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ACTIVE, MULTISITE, LABORATORY-BASED SURVEILLANCE FOR *CRYPTOSPORIDIUM PARVUM*

VANCE DIETZ, DUC VUGIA, RANDALL NELSON, JULIE WICKLUND, JOELLE NADLE, KATHERINE GIBBS MCCOMBS, SUDHA REDDY, AND THE FOODNET WORKING GROUP

Division of Parasitic Diseases, and Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; Division of Communicable Disease Control, California Department of Health Services, Berkeley, California; Connecticut Department of Public Health, Hartford, Connecticut; Minnesota Department of Health, Minneapolis, Minnesota; Division of Public Health, Georgia Department of Human Resources, Atlanta, Georgia

Abstract. *Cryptosporidium parvum* leaped to the attention of the United States following the 1993 outbreak in Milwaukee, Wisconsin, which sickened 400,000 people. Other outbreaks in the United States have been associated with drinking and recreational water, consumption of contaminated foods, contact with animals, and childcare attendance. Despite its public health importance, the number of people who become infected each year is not known. In 1997, active surveillance for *C. parvum* was added to the Foodborne Diseases Active Surveillance Network (FoodNet), a collaborative effort among the Centers for Disease Control and Prevention, selected state health departments, the U.S. Departments of Agriculture and Food and Drug Administration. During the first 2 years of surveillance, 1,023 laboratory-confirmed cases of cryptosporidiosis were detected in FoodNet (Connecticut, Minnesota, Oregon, and selected counties in California, Georgia, Maryland, and New York). The annual rate per 100,000 persons was 2.3. Sixteen percent of case-patients were hospitalized. A seasonal increase in case detection was noted in late summer among persons less than 15 years of age. These data represent the first active multistate ascertainment of laboratory-confirmed cryptosporidiosis cases and provide useful information on the burden of disease in the United States.

INTRODUCTION

First identified as a human pathogen in 1976, *Cryptosporidium parvum*, a coccidian protozoan parasite, has increasingly been recognized as an important cause of gastrointestinal illness.[1] In 1993, a massive outbreak of cryptosporidiosis in Milwaukee, Wisconsin, associated with contaminated city drinking water, made approximately 400,000 persons ill.[2] In the United States, outbreaks have also been associated with drinking water, recreational water use, consumption of contaminated foods, contact with animals, and child care attendance.[3–8] These outbreaks have heightened the awareness of cryptosporidiosis in this country.

Persons become infected with *C. parvum* through the ingestion of oocysts excreted in human or animal feces.[9] Infection can occur from person-to-person, animal-to-person, and through environmental transmission. Infection with *C. parvum* generally causes a self-limited diarrheal illness lasting 7–14 days. Symptoms can, however, last for weeks and may be severe. In immunocompromised persons, the disease can be chronic, severe and may even contribute to death.[10]

Despite the public health importance of cryptosporidiosis, good estimates of the number of people who become infected each year are not available. According to national routine (passive) surveillance data, approximately 3,000 cases are reported to the Centers for Disease Control and Prevention (CDC) each year (CDC, the National Electronic Telecommunications Surveillance System [NETSS], unpublished data). These data are probably an underestimate of the true magnitude of the disease. Possible reasons for this underestimate include the following: cryptosporidiosis is not a reportable disease in all states, laboratories and physicians fail to report all laboratory-confirmed cases, not all persons with a diarrheal illness seek medical care, not all providers request stools for testing, and in addition, not all laboratory testing includes *C. parvum*.

In 1997, to obtain better national and state-specific estimates of the burden of disease from *Cryptosporidium*, surveillance for *C. parvum* was added to the Foodborne Diseases Active Surveillance Network (FoodNet), which is part of the Emerging Infection Program (EIP).[11] FoodNet is a collaborative effort among CDC, the U.S. Department of Agriculture (USDA), the Food and Drug Administration (FDA), and selected EIP sites (Appendix 1). As opposed to passive national surveillance, in FoodNet staff regularly communicate with all laboratories in their surveillance areas to detect all laboratory-confirmed cases of cryptosporidiosis. This report summarizes the *Cryptosporidium* surveillance data from FoodNet for 1997 and 1998.

