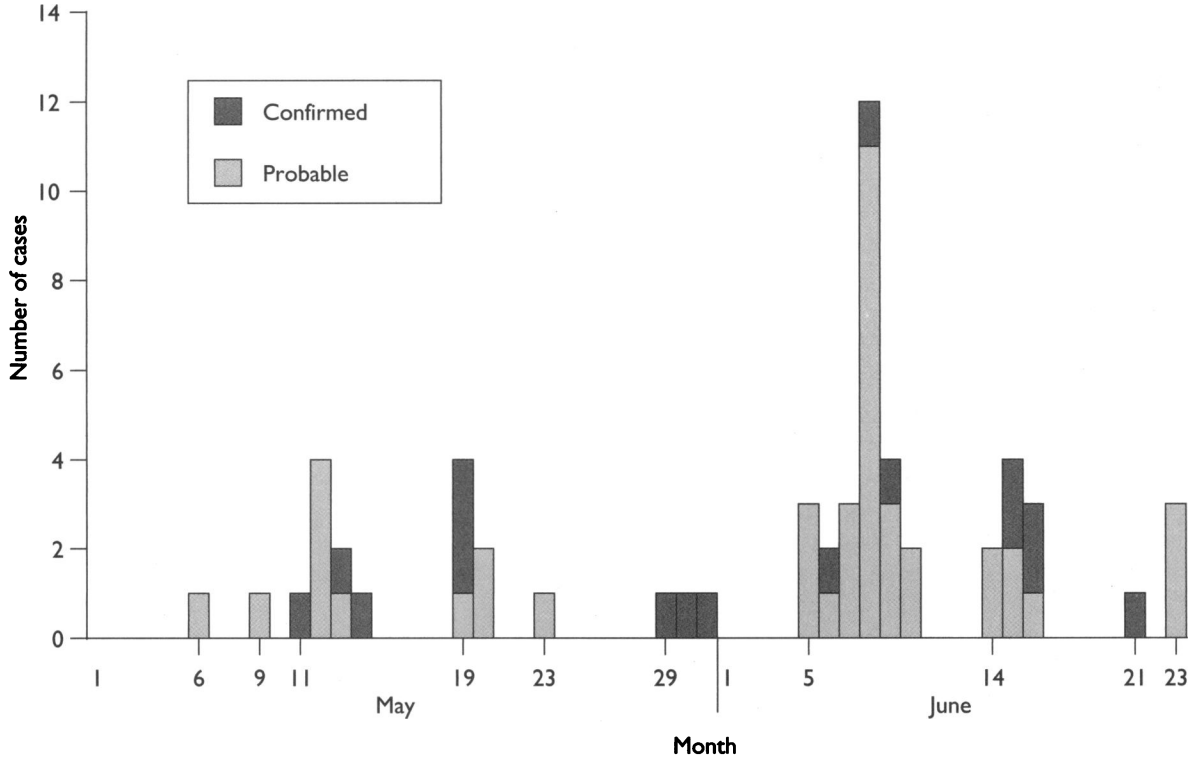
[a]Fisher's exact test

[b]A fruit salad containing strawberries, raspberries, and other non-berry fruits was also served; all 6 attendees ate some.

[c]A strawberry shortcake was also served; all 6 attendees interviewed ate some.

[d]Risk ratio for raspberries = 8.2 (95% confidence interval 1.2, 53.5); risk ratio for strawberries = 6.9 (95% confidence interval 1.1, 45.0)

Figure 2. Onset dates of confirmed and probable cluster-associated cyclosporiasis cases, Florida, May 1996 and June 1996



and probable cluster case subjects became ill a mean of 6.9 days (SD = ±2.1 days, range 1 day to 11 days) after the event, with symptoms including diarrhea, nausea, abdominal cramps, fatigue, and weight loss.

Table 4 lists the date of each event associated with a cluster of cases, the number of confirmed and probable cases associated with each event, and the fruit items served at each event. All events occurred in May and June 1996, when 93% of the sporadic cases also occurred (Figures 1 and 2). The number of confirmed and probable cases per event ranged from 2 to 22. Taking into account both confirmed and probable cases, the overall attack rate for all nine events was 60.6%, with a range per event from 33.3% to 100%; the median attack rate was 66.7%. Fresh raspberries were the only food common to all the events, were the only type of berry served at two events, and were significantly associated with illness at three events (Table 4). The overall attack rate among people who reported eating raspberries was 81% (59/73).

