A MASSIVE OUTBREAK IN MILWAUKEE OF CRYPTOSPORIDIUM INFECTION TRANSMITTED THROUGH THE PUBLIC WATER SUPPLY

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Abstract *Background.* Early in the spring of 1993 there was a widespread outbreak of acute watery diarrhea among the residents of Milwaukee.

Methods. We investigated the two Milwaukee water-treatment plants, gathered data from clinical laboratories on the results of tests for enteric pathogens, and examined ice made during the time of the outbreak for cryptosporidium oocysts. We surveyed residents with confirmed cryptosporidium infection and a sample of those with acute watery diarrhea consistent with cryptosporidium infection. To estimate the magnitude of the outbreak, we also conducted a survey using randomly selected telephone numbers in Milwaukee and four surrounding counties.

Results. There were marked increases in the turbidity of treated water at the city's southern water-treatment plant from March 23 until April 9, when the plant was shut down. Cryptosporidium oocysts were identified in water from ice made in southern Milwaukee during these weeks. The rates of isolation of other enteric pathogens remained stable, but there was more than a 100-fold increase in the rate of isolation of cryptosporidium. The median duration of illness was 9 days (range, 1 to 55). The median maximal number of stools per day was 12 (range, 1 to 90). Among 285 people surveyed who had laboratory-confirmed cryptosporidiosis, the clinical manifestations included watery diarrhea (in 93 percent), abdominal cramps (in 84 percent), fever (in 57 percent), and vomiting (in 48 percent). We estimate that 403,000 people had watery diarrhea attributable to this outbreak.

Conclusions. This massive outbreak of watery diarrhea was caused by cryptosporidium oocysts that passed through the filtration system of one of the city's water-treatment plants. Water-quality standards and the testing of patients for cryptosporidium were not adequate to detect this outbreak. (N Engl J Med 1994;331:161-7.)

HUMAN infection with cryptosporidium was first documented in 1976.[1,2] Since that time, cryptosporidium has been recognized as a cause of gastrointestinal illness in both immunocompetent[3-6] and immunodeficient people.[6,7] Infection with cryptosporidium results in watery diarrhea associated with varying frequencies of abdominal cramping, nausea, vomiting, and fever. In immunocompetent people, cryptosporidiosis is a self-limited illness, but in those who are immunocompromised, infection can be unrelenting and fatal.[5,8] Infection occurs in a variety of settings[8-11]; waterborne outbreaks of cryptosporidium infection have been documented in association with drinking water from a contaminated artesian well,[12] untreated surface water,[13] and filtered public water supplies.[14-16] We report our investigation of the largest documented outbreak of waterborne disease in the United States.

On April 5, 1993, the Wisconsin Division of Health was contacted by the Milwaukee Department of Health after reports of numerous cases of gastrointestinal illness that had resulted in widespread absenteeism among hospital employees, students, and schoolteachers. Little information was available about the nature of the illness or the results of laboratory tests of stool specimens from those who were ill. On April 7, two laboratories identified cryptosporidium oocysts in stool samples from seven adult residents of the Milwaukee area; none of the laboratories surveyed had found evidence of increased or unusual patterns of isolation of any other enteric pathogen.

The Milwaukee Water Works (MWW), which obtains water from Lake Michigan, supplies treated water to residences and businesses in the City of Milwaukee and nine surrounding municipalities in Milwaukee County. Either of two water-treatment plants, one located in the northern part of the city, and the other in the southern part, can supply water to the entire district; however, when both plants are in operation, the southern plant predominantly serves the southern portion of the district.

Examination of the two plants' records on the quality of untreated water (intake) and treated water (that supplied to customers) revealed an increase in the turbidity of treated water from the southern plant, beginning approximately on March 21, with increases to unprecedented levels of turbidity from March 23 through April 5. These findings pointed to the water supply as the likely source of infection and led to the institution, on the evening of April 7, of an advisory to MWW customers to boil their water. The southern plant was temporarily closed on April 9.

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METHODS

Investigation of Water-Treatment Plants

The policies, procedures, and physical plant of the southern MWW facility were reviewed and inspected in April 1993. Data on the monthly maximal turbidity of untreated and treated water from both plants were reviewed and analyzed for the period from January 1983 through April 1993. Data on the daily maximal turbidity and coliform count in untreated and treated water, as well as the pH and temperature of untreated water, were analyzed for the period from February through April 1993.