MATERIALS AND METHODS

In 1994, CDC implemented the EIP at selected sites around the nation. This program is conducted in collaboration with state and local health departments as well as academic centers and professional health associations. As part of the program, each participating site conducts population-based surveillance; FoodNet is the primary foodborne disease component. Its objectives are to estimate the burden of foodborne disease in the United States, to determine the proportion of foodborne diseases associated with specific food or other exposures, and to provide a framework to respond rapidly and collaboratively to emerging foodborne diseases.[11] In January 1996, active surveillance for seven bacterial pathogens began in five sites: Minnesota, Oregon, and selected counties in California, Connecticut, and Georgia. In 1997, selected counties in New York and Maryland were added. Surveillance for *C. parvum* began in January of 1997 in Connecticut, Minnesota, and in selected counties in California, and in July in Oregon. In 1998, surveillance began in selected counties in Georgia, Maryland, and New York.[12]

As part of the FoodNet program, each site identified all laboratories in the areas under surveillance that perform laboratory testing for the organism of interest. An initial survey

TABLE 1

Laboratory-confirmed cases of cryptosporidiosis, FoodNet, 1997–1998*

Site†	1997	1998	Total (%)
California	144	158	302 (30%)
Connecticut	42	44	86 (8%)
Georgia‡	—	93	93 (9%)
Maryland‡	—	12	12 (1%)
Minnesota§	242	173	415 (41%)
New York‡	—	20	20 (2%)
Oregon¶	26	69	95 (9%)
Total	454	569	1,023 (100%)

* Data for 1998 are preliminary.
† See text for description of geographic catchment areas.
‡ Began surveillance in 1998.
§ Includes outbreak-associated cases (1997 = 84, 1998 = 15).
¶ Oregon began surveillance in July 1997.
– = not participating at that time.

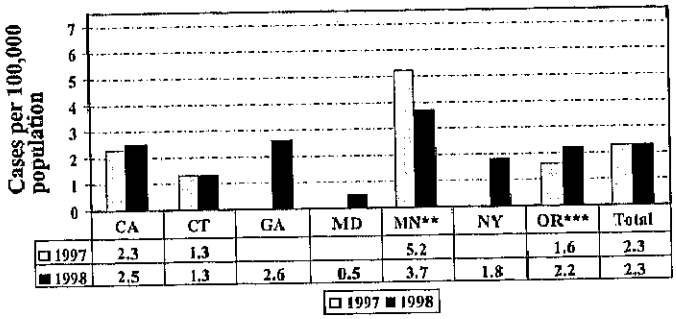

FIGURE 1. Cases of cryptosporidiosis per 100,000 population by site (Georgia, Maryland, and New York began surveillance in 1998). Collected by FoodNet, 1997 and 1998. **In 1997 and 1998, Minnesota experienced an outbreak. ***Oregon began surveillance in July 1997.

of all participating laboratories demonstrated that among those that tested for *C. parvum*; most, i.e., 119 (74%) used acid fast staining for detection of *C. parvum*, 35 (22%) used direct fluorescent antibody staining, and 15 (9%) used a commercial ELISA diagnostic kit. Overall positivity rates for each method were 1.3%, 1.4%, and 6.5%, respectively. The states did not differ in terms of overall testing methods, i.e., the majority of laboratories in each state used acid fast staining for the detection of *C. parvum*.