Fifty-three of the 60 confirmed and probable cases from all nine clusters met the criteria for inclusion in the summary analysis. An additional three case subjects and eight well subjects were excluded from the analysis because of missing information. With raspberries and strawberries included in the model, raspberries were strongly and significantly associated with illness (OR = 61.3; 95% CI 9.3, 405.8). The association with strawberries was much smaller and of borderline significance (OR = 3.2; 95% CI 1.0, 10.0).

People who prepared the foods for the events were asked whether the berries had been washed. The raspberries reportedly were washed before serving at seven of the nine events and were not washed before serving at one. No information was available about preparation of the raspberries served at one event.

Tracebacks. Complete tracebacks to the countries of origin were possible for raspberries served at seven of the nine events associated with cyclosporiasis cases. For six of the events, the raspberries definitely came from Guatemala; for one, either Guatemalan or Chilean raspberries could have been purchased, but the timing of the purchase made it most likely that the raspberries were from Guatemala. For the two remaining events, the indi-

viduals who bought the raspberries could not remember where they were purchased, although the purchaser for one event recalled that the raspberries were labeled as originating in Guatemala.

The raspberries clearly traceable to Guatemala were supplied by two different exporters. Raspberries served at the events came from shipments supplied to the exporter by as few as three or as many as 30 farms (Personal communication Marta-Louise Ackers, MD, CDC, July 1997). Therefore, it was impossible to trace the raspberries served at any of the events to a particular farm.

Figure 3 displays the weekly number of shipments of Guatemalan raspberries into the United States and the weekly totals of cyclosporiasis cases in Florida residents in 1996. The epidemic curve for *Cyclospora* infections follows the shape of the importation curve, with a time lag of 10 days to two weeks (Pearson correlation coefficient = 0.92, $P = 0.0001$).

DISCUSSION

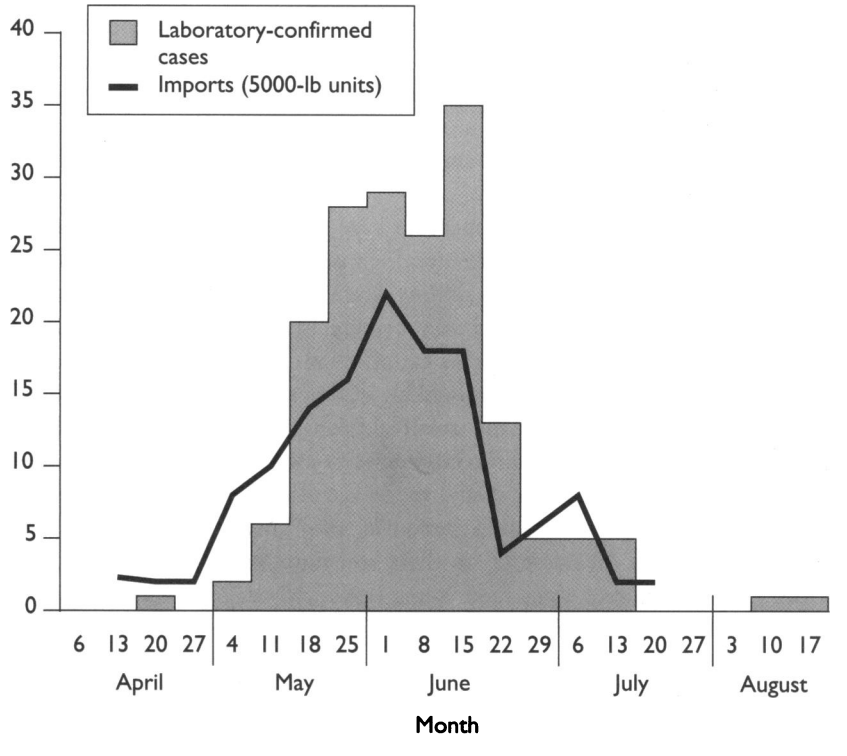
This investigation identified raspberries from Guatemala as the source of the 1996 cyclosporiasis outbreak in Florida, a conclusion supported by information from 19 other states, the District of Columbia, and two Canadian provinces. A total of 1465 confirmed and probable cases of cyclosporiasis were recorded in the two countries in the spring and early summer of 1996, and cluster and traceback investigations clearly implicated Guatemalan raspberries.[12–14] The North American outbreak of cyclosporiasis was the largest ever recorded, and the first to be conclusively linked to a food product.