Examination of Ice Made during the Outbreak

Water that had been frozen and stored by a southern Milwaukee company in 213-liter blocks on March 25 and April 9, 1993, was melted and examined. From ice produced on each of those dates, three aliquots of water totaling 639 liters (three melted blocks) were filtered with peristaltic pumps and two types of filter: spun-polypropylene cartridge filters with a nominal porosity of 1 μm (approximate flow rate, 4 liters per minute), and 29.2-cm Millipore filters with a porosity of 0.45 μm (approximate flow rate, 2 liters per minute). The filters were eluted, the eluates centrifuged, and the pellets resuspended with the use of a standard procedure; the suspensions were examined for cryptosporidium oocysts with an immunofluorescent technique.[17]

Laboratory Surveillance

On April 7, surveillance for enteric pathogens was begun among 14 clinical laboratories in Milwaukee County. The laboratories reported the retrospective (March 1 through April 6, 1993) and prospective (April 7 through 16, 1993) test results for all stool specimens submitted for bacterial or viral culture and examination for ova and parasites. All 14 laboratories routinely tested all stool specimens submitted for bacterial culture for salmonella, shigella, and campylobacter, at a minimum. At our request, the laboratories reported, both retrospectively and prospectively, all positive tests for cryptosporidium from March 1 through May 30. Before April 7, 12 of the 14 laboratories tested for cryptosporidium only at the request of a physician; beginning on April 7, these 12 laboratories began to test all stool specimens for this coccidian protozoan. Cryptosporidium testing was performed according to standard concentration techniques with either modified acid-fast staining[18] (13 laboratories) or direct fluorescent antibody staining[19] (1 laboratory).

Examination for Enteric Infection

On April 13, stool specimens were solicited from 11 Milwaukee residents with gastrointestinal illness that had begun within the previous 48 hours. Stool specimens from these residents were tested for enteric pathogens with the use of routine procedures for enteric bacterial and viral culture, examination for ova and parasites, and modified acid-fast staining after formalin–ether sedimentation. The stool specimens were examined by electron microscopy. Serum samples obtained during the acute and convalescent phases of illness in 8 of the 11 residents were tested for antibody to the Norwalk virus.[20]

Laboratory-Confirmed Cryptosporidium Infection

A total of 739 people were found to have cryptosporidium in stool samples tested by the 14 participating laboratories between March 1 and May 30. Telephone numbers were available for 567 (77 percent) of these 739 people with laboratory-confirmed cryptosporidium infection, and 312 (55 percent) were interviewed by telephone. Of these 312 people, 285 (91 percent) reported an onset of illness between March 1 and May 15, 1993, and were considered case patients; the other 27 people were excluded from the study because their illnesses had begun before March 1. Telephone interviews were completed during two periods: from April 9 through April 13 (phase 1), 101 case patients were interviewed; and from April 17 through June 2 (phase 2), 200 were interviewed, including 16 of those who had been interviewed during phase 1. The same questionnaire was used in both phases to collect information on demographic characteristics and clinical illness. During the second phase, however, additional questions were asked about preexisting chronic diseases, weight loss, recurrent diarrhea, and length of hospital stay. People were considered to be immunocompromised if they reported having had a positive test for the human immunodeficiency virus or if they were being treated with immunosuppressive drugs, cancer chemotherapy, radiation therapy, or renal dialysis.

Clinical Cryptosporidium Infection in the MWW Service Area

To determine representative clinical characteristics of illness among the people affected by the outbreak, a telephone survey was conducted on April 9, 10, and 12 with the use of randomly selected telephone numbers from the MWW service area. The first adult (≥18 years of age) to answer the telephone was interviewed with the same questionnaire used in phase 1 to collect demographic and clinical information from the people with laboratory-confirmed cryptosporidiosis. Survey respondents were identified as having clinical cryptosporidium infection if they reported the occurrence of watery diarrhea between March 1, 1993, and the time of the interview.

