

# A Multistate Outbreak of Cyclosporiasis

## A Classroom Case Study

### STUDENT'S VERSION

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*NOTE: This case study is based on real-life investigations undertaken in 1996 and 1997 in the United States and abroad that were published in the Morbidity and Mortality Weekly Report, the New England Journal of Medicine, and the Annals of Internal Medicine. The case study, however, is not a factual accounting of the details from these investigations. Some aspects of the investigations (and the circumstances leading up to them) have been altered to assist in meeting the desired teaching objectives. Some details have been fabricated to provide continuity to the storyline.*

**Target audience:** students with minimal knowledge of basic epidemiologic concepts who are interested in learning more about the practice of epidemiology including participants in the Knight Journalism Fellowship Program.

**Level of case study:** basic

**Teaching materials required:** none

**Time required:** approximately 3 hours

**Language:** English

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**STUDENT'S VERSION**  
**A Multistate Outbreak of Cyclosporiasis**

<p><b>Learning objectives:</b> After completing this case study, the participant should be able to:</p> <ol style="list-style-type: none"><li>1) use the modes of transmission and incubation period for a disease to focus the search for the source of an outbreak</li><li>2) describe the two most common types of epidemiologic studies routinely used to investigate outbreaks</li><li>3) interpret the results of an epidemiologic study</li><li>4) consider potential sources of error in designing or carrying out an epidemiologic study</li><li>5) apply the criteria for causation to the results of an outbreak investigation</li><li>6) list considerations in implementing control measures before confirmation of the source of an outbreak</li><li>7) describe the occurrence, signs and symptoms, and control of cyclosporiasis</li></ol>
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**Part I – Background**

On May 20, 1996, the following article appeared on the front page of the Toronto Sun:

<p><b>Exotic Parasite Sickens Canadian Businessmen</b> By Xavier Onnasis</p> <p>TORONTO - Public health officials today confirmed that three Canadian businessmen, two from Toronto and one from Ottawa, were diagnosed with cyclosporiasis, a parasitic disease seen only in tropical countries and overseas travelers. The three men, who had recently traveled to the United States, became seriously ill with diarrhea over the weekend (May 16-18). One of the men was hospitalized at Princess Margaret Hospital when he collapsed due to severe dehydration.</p> <p>Dr. Richard Schabas, Ontario's Chief Medical Officer, reported that cyclosporiasis was exceedingly rare in North American and that much was still unknown about this disease. Cyclosporiasis is caused by the</p>	<p>microorganism <i>Cyclospora cayetanensis</i>. <i>Cyclospora</i> infects the small bowel and usually causes watery diarrhea, with frequent, sometimes explosive, bowel movements. Symptoms can include bloating, increased gas, stomach cramps, nausea, loss of appetite, and profound weight loss. The illness is diagnosed by examining stool specimens in the laboratory.</p> <p>Dr. Schabas declined to identify a source of infection for the three businessmen but indicated that the parasite is transmitted through contaminated food or water but not by direct person-to-person spread. The time between exposure to the parasite and becoming sick is usually about 7 days.</p> <p>Dr. Schabas reported that all three men had attended a meeting in Texas on May 9-10. He said Ontario Health Department staff would be investigating leads locally and in Texas.</p>
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See Appendix 1 for "Cyclosporiasis Fact Sheet".

**Question 1:** What is the incubation period for cyclosporiasis? How will it be used in the investigation?

**Question 2:** On what sources of infection should public health officials focus for the three cases of cyclosporiasis? Is it possible that one of the men was the source of infection for the others? Do you think that it is likely that the businessmen became infected with cyclosporiasis in Texas?

## Part II – Outbreaks in Texas

The chief medical officer of the Ontario Health Department notified the Texas Department of Health (TDH) about the *Cyclospora* infections in the three Canadian businessmen. The businessmen had attended a meeting at a private club in Houston, Texas on May 9-10.

A total of 28 people had attended the Houston business meeting. Participants came from three U.S. states and Canada. Meals served during the meeting were prepared at the restaurant operated by the private club. Rumors among restaurant staff suggested that other attendees at the meeting had also become ill.

TDH, the Houston Health & Human Services Department, and the Centers of Disease Control and Prevention (CDC) initiated an epidemiologic investigation to identify the source of the cyclosporiasis outbreak.