Evidence pointing to Guatemalan raspberries as the cause of the Florida outbreak came from ecological data, from two different kinds of epidemiologic investigations (case control and cohort), and from detailed traceback investigations. The requirement that a reference laboratory reconfirm all laboratory-confirmed cases provided further reason for confidence in the results of the epidemiologic findings.

The epidemic curve for the cyclosporiasis outbreak in Florida closely matched the import curve for Guatemalan raspberries, with a 10-day to two-week lag time between the curves that allowed for distribution and purchase of the berries and a median seven-day incubation period after consumption (see Figure 3). The rates of cyclosporiasis were highest in the counties with the state's highest per capita incomes, consistent with consumption of an expensive food item. Raspberries are a relatively expensive fruit, with wholesale prices approximately three times higher than prices for strawberries.[25]

The case control study found a strong association between *Cyclospora* infection and consumption of raspberries (multivariate matched OR = 31.9; 95% CI 7.4, 138.2) and a much weaker association with consumption of strawberries (OR = 4.7; 95% CI 1.6, 13.6). While we cannot rule out the possibility that some strawberries may have been separately contaminated or cross-contaminated during handling or preparation, the more likely

Figure 3. Temporal association of confirmed Florida *Cyclospora* infections with Guatemalan raspberry imports into the US: number of cases by week of onset of symptoms and weekly imports, April–August 1996



explanation is recall bias related to extensive media publicity linking strawberries and *Cyclospora* infection. Beginning at least as early as August 1995 and continuing through July 1996, local and national news media reported concerns on the part of officials in various states that strawberries were the cause of both the 1995 outbreak of cyclosporiasis in Florida and the 1996 international outbreak.[26–33] Little publicity appeared about the association of cyclosporiasis with raspberries until July 3, when the state of Florida issued a consumer warning based on preliminary results of the case control study, using data on the first 72 cases. It would not be surprising if the months-long publicity about strawberries resulted in a bias toward recall of strawberry consumption among infected individuals. What is remarkable is that, despite a possible bias toward recall of strawberry consumption, our case control study documented an extremely strong association between self-reported raspberry consumption and *Cyclospora* infection.

The results of the case control study were supported by evidence from investigations of nine clusters of cyclosporiasis cases. Taken together, these clusters point strongly to raspberries as the vehicle of infection. The clusters occurred during the peak of the outbreak of sporadic cases, suggesting a common vehicle for the sporadic and cluster cases. Raspberries were the only food item common to all nine events. The attack rate among those who reported eating raspberries or fruit mixtures containing raspberries was 81%, and only one of 60 probable and confirmed cases reported no consumption of raspberries. The summary analysis showed a strong association between infection and raspberries and only a borderline association with strawberries.

Only about two-thirds of the sporadic case subjects who were interviewed about their food consumption reported eating raspberries. Such a finding is not uncommon in foodborne outbreaks[34] and may be due to poor recall, recall bias, or to other vehicles of infection. Poor recall and recall bias were particularly likely in this situation, for three reasons. First, the relatively long time between onset of symptoms and the interviews (a median of 17 days for the case control study) made recall difficult. Second, raspberries are often served in salad mixtures or as garnishes on desserts, so their consumption was harder to remember than food items served alone. Third, as noted above, the investigations were complicated by media publicity about strawberries.

The epidemiologic investigations were supplemented by detailed traceback information that identified Guatemala as the country of origin of the implicated raspberries. Although Guatemala accounted for less than 10% of domestic and imported raspberries shipped to the United States in May and June 1996,[12] it was the sole source of raspberries for six of seven events in Florida in May and June for which complete traceback documentation was available, and the most likely source for the seventh.

In retrospect, the 1995 outbreak of cyclosporiasis in Florida presaged the more extensive outbreak in 1996. While no single exposure was identified as the cause of the 1995 outbreak, it included two clusters (a total of seven laboratory-confirmed and seven probable cases) related to social events at which raspberries were served; no exposure was significantly related to illness at either event.[11] Tracebacks of the berries served at the two events indicated they could have come from either Guatemala or Chile.