Survey of Households in the Greater Milwaukee Area

To determine the extent of the outbreak, we conducted a telephone survey of households in the greater Milwaukee area (Milwaukee County and the four surrounding counties) with the use of a random-digit dialing method.[21,22] Households in the sample were contacted by interviewers from the Wisconsin Survey Research Laboratory during the period from April 28 through May 2. For each household, the interviewer asked to speak with the person most knowledgeable about the health of all members of the household. For each household member, this person provided information about demographic characteristics; employment or school attendance outside the home; the ZIP Code of the residence and workplace or school; the occurrence of diarrhea since March 1, 1993; and the onset, duration, and character of the diarrhea. We defined a case of probable cryptosporidium infection as the onset of watery diarrhea during the period from March 1 through April 28, 1993.

The residential ZIP Code was used to assign each person in the survey to one of four regions. The southern region was defined as the region that received water predominantly from the southern water-treatment plant, the northern region as that receiving water predominantly from the northern plant, and the middle zone as that receiving water from either plant, depending on supply and demand. In our analysis, all three of these regions were considered part of the MWW service area. All surveyed areas not receiving MWW water were considered in aggregate as the non-MWW region.

Results

Investigation of Water-Treatment Plants

At the time of the outbreak, both MWW plants treated water by adding chlorine and polyaluminum chloride (a coagulant to enhance the formation of larger particulates), rapid mixing, mechanical flocculation (which promotes the aggregation of particulates to form floc), sedimentation, and rapid sand filtration. After filtration, the effluent (treated water) was stored in a large clear well until it was supplied to customers. Filters were cleaned by backwashing them with water, which was then recycled through the treatment process.

From January 1983 through January 1993, the turbidity of treated water at the southern plant did not exceed 0.4 nephelometric turbidity unit (NTU). During the period from February through April 1993, the turbidity of treated water at the southern plant did not exceed 0.25 NTU until March 18, when it increased to 0.35 NTU. From March 23 to April 1, the maximal daily turbidity of treated water was consistently 0.45

NTU or higher, with peaks of 1.7 NTU on March 28 and 30, despite an adjustment of the dose of polyaluminum chloride (Fig. 1). Although marked improvement in the turbidity of treated water had been achieved by April 1 with the use of polyaluminum chloride, on April 2 the southern plant began to use alum instead of polyaluminum chloride as a coagulant. On April 5, the turbidity of treated water increased to 1.5 NTU. During the period from February through April 1993, the turbidity of treated water at the northern plant did not exceed 0.45 NTU. There was no correlation between the turbidity of treated water and the turbidity or temperature of untreated water.

Throughout the period from February to April 1993, samples of treated water from both plants were negative for coliforms and were within the limits set by the Wisconsin Department of Natural Resources for water quality. Inspection of the southern plant revealed that a streaming-current monitor, which can aid plant operators in adjusting the dose of coagulant, had been incorrectly installed and thus was not in use. In addition, monitors designed for continuous measurement of the turbidity of filtered water were not in operation. Turbidity was monitored once every eight hours.

Examination of Ice Made during the Outbreak

Water obtained by melting ice blocks produced on March 25 and April 9, 1993, contained cryptosporidium in concentrations of 13.2 and 6.7 oocysts per 100 liters, respectively, when filtered through a membrane filter with an absolute porosity of 0.45 μm and 2.6 and 0.7 oocysts per 100 liters, respectively, when filtered through a polypropylene cartridge filter with a nominal porosity of 1 μm.

Laboratory Surveillance

During the period from March 1 through April 16, 1993, a total of 2300 stool specimens were submitted to the 14 clinical laboratories in the Milwaukee vicinity for routine culture for bacterial enteric pathogens. Twenty specimens (0.9 percent) were positive for salmonella, 10 (0.4 percent) for shigella, and 11 (0.5 percent) for campylobacter; 1 of 80 specimens (1.3 percent) cultured for yersinia and 1 of 73 (1.4 percent) cultured for aeromonas were positive. During the same period, 14 of 1744 stool specimens examined for ova and parasites (0.8 percent) were found to have giardia, and 5 of 266 specimens cultured for enteric viruses (2 percent) were positive. An enzyme immunoassay kit for rotavirus was used to test 96 specimens, 3 of which (3 percent) were positive. From March 1 through April 6, 12 of 42 stool specimens (29 percent) tested for cryptosporidium were positive; from April 8 through April 16, 331 of 1009 specimens (33 percent) were positive. We found no evidence of cyclospora infection. Oocysts examined by the Centers for Disease Control and Prevention were