**Question 3:** What are the two most common types of epidemiologic studies used to investigate the source of an outbreak (or other public health problem)? Which would you use to investigate the source of the cyclosporiasis outbreak in Texas? Why?

Because the outbreak appeared to affect a small, well-defined group of individuals (i.e., meeting attendees), investigators undertook a retrospective cohort study to investigate the source of the cyclosporiasis.

Investigators first surveyed people who attended the meeting to characterize the illness associated with the outbreak. (Twenty-seven of the 28 meeting attendees were interviewed.) All ill people experienced severe diarrhea and weight loss. In addition, 87% reported loss of appetite; 87% reported fatigue; 75% reported nausea; 75% reported stomach cramps; and 25% reported fever. Five ill people had stool specimens positive for *Cyclospora*.

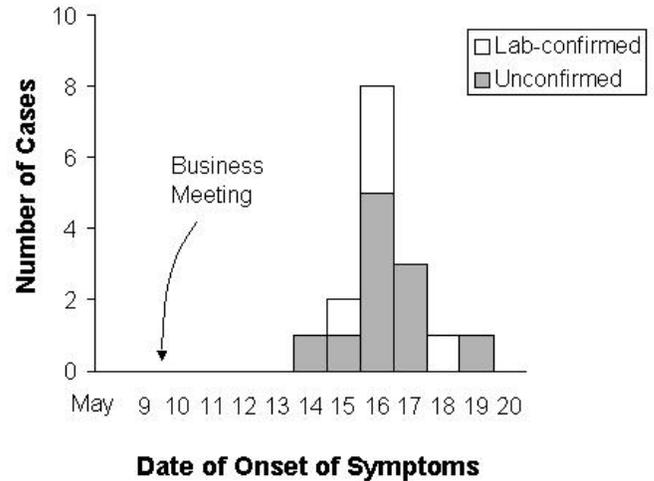
Based on this information, investigators defined a case of cyclosporiasis for the cohort study as diarrhea of at least 3 days duration in someone who had attended the business meeting. Laboratory confirmation of *Cyclospora* infection was not required.

Of the 27 meeting attendees who were interviewed, 16 (59%) met the case definition for cyclosporiasis. Onsets of illness occurred from May 14 through May 19. (Figure 1)

Investigators questioned both ill and well meeting attendees about travel history and food and water exposures during the meeting.

**Question 4:** Why would you question people who did not become ill about possible sources of infection with *Cyclospora*?

Figure 1. Onset of illness among patients with cyclosporiasis, Houston business meeting, May 1996.



Restaurant management at the private club refused to take calls from investigators or cooperate with the investigation. As a result, a list of foods served at meals during the meeting was obtained from the meeting organizer. No menu items were confirmed by restaurant staff.

Twenty-four meeting attendees provided information on foods eaten during the meeting. (Four attendees, including three cases, did not provide the information.) Investigators examined the occurrence of illness among people who ate different food items.

Twelve (92%) of 13 attendees who ate the berry dessert became ill. Only one (9%) of 11 attendees who did not eat the berry dessert became ill. The relative risk for eating berries was 10.2 (p-value <0.0001). No other exposures were associated with illness.

Case-patients reported that the berry dessert contained strawberries.

**Question 5:** In your own words, interpret the results of the cohort study.

**Question 6:** What problems in study design or execution should you consider when reviewing the results of this study (or any epidemiologic study)?

On June 4, before the first investigation had been completed, TDH was notified of another outbreak of cyclosporiasis involving physicians who attended a dinner on May 22 at a Houston, Texas restaurant. A second cohort study was undertaken. Nineteen attendees were interviewed. Ten met the case definition for cyclosporiasis (i.e., diarrhea of at least 3 days duration).

Attendees who ate dessert at the dinner were more likely to become ill than attendees who did not. Illness, however, was not associated with eating a particular type of dessert. No other exposures were associated with illness.

All desserts were garnished with either one fresh strawberry (for regular patrons) or with a strawberry, blackberry, and raspberry (for VIPs). Of the 7 attendees who reported eating a strawberry, all seven became ill. Of the eight attendees who reported not eating a strawberry, only one became ill (relative risk = 8.0, p-value = 0.001). (Note: four attendees, including two cases, could not recall whether they had eaten a strawberry and were excluded from this analysis.)