The history of Guatemalan raspberry cultivation also suggests that the 1995–1996 outbreaks in Florida were not chance events. Raspberries have been an export crop in Guatemala only since 1988, and imports increased substantially in 1995 and 1996. Monthly fruit and vegetable imports into the United States are not recorded in the database of the Department of Agriculture's Agricultural Marketing Service unless they are in amounts of 50,000 pounds or greater (Personal communication, Douglas Edwards, Market News Branch, US Department of Agriculture, August 1997). The Guatemalan raspberry imports reached the 50,000-pound mark for the first time in November 1994, when approximately 200,000 pounds were imported.[35–41] Cyclosporiasis shows a marked seasonality in Guatemala, peaking in the springtime. The first large-scale springtime imports of Guatemalan raspberries were in 1995; approximately 100,000 pounds were imported in May of that year.[42] The first Florida outbreak began that same month and peaked in June. In 1996, estimated spring imports of Guatemalan raspberries quadrupled, to approximately 400,000 pounds imported in May and June.[43]

Following a second multistate outbreak of cyclosporiasis associated with Guatemalan raspberries in May 1997, the Guatemalan government announced a voluntary suspension of exports of fresh raspberries to the United States.[44] No outbreaks associated with Guatemalan raspberries occurred during Guatemala's fall and winter export seasons in 1996 and 1997. In the spring and summer of 1998, the US Food and Drug Administration (FDA) prohibited importation of fresh Guatemalan raspberries, but Guatemalan raspberries were exported to Canada. A multicluster outbreak of cyclosporiasis in Ontario in May 1998 was linked to Guatemalan raspber-

ries.[45] For the 1999 spring-summer import season, the FDA approved importation of fresh raspberries from four Guatemalan farms that met new hygiene standards developed by the Guatemalan government and the Guatemalan Berry Commission (Personal communication, George J. Jackson, PhD, Acting Director, Office of Special Research Skills, FDA, July 1999).

It is not known how Guatemalan raspberries may have become contaminated with *Cyclospora* oocysts. Tracebacks in 1996 and 1997 indicated that no single farm, grower, or exporter could account for the outbreak.[12,44] One hypothesis is that contaminated water was used to dilute the insecticides and fungicides that are typically applied to the berries as late as the day of harvest.[12] This explanation is attractive because water has previously been implicated as a vehicle for human infection.[6,9,10] The Guatemalan Berry Commission's export standards for raspberry farms now require installation of filters to exclude *Cyclospora* oocysts from water used on berries.

The magnitude of the 1996 outbreak is unclear, but it certainly was broader than the 180 confirmed cases in Florida and the 800 confirmed and 445 probable cases reported elsewhere in the US and Canada.[12] Florida was the only state where cyclosporiasis was a reportable illness at the time of the outbreak, and Florida's public health laboratories were routinely testing for *Cyclospora* oocysts in stool samples submitted for ova and parasite examinations. Even in Florida, many cases were likely to have been missed because ill persons did not seek medical care, because physicians did not order testing for *Cyclospora*, or because private laboratories did not test for the parasite. One of the nine clusters we investigated included 15 physicians who had attended a seminar. At the time of their interviews, none of their illnesses were laboratory-confirmed and only two had submitted stool samples, which had not been tested for *Cyclospora*.

The Florida investigation of the 1996 cyclosporiasis outbreak highlights a number of important clinical and public health issues. First, clinicians should be alert to the possibility of cyclosporiasis in patients with prolonged diarrhea and should order the specialized tests needed for identification before prescribing curative treatment. Stool testing and mandatory reporting are important tools in the identification of outbreaks. A community laboratory that began screening for *Cyclospora* provided the first evidence of the Florida cyclosporiasis outbreaks of 1995 and 1996.

Second, this outbreak demonstrates the usefulness of epidemiologic methods in identifying vehicles when laboratory data are unavailable. *Cyclospora* does not multiply outside its host, and laboratory techniques are not sufficiently sensitive or standardized to reliably identify *Cyclospora* except in stool. Guatemalan raspberries were identified as the vehicle for this outbreak using epidemiologic approaches and product tracebacks.

Finally, this and other investigations of the 1996 outbreak establish *Cyclospora* cayetanensis as a foodborne pathogen and highlight the potential for widespread dissemination of exotic pathogens in food. Although raspberries were the identified vehicle in this outbreak, a Florida outbreak in 1997 was associated with baby greens (mesclun),[46] and a 1997 outbreak in the District of Columbia, Baltimore, and northern Virginia was associated with fresh basil.[47] Other raw fruits or vegetables could be vehicles for future cyclosporiasis outbreaks. While it is tempting to make public health recommendations about washing produce, our findings show that washing fruit was not a reliably protective measure; persons (most were not workers) who prepared food for seven of the nine events associated with cyclosporiasis cases reported washing the raspberries before serving. In that respect, this outbreak illustrates the need for new ways to protect our food supply as expanded trade brings in produce from all parts of the world.

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