FoodNet staff maintains regular communication with each laboratory. The frequency of communication depends on the site and organism included in surveillance. Laboratories report to a central FoodNet office in each site. Only laboratory-confirmed cases are reported to the FoodNet office. These sites report electronically to CDC on an ongoing and regular basis via the Public Health Laboratory Information System (PHLIS).[13] FoodNet collects information on both the number of specimens positive for *C. parvum* and the number of persons infected. However, data included in the analysis presented here include only the number of persons infected. Information transmitted to CDC for each case of cryptosporidiosis includes age, sex, race, and ethnicity data, as well as the laboratory test used to identify the organism. Additional information is collected on hospitalization and outcome. FoodNet obtains information on an individual's hospitalization status in several ways, e.g., from a physician report, by contacting the physician who requested the test that identified *C. parvum*, directly from the patient, or, in the case of hospital-based laboratories, directly from a laboratory. Some sites obtain information on human immunodeficiency virus (HIV) status. However, this is not collected consistently and may be obtained differently by sites. For example, in Connecticut, all case-patients with cryptosporidiosis are interviewed by telephone and questioned about their HIV status. In Minnesota, FoodNet staff provide a list of laboratory-confirmed cases of cryptosporidiosis to the state HIV unit, which in turns supplies FoodNet with the number of persons with cryptosporidiosis who are HIV-positive, along with basic demographic information. In California, legal statutes prevent health officials from seeking information on the HIV status of any individual. In Oregon, FoodNet staff request information on a patient's HIV status from the patient's physician but it is often not available. In Maryland, the information is not collected.

Annual incidence rates were calculated using the number of cases detected in the FoodNet surveillance area as the numerator and the 1997 postcensus estimates from the FoodNet population under surveillance as the denominator.[14] For Oregon, to calculate the 1997 incidence, the number of cases detected during the 6 months of surveillance in 1997 was doubled. Monthly incidence data is calculated based on the date of specimen collection. The total population under FoodNet surveillance was 20,928,056 in 1997 and 24,476,487 in 1998.

Data collection for a given year is finalized early the following year. Thus, while the number of cases presented here for 1998 are final, data on demographics, hospitalization, outcome, and HIV status are preliminary.

RESULTS

Characteristics of all laboratory-confirmed cases. In 1997 and 1998, 1,023 cases of *C. parvum* were detected by FoodNet (Table 1). Of these, Minnesota reported 415 or 41% of all cases. In 1997, 84 of these cases were known to be outbreak-associated, and in 1998, 15 cases were outbreak-associated. California reported 302 (30%) cases. Cases per 100,000 population in 1997 ranged from 1.3 in Connecticut to 5.2 in Minnesota for an overall rate of 2.3 per 100,000 per year (Figure 1). During 1998, the overall rate was also 2.3 per 100,000 population (range = 0.5 in Maryland to 3.7 in Minnesota). Of all cases, 587 (57%) persons were male and 429 (43%) persons were female (Table 2). All age groups were represented. However, 37% of cases were in

TABLE 2

Laboratory-confirmed cases of cryptosporidiosis by age in years and by sex. Collected by FoodNet, 1997 and 1998*

Age (years)	Female	Male	Unknown	Total (%)
0–4	81	115	0	196 (19%)
5–14	87	97	1	185 (18%)
15–24	31	40	0	71 (7%)
25–44	142	255	1	398 (39%)
45–60	56	59	0	115 (11%)
≥61	32	21	0	53 (5%)
Unknown	0	0	5	5 (0.5%)
Total	429	587	7	1,023 (100%)

* Data for 1998 are preliminary.

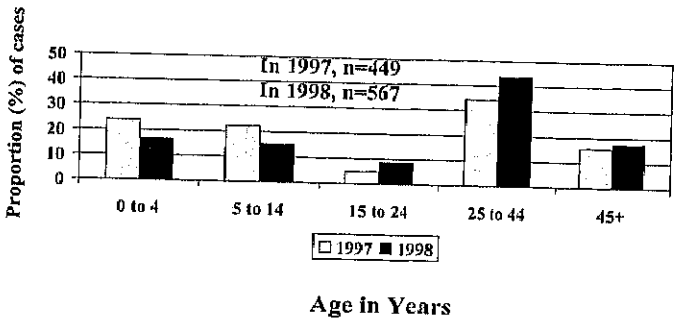

FIGURE 2. Age distribution of laboratory-confirmed case of cryptosporidiosis. Collected by FoodNet, 1997–1998. The year of onset was unknown for 7 cases.