Based on the results of the two cohort studies, investigators hypothesized that strawberries were the source of the cyclosporiasis outbreaks in Houston.

**Question 7:** What additional studies might confirm (or refute) the hypothesis that strawberries were the source of the cyclosporiasis outbreaks?

TDH staff examined invoices and other records from the two restaurants involved in the Texas cyclosporiasis outbreaks. The strawberries consumed at both the May 9-10 business meeting and the May 22 physician dinner were grown in California. The individual producers/distributors of the strawberries, however, were not determined.

On May 31, TDH released a public health advisory about the presumed link between the consumption of California strawberries and the cyclosporiasis outbreak. The State Health Officer advised consumers to wash strawberries "very carefully" before eating them, and recommended that people with compromised immune systems (e.g., people with HIV infection, patients on cancer chemotherapy) avoid them entirely.

A few days later, Ontario's chief medical officer reported on an outbreak of cyclosporiasis in the Metro Toronto area affecting 40 people. Ontario public health officials believed California strawberries were also the source of the Toronto outbreak. A public health advisory, similar to the one from Texas, was issued.

Concurrent with the announcements from Texas and Ontario, CDC encouraged physicians from across the United States to report cases of cyclosporiasis to their local or state health department so that the source of the *Cyclospora* could be investigated further.

**Question 8:** You are writing a newspaper article about the cyclosporiasis outbreaks in Texas and Ontario. It is thought that the cyclosporiasis problem is ongoing. Four people are available for interview: the CDC expert on cyclosporiasis, one of the Canadian businessmen who became ill following the meeting in Houston, the owner of the private club in Houston where the first outbreak occurred, and the attorney for the California Strawberry Grower's Association. Your deadline is looming. You have time to ask each of these people only three questions. What would you ask them?

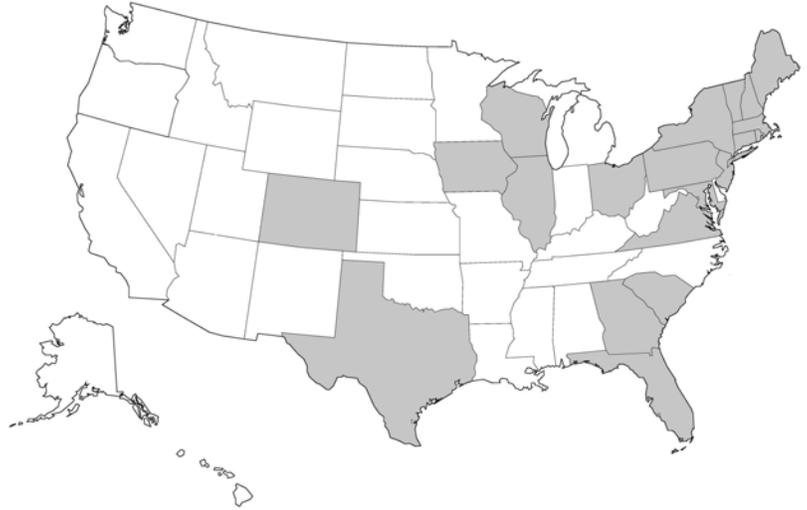
### Part III – Outbreaks in Other States

Despite recommendations by health departments in Texas and Ontario to wash strawberries carefully before eating them, cases of cyclosporiasis continued to occur nationwide. By the end of June, over 800 laboratory-confirmed *Cyclospora* infections were reported to CDC from 20 states, the District of Columbia, and two Canadian provinces. (Figure 2)

Discrepancies began to appear in the link between California strawberries and the *Cyclospora* infections. Investigations undertaken by the New York City Health Department and South Carolina Department of Health and Environmental Control pointed toward raspberries as the source of the cyclosporiasis outbreaks in their jurisdictions.

In late June, the New Jersey Department of Health and Senior Services (NJDHSS) initiated an epidemiologic investigation to identify the source of infection among cyclosporiasis cases in New Jersey residents. The cases to be included in the New Jersey study were not linked together by a common event and did not occur in a well-defined group of people.

Figure 2. States with laboratory-confirmed *Cyclospora* infections (shaded), May and June, 1996.