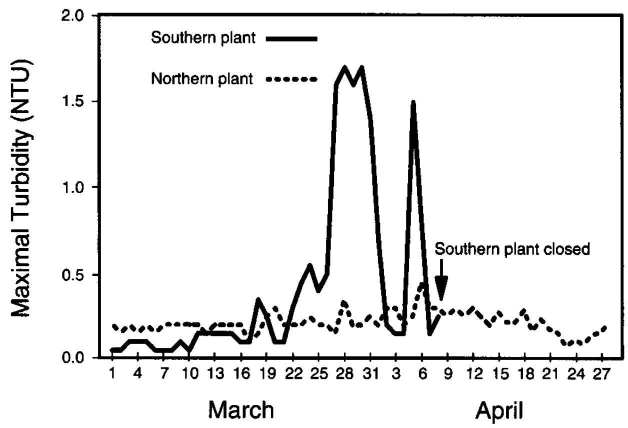

Figure 1. Maximal Turbidity of Treated Water in the Northern and Southern Water-Treatment Plants of the Milwaukee Water Works from March 1 through April 28, 1993.
NTU denotes nephelometric turbidity units.

4 to 6 μm in diameter and were positive for cryptosporidium with monoclonal-antibody staining.

Examination for Enteric Infection

Cryptosporidium was identified in stool specimens from 8 of the 11 people with gastrointestinal illness (73 percent) whose specimens were obtained within 48 hours after the onset of illness. Stool cultures for enteric bacterial and viral pathogens, electron microscopical studies, and stool examination for other ova and parasites, including cyclospora and microsporida, were negative. None of the pairs of serum samples (obtained during the acute and convalescent phases of illness) had a fourfold rise in antibody to the Norwalk virus.

Laboratory-Confirmed Cryptosporidium Infection

Of the 285 patients with laboratory-confirmed cryptosporidium infection, 170 (60 percent) were female, 130 (46 percent) were hospitalized during the course of their illness, and 48 (17 percent) were immunocompromised; their mean age was 41 years (range, 2 months to 93 years). All 285 patients had diarrhea, and 265 (93 percent) characterized it as watery (Table 1). The median duration of diarrhea was 9 days (range, 1 to 55), with a median reported maximum of 12 stools per day (range, 1 to 90). Among people with fever, the median reported maximal temperature was 38.3°C (101°F) (range, 37.2 to 40.5°C [99 to 105°F]). The date of the onset of illness was available for 254 confirmed cases with an onset during the period from March 1 through April 15 (Fig. 2, upper panel).

Of the 200 patients with laboratory-confirmed infection who were interviewed with the longer questionnaire, 150 (75 percent) reported weight loss, with a median loss of 4.5 kg (10 lb) (range, 0.45 to 18 kg [1 to 40 lb]), and 81 (41 percent) were hospitalized with cryptosporidium infection for a median of 5 days (range, 1 to 55). Seventy-seven patients (39 percent) reported a recurrence of diarrhea after at least 2 days of normal stools, with a median interval of 2 days of normal stools (range, 2 to 14) before the diarrhea recurred. Recurrence of diarrhea after at least five days of normal stools was reported by 11 (6 percent) of the patients.

In general, the frequencies of signs and symptoms of illness were similar in immunocompromised and immunocompetent patients. However, the immunocompromised patients had more diarrheal stools per day (mean, 15 vs. 12; P = 0.08 by the Kruskal–Wallis test), were more likely to be hospitalized (odds ratio, 1.9; 95 percent confidence interval, 0.95 to 3.9; P = 0.07), and were less likely to have a recurrence of diarrhea after at least two days of normal stools (odds ratio, 0.5; 95 percent confidence interval, 0.2 to 1.1; P = 0.09).

Clinical Cryptosporidium Infection in the MWW Service Area

Of the 482 respondents to the telephone survey of the MWW service area, 235 (49 percent) reported having had diarrhea since March 1, 1993; 201 of the 235 (86 percent) had watery diarrhea and thus met our case definition of clinical cryptosporidiosis. The mean age of the people with clinical cryptosporidiosis was 45 years (range, 18 to 84), and 138 (69 percent) were women. The rate of watery diarrhea was similar among men and women. Table 1 shows the clinical characteristics of the people with clinical cryptosporidiosis, as compared with those of the people with laboratory-confirmed cryptosporidium infection. Those with laboratory-confirmed infection had a significantly longer duration of diarrhea and more stools per day; the frequency of fever, fatigue, nausea, vomiting, and loss of appetite was also higher in this group. Among people with clinical cryptosporidiosis, the median duration of watery diarrhea was 3 days (range, 1 to 38), with a median reported maximum of 5 stools per day (range, 1 to 60). Among people with fever, the median reported maximal temperature was 37.7°C (range, 37.2 to 40.0°C). Thirteen people with clinical cryptosporidiosis (6.5 percent) reported having visited a physician because of their illness. The dates of the onset of illness in those with clinical cryptosporidium infection are shown in Figure 2, lower panel.