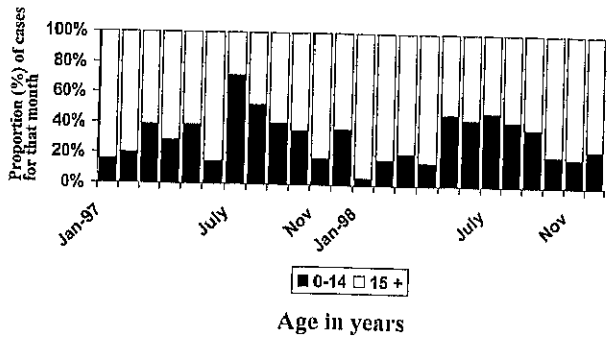

FIGURE 4. Age distribution for each month of surveillance for cases of cryptosporidiosis by month of collection. Collected by FoodNet, 1997–1998.

persons less than 15 years of age (Figure 2). Information on race was available in 646 (63%) cases. Of these, 538 (83%) were white and 94 (15%) were African-American. Persons in most cases (54%) did not provide information on ethnicity. Persons in 40 (4%) cases were identified as Hispanic.

Cases were detected during all months of the year with increases noted in the summer months of both years of surveillance, when 40% of all cases were detected (Figure 3). When evaluated by age, this increase was seen primarily among individuals less than 15 years of age (Figure 4). For example, when evaluated monthly from January through June of 1997, persons less than 15 years of age accounted for less than 40% of all cases during any month. In July, however, they accounted for 72% of all cases and for 53% of all cases in August. In 1998, from January through April, less than 21% of cases were in persons less than 15 years of age in a given month. In June, however, they accounted for 44% of all cases, 48% in July, and 43% in August.

A total of 161 case-patients were hospitalized (79 in 1997 and 82 in 1998) and 6 died. The annual hospitalization rate was 17.4% in 1997 and 14.4% in 1998 for an average of 15.7%. The overall case-fatality rate was 0.6%.

The HIV status was available only for 236 (23%) of all cases. Of these 236 cases, 103 persons (44%) were HIV-positive. Three percent died and 32% were hospitalized. When compared with all cases, no seasonal trend in the number of cases of cryptosporidiosis in HIV-positive persons was observed. When HIV status was evaluated by seasonality, the increased number of cases during the summer months was only seen in HIV-negative individuals (Figure 5).

Severe cases. Hospitalized case-patients with cryptosporidiosis were detected in all FoodNet sites (Table 3). Most were male and persons ≥ 25 years of age. Of the hospitalized cases, 25% were persons 5–14 years of age. Information about HIV status was available for 43 hospitalized cases; 32 (74%) were HIV-positive. Five of these hospitalized persons died; data on the cause was not obtained.

All fatal cases (five hospitalized and one not hospitalized) were in persons between 25 and 44 years of age; 83% were male. Three fatal cases were reported form California, two from Connecticut, and one from New York. The HIV status was known for three; all three were positive.

Minnesota 1997 outbreak. In early July 1997, an outbreak of cryptosporidiosis with 84 cases was reported in Minnesota.[15] The outbreak was associated with a water sprinkler fountain in a zoo. Cases were detected from July 6 through August 3 with the peak on July 15 when 18 cases occurred. Most (87%) of cases were in persons ≤ 10 years of age. Half were male. There were 12 hospitalizations and no deaths.

DISCUSSION

Cryptosporidiosis has emerged as an important cause of gastrointestinal illness in the United States. Unfortunately, surveillance for cryptosporidiosis is hampered by many factors. First, few individuals with a diarrheal illness seek medical attention. Of those who do, only a minority has stool examinations requested by their provider. Second, of providers who request a stool examination, not all request examination for parasitic diseases. Of those who do, not all may

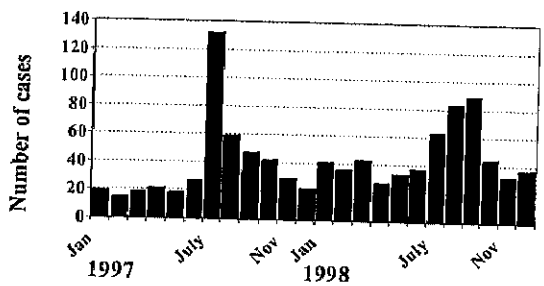

FIGURE 3. Number of laboratory-confirmed cases of cryptosporidiosis by month of collection. Collected by FoodNet, 1997–1998.