**Question 9:** Would you undertake a case-control or a cohort study to investigate the source of the cyclosporiasis cases in New Jersey? Why?

To assess possible risk factors for infection among the cases of cyclosporiasis in New Jersey, NJDHSS conducted a case-control study. In contrast to the Texas investigation, a case of cyclosporiasis for this study was defined as a patient with laboratory-confirmed *Cyclospora* infection and a history of diarrhea.

**Question 10:** How might you identify cases of cyclosporiasis for the case-control study? Who would you use as controls?

For the New Jersey case-control study, cases were identified by reviewing laboratory records from all clinical laboratories in the state. Forty-two cases were identified. Two controls were identified for each case through telephone calls to randomly selected households in the community. To be eligible for the study, controls could not have had loose stools during the previous 30 days.

Investigators interviewed 30 case-patients and 60 controls by telephone using a standardized questionnaire that asked about possible exposures (including consumption of 17 fruits and 15 vegetables, water and soil exposures, and animal contact) during the period of interest.

Case-patients and controls were similar with respect to age, sex, and level of education. Twenty-one (70%) of 30 case-patients and four (7%) of 60 controls had eaten raspberries. The odds ratio for eating raspberries was 32.7 (p-value <0.000001). No other exposures (including strawberries) were associated with illness.

**Question 11:** In your own words, interpret the results of the New Jersey case-control study.

Studies from other states and Canada supported the results from New Jersey, New York City, and South Carolina. A total of 725 cases of cyclosporiasis associated with 55 different events (e.g., wedding receptions, parties, buffets) were investigated. The only exposure consistently associated with cyclosporiasis was the consumption of raspberries.

Raspberries were served at 54 of the 55 events and were the only berries served at 11 events. (Reexamination of the events associated with the initial outbreaks in Texas and Ontario indicated that raspberries were included among the implicated berry items served at those events.) The median attack rate for cyclosporiasis among persons who ate items that contained raspberries at the different events was 93%. Furthermore, for 27 of the 41 events for which adequate data were available, the associations between the consumption of raspberries and cyclosporiasis were statistically significant ( $p$ -value $<0.05$ ).

The origin (i.e., producer) and mode of contamination of the raspberries served at the events were unknown. Due to the large number of raspberry producers at the time of the outbreaks (both domestic and international), public health officials could not recall the implicated raspberries or remove them from the marketplace. Traceback investigations were planned.

**Question 12:** Would you alert the public of this possible public health threat? Defend your answer.

## Part IV – Traceback and Environmental Investigations

To identify the sources of raspberries served at the 54 events linked to outbreaks of cyclosporiasis, CDC, the U.S. Food and Drug Administration (FDA), and health departments from the affected states obtained information on the place and dates of purchase of the implicated raspberries. Distributors and importers of the raspberries were identified through invoices and shipping documents. Airway bill numbers and importation documents (e.g., Custom's forms), supplied by importers, were used to identify overseas shipments and exporters.

By the third week of July, investigators had documented the source of the raspberries for 29 of the 54 cyclosporiasis-associated events. For 21 of these events, the raspberries definitely came from Guatemala. For 8 events, the raspberries could have originated there. No commonalities were found in the U.S. ports of entry for the implicated raspberries.

During the outbreak period, raspberries had been imported from a number of countries. Based on monthly data from the U.S. Department of Agriculture, Guatemalan raspberries represented 4-20% of fresh raspberries (domestic and imported) shipped within the United States in April-June of 1996.

**Question 13:** Does the traceback information support raspberries as the source of the cyclosporiasis outbreak?

At the time of the investigation, seven Guatemalan exporters, of which A and B were the largest, shipped raspberries to the United States. The raspberries for 25 of the 29 events were traced to only one Guatemalan exporter per event:

- 18 of 25 (72%) to Exporter A
- 5 (20%) to Exporter B
- 1 (4%) to Exporter C
- 1 (4%) to Exporter D

Using exporter records, the raspberries were traced back to the farm where they were grown. Because exporters typically combined raspberries from multiple farms in a shipment, investigators could identify only a group of contributing farms (an average of 10 farms with a range of 2 to 30) rather than one source farm per event. More than 50 farms could have contributed to implicated shipments of raspberries.