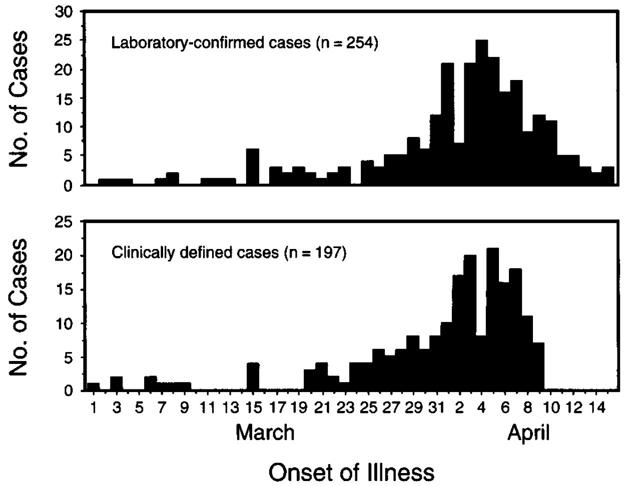

Figure 2. Reported Date of the Onset of Illness in Cases of Laboratory-Confirmed or Clinically Defined Cryptosporidium Infection during the Period from March 1 through April 15, 1993.

The clinically defined cases were identified during a telephone survey begun on April 9 of residents in the area served by the Milwaukee Water Works.

Table 1. Clinical Characteristics of Case Patients with Laboratory-Confirmed Cryptosporidium Infection and Survey Respondents with Clinical Infection.

Characteristic	Laboratory-Confirmed Infection (N = 285)		Clinical Infection* (N = 201)		P Value†
Symptoms — no. of patients or respondents (%)					
Diarrhea	285	(100)	201	(100)	NA
Watery diarrhea	265	(93)	201	(100)	NA
Abdominal cramps	238	(84)	168	(84)	0.9
Fatigue	247	(87)	145	(72)	<0.001
Loss of appetite	230	(81)	147	(73)	0.03
Nausea	199	(70)	119	(59)	0.01
Fever	162	(57)	72	(36)	<0.001
Chills	65	(64)‡	91	(45)	0.04
Sweats	55	(54)‡	83	(41)	0.04
Muscle or joint aches	152	(53)	100	(50)	0.6
Headache	53	(52)‡	122	(61)	0.2
Vomiting	136	(48)	37	(18)	<0.001
Cough	68	(24)	56	(28)	0.3
Sore throat	48	(17)	35	(17)	0.7
Mean duration of diarrhea — days	12		4.5		0.001§
Mean maximal no. of stools/day	19		7.7		0.001§
Mean maximal temperature — °C	38.3		38.1		0.09§
Mean duration of vomiting — days	2.9		2.0		0.07§
Mean maximal no. of vomiting episodes/day	3.9		2.6		0.36§

*The criterion for clinical infection was the reported presence of watery diarrhea.

†Unless otherwise noted, Yates' correction has been applied to P values. NA denotes not applicable.

‡Data are from 101 case patients interviewed during phase 1 of the study.

§By Kruskal–Wallis test.