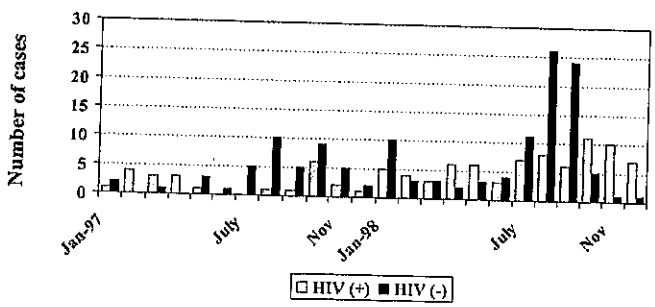

FIGURE 5. Number of cases of cryptosporidiosis by month of collection and human immunodeficiency virus (HIV) status, FoodNet, 1997–1998. HIV status was not consistently collected. Status was known for 236 (23%) of 1,023. See Materials and Methods for explanation.

TABLE 3

Characteristics of hospitalized laboratory-confirmed cases of cryptosporidiosis: site, age in years, sex, human immunodeficiency (HIV) status, and clinical outcome. Collected by FoodNet, 1997 and 1998*

Characteristic		Number	Percent of total
Site†	California	22	14
	Connecticut	23	14
	Georgia‡	16	10
	Maryland‡	2	1
	Minnesota	82	51
	New York‡	5	3
	Oregon	11	7
Age (years)	0–4	20	12
	5–14	39	24
	15–24	14	9
	25–44	62	39
	45–60	13	8
	≥61	13	8
Sex	Female	65	40
	Male	96	60
Outcome	Alive	151	94
	Died	5	3
	Unknown	5	3
HIV status§	Positive	32	20
	Negative	11	7
	Unknown	118	73

* Data for 1998 are preliminary.
† See text for description of geographic catchment areas.
‡ Began surveillane in 1998.
§ HIV status not consistently collected; see text for explanation.

request tests specific for *C. parvum*. Increased testing of specimens for *Cryptosporidium* is hampered by the concern of low positivity rates, costs, need for technician time, and lack of appropriate equipment.[16]

Surveillance activities in FoodNet attempt to address at least some of the deficiencies in the routine surveillance and reporting of cryptosporidiosis. While not currently addressing the impact of deficiencies in testing practices on surveillance, FoodNet surveillance may result in increased sensitivity over traditional passive reporting. As opposed to routine passive reporting, all laboratories in FoodNet surveillance areas are routinely contacted to ensure that all identified cases are reported. FoodNet data suggests that cryptosporidiosis is widespread and may be more common than previously thought. In addition, these data suggest that cryptosporidiosis causes significant and severe illness, with a 16% hospitalization rate in our surveillance sites. However, since hospitalized cases may be more likely to be detected than non-hospitalized cases, this hospitalization rate may be artificially high.

Data reported here suggest a seasonal trend in *C. parvum* infections. This has been observed at the national level as well (CDC, unpublished data). The increased identification of *C. parvum* in the summer among both young persons and persons who are HIV-negative could represent increased transmission from recreational water use. To address this and other questions, in 1999 FoodNet sites began conducting a case-control study of sporadic cases. Persons with laboratory-confirmed *C. parvum* infection are interviewed along with two age and geographically matched controls. Information on water use and consumption, travel, and contact with childcare attendees or with animals is obtained. This will provide insight into vehicles of transmission including those that cause seasonal increases, which will aid the development of appropriate public health interventions.

Many questions remain unanswered about cryptosporidiosis. A critical question for the understanding and control of cryptosporidiosis relates to the relative roles of drinking water and recreational water, food, and person-to-person or animal-to-person contact in the transmission of *C. parvum*. Active surveillance for *Cryptosporidium* in conjunction with the case-control study of detected cases will provide useful information. In addition, the Environmental Protection Agency (EPA) and CDC, in collaboration with state and local health departments, will conduct studies to assess the burden of the disease attributable to drinking water. If we are to have the necessary information to assess the burden of disease from *Cryptosporidium*, more rapid and sensitive serologic and molecular diagnostic tests are needed for the detection of *Cryptosporidium* in humans and in the environment.[1] For example, improved surveillance techniques are needed to address the potential for transmission via water before it occurs and studies are needed to determine the public health significance of low levels of oocysts frequently found in municipal drinking water. Finally, new drugs are needed to treat cryptosporidiosis not only to reduce the illness associated with infection, particularly in immunosuppressed persons, but to provide added impetus to physicians to request stool examinations for *C. parvum*, thereby improving the likelihood of better disease ascertainment.