To investigate how raspberries were grown and handled in Guatemala, CDC and FDA investigators visited Exporters A, B, C, and D and the seven most commonly implicated raspberry producing farms (six supplying Exporter A and one supplying Exporter B).

**Question 14:** Given what you know about the transmission of cyclosporiasis, on what cultivation or harvesting practices would you focus in the investigation of the raspberry-producing farms?

The six most commonly implicated farms supplying Exporter A were in the same region of Guatemala. All six began harvesting for the first time in 1996 and often had raspberries in the same shipment. Five of the farms obtained agricultural water from wells. These wells varied in construction, depth, and quality. Two of the five farms also stored well water in reservoirs constructed of concrete blocks and covered with concrete. The sixth farm used river water. The farm that supplied raspberries to Exporter B was 25 km from the closest of the six farms that sold raspberries to Exporter A. That farm used well water, which was stored in a mesh-covered, plastic-lined, man-made reservoir.

At all seven farms, ground-level drip irrigation was used (primarily during the dry season) to avoid direct contact between raspberries and water. Agricultural water was also used to mix insecticides and fungicides that were sprayed directly onto raspberries, sometimes as late as the day they were harvested. At all farms, the raspberries were picked and sorted by hand, packed in plastic containers, and flown to the United States within 36 hours of picking.

Agricultural water at the seven farms (and on Guatemalan raspberry farms, in general) was filtered to remove debris but not microbes. Testing of agricultural-water samples from the seven farms indicated at least intermittent contamination with bacteria commonly found in sewage and human wastes (i.e., “coliforms” such as *Escherichia coli*). No *Cyclospora* were found.

No *Cyclospora* were found in samples of Guatemalan raspberries obtained from the farms during the traceback investigation.

**Question 15:** *Cyclospora* were not found in any Guatemalan raspberries or water samples. If the Guatemalan raspberries were the source of the cyclosporiasis outbreaks, list plausible explanations for this finding.

Investigators hypothesized that the raspberries became contaminated through spraying with insecticides and fungicides that had been mixed with contaminated water from improperly constructed or maintained wells near deep pit latrines or seepage pits. The wells may have been particularly vulnerable to contamination during the rainy season (e.g., from surface-water runoff), when the 1996 outbreak occurred. Once contaminated, the raspberries remained contaminated until eaten because they were too fragile and covered with crevices to be washed thoroughly.

By July 18, 1996, CDC and FDA declared that raspberries from Guatemala were the likely source of the *Cyclospora* outbreak.

## Part V – Control and Prevention Measures

Although skeptical of study findings and suspicious of potential trade barriers, the government of Guatemala, Guatemalan raspberry growers and exporters, and the Guatemalan Berries Commission (a growers' organization) collaborated with CDC and FDA to decrease the risk of contamination of Guatemalan raspberries during growth, harvest, and packaging.

**Question 16:** What specific measures would you suggest to decrease the likelihood of contamination of raspberries from the Guatemalan farms?

The Guatemalan raspberry growers voluntarily improved employee hygiene, sanitation, and water quality. They implemented systems to monitor the production of the raspberries so that potential points of contamination could be identified and addressed (i.e., Hazard Analysis and Critical Control Point systems). The Guatemalan Berries Commission established a farm classification system (with only farms in the best class permitted to export) in an attempt to minimize the exportation of *Cyclospora*-contaminated raspberries to the United States.

During the fall and winter of 1996, no outbreaks of cyclosporiasis in the United States were linked to Guatemalan raspberries. In the spring of 1997, however, another multistate outbreak occurred. By the end of May, more than a thousand new cases of cyclosporiasis had been reported from 18 states and two provinces in Canada. Consumption of raspberries was strongly associated with the outbreaks and the preponderance of the traceback data implicated Guatemala as the source of the raspberries, suggesting either some farms did not fully implement the control measures or the contamination was associated with a source against which these measures were not directed.

In the face of warnings by U.S. public health authorities on the danger of eating Guatemalan raspberries, the government of Guatemala and the Guatemalan Berries Commission voluntarily suspended exports of fresh raspberries to the United States on May 30, 1997. (See "FDA Talk Paper".) The interruption of exportation caused large economic losses for the producers, especially small and medium-sized ones.

**FDA**

**TALK PAPER**

*Food and Drug Administration  
U.S. Department of Health and Human Services  
Public Health Service 5600 Fishers Lane Rockville, MD 20857*

T97-22

June 10, 1997

OUTBREAKS OF CYCLOSPORIASIS AND GUATEMALAN RASPBERRIES

We have been receiving inquiries about recent U.S. outbreaks of cyclosporiasis, a diarrheal illness resulting from ingestion of the *Cyclospora* parasite. The following may be useful for answering questions.

According to the U.S. Centers for Disease Control and Prevention, fresh raspberries from Guatemala are the likely cause of outbreaks of cyclosporiasis that have occurred since mid-April in at least seven states including California, Maryland, Nebraska, Nevada, New York, Rhode Island and Texas. CDC and FDA are cooperating in investigating the outbreaks, examining epidemiological evidence and tracing the source of implicated raspberries.

FDA and CDC were informed by the Guatemalan government and the Guatemalan Berries Commission on May 30 that the country's growers voluntarily suspended shipment of fresh raspberries to the United States. FDA is working with CDC, the Guatemalan government and the Guatemalan Berries Commission to determine when the country may resume shipment of fresh raspberries to the United States.

FDA believes that few if any fresh raspberries from Guatemala remain on the U.S. market due to the short shelf life of the commodity. However, if any consumers, distributors, caterers, restaurateurs or retail establishments are holding fresh raspberries labeled as Product of Guatemala, they should not serve, sell or eat them.

FDA is advising consumers who have recently eaten fresh raspberries from Guatemala and who are suffering diarrheal illness to see a doctor for diagnosis and possible treatment for cyclosporiasis.

*Cyclospora* infects the small intestine and causes watery diarrhea with frequent, sometimes explosive bowel movements. Other symptoms include loss of appetite, substantial loss of weight, bloating, increased gas, stomach cramps, nausea, vomiting, muscle aches, low-grade fever and fatigue. Symptoms usually develop about a week after consuming contaminated product. *Cyclospora* infection can be successfully treated with appropriate antibiotics.

FDA will convene a public meeting in July to review the science on *Cyclospora* on fresh produce and its control. The date and other details of that meeting will be made public when they are available.

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CDC and FDA continued to work with the government of Guatemala and the Berries Commission to determine when the safety of Guatemalan raspberries could be assured and exports could resume. The exportation of raspberries resumed in mid-June; however, U.S. public health authorities continued to warn of the dangers of eating Guatemalan raspberries.

In December 1997, amid objections from the Guatemalan government, FDA announced that it was blocking imports of raspberries from Guatemala for 1998. Before this time, FDA rarely denied imports without physical evidence, and this ban was based only on epidemiological evidence about past outbreaks and FDA observations on current raspberry production practices. Congressional representatives and supporters of free trade railed about protectionism and questioned the science behind the decision since *Cyclospora* had not been identified on any raspberries from Guatemala.

**Question 17:** Do you believe that the raspberries were the source of the multistate outbreaks of cyclosporiasis? Which of the criteria for causality (i.e., strength of association, biological plausibility, consistency with other studies, exposure precedes disease, and dose-response effect) have been satisfied in the linkage between raspberries and cyclosporiasis? How would you convince others on the validity of these findings?

The U.S. ban on importation of Guatemalan raspberries became effective on March 15, 1998 and continued through August 15, the normal Guatemalan raspberry exporting season. With the ban in place, outbreaks of cyclosporiasis did not occur in 1998 in the United States.

Canadian officials decided not to block the importation of Guatemalan raspberries in 1998. In May and June, a multicluster outbreak of cyclosporiasis occurred in Ontario involving over 300 people. Investigations linked the outbreak to raspberries from Guatemala.

Beginning in the spring of 1999, the United States allowed entry of raspberries from farms that complied with a detailed program of food safety practices and successfully passed Guatemalan government inspections and FDA audits. That spring, there were several cyclosporiasis outbreaks in the United States and Canada; however, Guatemalan raspberries were not implicated as a source for any. In 2000, two outbreaks of cyclosporiasis were linked to raspberries traced to one Guatemalan farm. That farm discontinued exportation of raspberries.

As of June 2004, no further outbreaks of cyclosporiasis have been associated with Guatemalan raspberries. However, only three of the original 85 Guatemalan raspberry growers continue to export raspberries.