Authors' addresses: Vance Dietz, Division of Parasitic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Mailstop F-22, 4770 Buford Highway, NE, Atlanta, GA 30341-3724. Duc Vugia, Division of Communicable Disease Control, California Department of Health Services, 2151 Berkeley Way, Berkeley, CA 94707-1101. Randall Nelson, Epidemiology Program, Connecticut Department of Public Health, 410 Capitol Avenue, MS# 11EPI, Hartford, CT 06134-0308. Julie Wicklund, 7037 25th Avenue NW, Seattle, WA 98117. Joelle Nadle, California Emerging Infections Program, 1212 Broadway, #704, Oakland, CA 94612. Katherine Gibbs McCombs, Notifiable Diseases Unit, Division of Public Health, 2 Peachtree Street NW, Suite 14-263, Atlanta, GA. Sudha Reddy, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Mailstop A-38, 1600 Clifton Road, Atlanta, GA 30333.

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Appendix 1

1998 FoodNet Working Group

CDC
Frederick Angulo
Thomas Van Gilder
Patricia Griffin
Robert Tauxe
Drew Voetsch
Sudha Reddy
Samantha Yang
David Wallace
Nina Marano
Paul Mead
David Swerdlow
Laurence Slutsker
Cindy Friedman
Vance Dietz
Bill MacKenzie
Kate Glynn
Thomas Hennessy
Sarah Pichette
Karen Stamey
Peggy Hayes
Timothy Barrett
Bala Swaminathan
John Hatmaker
Richard Bishop
Kathleen Maloney
Mike Hoekstra
Nancy Bean
Laura Conn
Robert Pinner

California
Duc Vugia
Michael Samuel
Ben Werner
Kevin Reilly
Sharon Abbott
Sue Shallow
Gretchen Rothrock
Pam Daily
Alexander McNees
Nandeeni Mukerjee
Joelle Nadle
Mary Ann Davis
Lisa Gelling
Ben Silk

Connecticut
James Hadler
Matthew Cartter
Ruthanne Marcus
Terry Fiorentino
Gazala Kazi
Robin Ryder
Patricia Mshar
Robert Howard
Donald Mayo

Georgia
Paul Blake
Jane Koehler
Monica Farley
Susan Ray
Wendy Baughman
Suzanne Segler
Shama Desai
Matthew Sattah
Sabrina Whitfield
Molly Bardsley
Katherine Gibbs McCombs
Laura Gilbert

Maryland
Kelly Henning
Peggy Pass
Lora Gay
Michael Carter
Dale Rohn
Jeffery Roche
Diane Dwyer
Althea Glenn
Jafar Razeq
Yongyu Wong
Alexander Sulakvelidze
J. Glenn Morris, Jr.

Minnesota
Michael Osterholm
Craig Hedberg
Julie Wicklund
Valerie Deneen
Heidi Kassenborg
Jeff Bender
Kirk Smith
John Besser

New York
Dale Morse
Perry Smith
Shelley Zansky
Nellie Dumas
Barbara Damaske
Hwa-Gan Chang
Candace Noonan
Brian Sauders
Karim Hechemy

Oregon
David Fleming
Paul Cieslak
Bill Keane
Beletshachew Shiferaw
Maureen Cassidy
Teresa McGivern
Regina Stanton
Steve Mauvais
Stephen Ladd-Wilson
Bob Sokolow
Vijay Balan

Tennessee
William Moore
Allen Craig
Timothy Jones
William Schaffner
Brenda Barnes

USDA
Kaye Wachsmuth
Phyllis Sparling
Ruth Etzel

FDA
Ken Falci
Bing Garthright
Clifford Purdy