## Epilogue

Announcements by Texas and Ontario public health officials implicating California strawberries as the source of the cyclosporiasis outbreaks in May of 1996 had a devastating effect on the strawberry industry. Supermarket chains took California strawberries off their shelves, in response to pressure from consumers. Consumers stopped buying strawberries from all sources. Truckloads of strawberries headed for market rotted as they were turned away by produce and grocery store managers. Strawberry sales around the United States and Canada crashed, causing \$40 million in losses for the industry and the loss of 5,000 jobs.

And, in the end, the actual vehicle for the outbreak turned out to be Guatemalan raspberries, not strawberries.

**Question 18:** To prevent additional cases of a health problem (and possible hospitalizations and deaths), public health authorities are often required to make decisions on control measures when data are suggestive of the source of the problem but are, perhaps, not conclusive. What criteria would cause you to implement control measures for a health problem before you were absolutely certain of the source?

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## **APPENDIX 1: CDC Cyclosporiasis Fact Sheet** (available at <http://www.cdc.gov/az.do>)

*Cyclospora cayetanensis* (SIGH-clo-SPORE-uh KYE-uh-tuh-NEN-sis) is a parasite composed of one cell, too small to be seen without a microscope. The first known human cases of illness caused by *Cyclospora* infection (i.e., cyclosporiasis) were reported in 1979. Cases began being reported more often in the mid-1980s. In the last several years, outbreaks of cyclosporiasis have been reported in the United States and Canada.

### **How is *Cyclospora* spread?**

*Cyclospora* is spread by people ingesting something, for example, water or food that was contaminated with infected stool. For example, outbreaks of cyclosporiasis have been linked to various types of fresh produce. *Cyclospora* needs time (days or weeks) after being passed in a bowel movement to become infectious. Therefore, it is unlikely that *Cyclospora* is passed directly from one person to another. It is unknown whether animals can be infected and pass infection to people.

### **Who is at risk for infection?**

People of all ages are at risk for infection. In the past, *Cyclospora* infection was usually found in people who lived or traveled in developing countries. However, people can be infected worldwide, including the United States.

### **What are the symptoms of infection?**

*Cyclospora* infects the small intestine (bowel) and usually causes watery diarrhea, with frequent, sometimes explosive, bowel movements. Other symptoms can include loss of appetite, substantial loss of weight, bloating, increased gas, stomach cramps, nausea, vomiting, muscle aches, low-grade fever, and fatigue. Some people who are infected with *Cyclospora* do not have any symptoms.

### **How soon after infection will symptoms begin?**

The time between becoming infected and becoming sick is usually about 1 week.

### **How long will symptoms last?**

If not treated, the illness may last from a few days to a month or longer. Symptoms may seem to go away and then return one or more times (relapse).

### **What should I do if I think I may be infected?**

See your health care provider.

### **How is *Cyclospora* infection diagnosed?**

Your health care provider will ask you to submit stool specimens to see if you are infected. Because testing for *Cyclospora* infection can be difficult, you may be asked to submit several stool specimens over several days. Identification of this parasite in stool requires special laboratory tests that are not routinely done. Therefore, your health care provider should specifically request testing for *Cyclospora*. Your health care provider may have your stool checked for other organisms that can cause similar symptoms.

### **How is infection treated?**

The recommended treatment for infection with *Cyclospora* is a combination of two antibiotics, trimethoprim-sulfamethoxazole, also known as Bactrim\*, Septra\*, or Cotrim\*. People who have diarrhea should rest and drink plenty of fluids.

### **I am allergic to sulfa drugs; is there another drug I can take?**

No alternative drugs have been identified yet for people who are unable to take sulfa drugs. See your health care provider for other treatment recommendations.

### **How is infection prevented?**

Avoiding water or food that may be contaminated with stool may help prevent *Cyclospora* infection. People who have previously been infected with *Cyclospora* can become infected again.

### **For more information:**

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## APPENDIX 2: Calculating Measures of Association

### Cohort studies

The **relative risk** is the measure of association for a cohort study. It tells us how much more likely (or less likely) it is for people exposed to a factor to develop a disease compared to people not exposed to the factor.

The relative risk is the **ratio of the attack rates** of a disease among people exposed to the factor and those not exposed to that factor. (The **attack rate** is the incidence of disease in a group [i.e., the number of people in the group who became ill divided by the total number of people in the group].)

$$\begin{aligned} \text{attack rate} &= \frac{\text{\# ill people in group}}{\text{\# people in group}} \\ \text{relative risk} &= \frac{\text{attack rate for exposed persons}}{\text{attack rate for unexposed person}} \end{aligned}$$

A relative risk of:

- **1.0** (or close to 1.0) means the risk of disease is similar in the exposed and unexposed group and exposure is not associated with disease.
- **Greater than 1.0** means the risk of disease is greater in the exposed than the unexposed group and the exposure could be a risk factor for the disease.
- **Less than 1.0** means the risk of disease is less in the exposed group than the unexposed group and the exposure could be a protective factor.

In the Texas cohort study:

Twelve of 13 attendees who ate the berry dessert became ill. Only one of eleven attendees who did not eat the berry dessert became ill. Inserting these numbers into the 2x2 table:

Ate Berry Dessert	Ill	Well	TOTAL
Yes	12	1	13
No	1	10	11
TOTAL	13	11	24

$$\text{attack rate (ate berries)} = \frac{\text{\# people who ate berries who became ill}}{\text{\# people who ate berries}}$$

$$= \frac{12}{13} = 92\%$$

$$\text{attack rate (did not eat berries)} = \frac{\text{\# people who did not eat berries who became ill}}{\text{\# people who did not eat berries}}$$

$$= \frac{1}{11} = 9\%$$

$$\text{relative risk (eating berries)} = \frac{\text{attack rate for people exposed to berries}}{\text{attack rate for people not exposed to berries}}$$

$$= \frac{92\%}{9\%} = 10.2$$

Interpretation: People exposed to the berry dessert were 10 times more likely to develop illness than people not exposed to the berry dessert.

## Case-control studies

The **odds ratio** is the measure of association for a case-control study. It tells us how much higher the odds of exposure is among cases of a disease compared with controls.

The odds ratio compares the **odds of exposure** to the factor of interest **among cases** to the odds of exposure to the factor **among controls**. (The **odds** is the probability that an event will happen divided by the probability that it won't happen.)

For an unmatched case-control study, the data look like this:

Exposed	Case	Control	TOTAL
Yes	a	b	a+b
No	c	d	c+d
TOTAL	a+c	b+d	a+b+c+d

$$\text{odds of exposure (cases)} = \frac{\text{number of cases with the exposure}}{\text{number of cases without the exposure}} = \frac{a}{c}$$

$$\text{odds of exposure (controls)} = \frac{\text{number of controls with the exposure}}{\text{number of controls without the exposure}} = \frac{b}{d}$$

$$\text{odds ratio} = \frac{\text{odds of exposure (cases)}}{\text{odds of exposure (controls)}} = \frac{ad}{bc}$$

An odds ratio of:

- **1.0 (or close to 1.0)** means that the odds of exposure among cases is the same as the odds of exposure among controls. The exposure is not associated with the disease.
- **Greater than 1.0** means that the odds of exposure among cases is greater than the odds of exposure among controls. The exposure may be a risk factor for the disease.
- **Less than 1.0** means that the odds of exposure among cases is lower than the odds of exposure among controls. The exposure may be protective against the disease.

In the New Jersey case-control study:

Twenty-one of 30 case-patients and four of 60 controls had eaten raspberries. Inserting these numbers into the 2x2 table:

Ate Raspberries	Case	Control	TOTAL
Yes	21 (a)	4 (b)	25
No	9 (c)	56 (d)	65
TOTAL	30	60	90

$$\text{odds of exposure (cases)} = \frac{21}{9} = 2.3$$

$$\text{odds of exposure (controls)} = \frac{4}{56} = 0.07$$

$$\text{odds ratio} = \frac{\text{odds of exposure (cases)}}{\text{odds of exposure (controls)}} = \frac{2.3}{0.07} = 32.7$$

or

$$\text{odds ratio} = \frac{ad}{bc} = \frac{(21)(56)}{(4)(9)} = 32.7$$

Interpretation: The odds of exposure to raspberries was over 30 times higher among cases than controls.