Survey of Households in the Greater Milwaukee Area

Illness in the Survey Sample

Interviews were completed for 613 of the 840 households that were contacted (73 percent). The surveyed households were very similar to the 601,458 households reported in the 1990 Census, in terms of the sex, age, and geographic distributions of people in the greater Milwaukee area and the number of members per household. Among the 1663 household members surveyed, 493 (30 percent) were reported to have had diarrhea beginning during the period from March 1 through April 28, 1993, and in 436 the diarrhea was characterized as watery. Among these 436 people, the median duration of diarrhea was 3 days (range, 1 to 45). The occurrence of diarrhea among survey participants peaked from April 3 through April 5, and by April 16 it had decreased to the level before the out-

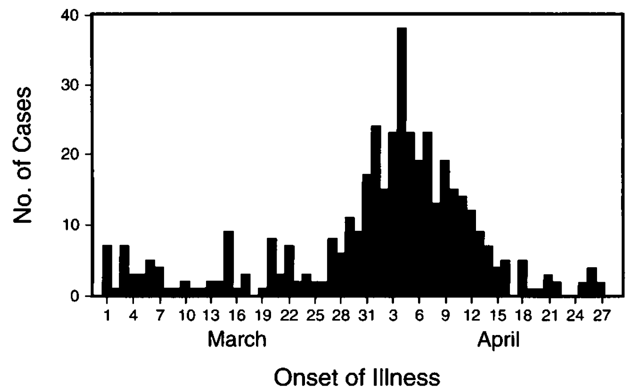

Figure 3. Reported Date of the Onset of Watery Diarrhea during the Period from March 1 through April 28, 1993, in 436 Cases of Infection Identified by a Random-Digit Telephone Survey of the Greater Milwaukee Area.

break (Fig. 3). The attack rate was similar for males and females and was highest among household members who were 30 to 39 years of age (Table 2).

The rate of watery diarrhea was highest among the residents of the MWW southern region (52 percent), less high in the middle zone (33 percent) and northern region (26 percent), and lowest outside the MWW service area (15 percent) (Table 2). The risk of watery diarrhea was higher among residents of the MWW service area than among residents of areas outside the MWW region (relative risk, 2.7; 95 percent confidence interval, 2.2 to 3.2; $P<0.001$). As compared with the risk of watery diarrhea among people living outside the MWW service area, the risk was more than three times higher among residents of the MWW southern region (relative risk, 3.6; 95 percent confidence interval, 3.0 to 4.3; $P<0.001$), more than two times higher among those in the middle zone (relative risk, 2.4; 95 percent confidence interval, 1.8 to 3.3; $P<0.001$), and almost two times higher among those in the northern region (relative risk, 1.8; 95 percent confidence interval, 1.39 to 2.3; $P<0.001$). Among the 644 people who resided outside the MWW service area and worked outside the home, 11 of the 28 (39 percent) who worked in the southern region had watery diarrhea, as compared with 94 of the 616 (15 percent) who worked outside the southern region (relative risk, 2.6; 95 percent confidence interval, 1.6 to 4.2; $P = 0.002$).

Estimate of the Magnitude of the Outbreak

By applying the rate of watery diarrhea among the survey participants (26 percent) to the total population of the greater Milwaukee area (1,610,000 people), we estimated that 419,000 people (95 percent confidence interval, 386,000 to 451,000) in this area had watery diarrhea during the survey period. Using a background rate of 0.5 percent per month for cases of watery diarrhea among residents, we estimated that 16,000 cases of watery diarrhea unrelated to the waterborne outbreak could have been expected during March and April 1993 (unpublished data). Thus, an estimated 403,000 people had watery diarrhea that could be attributed to this outbreak.

Discussion

A massive outbreak of waterborne cryptosporidium infection occurred in the greater Milwaukee area during late March and early April 1993. We estimate that more than 400,000 people were affected during this outbreak; however, by limiting the case definition to watery diarrhea in our survey, we may have underestimated the size of the affected population. Cryptosporidium infection was confirmed in more than 600 people with gastrointestinal illness in association with this outbreak, and despite intensive investigation, no other enteric pathogen could be found to account for the illness.

More than half the people who received residential drinking water predominantly from the MWW's southern water-treatment plant became ill, which was twice the rate of illness among people whose residential drinking water came mainly from the MWW's northern water-treatment plant. The intermediate attack rate among residents of the middle zone was expected, since the MWW distribution system, adjusting for variations in flow, would have intermittently allowed water from the southern plant to reach their residences. Diarrhea among people not living in the MWW service area may have resulted from consumption of water while they were working in or visiting the area. Among nursing home residents in the northern region, who were unlikely to travel, there was no increase in diarrheal illness associated with the out-

Table 2. Rate of Watery Diarrhea from March 1 through April 28, 1993, among Respondents in a Random-Digit Telephone Survey of Households in the Greater Milwaukee Area, According to Sex, Age, and Water Works Region.

Characteristic	No. of Respondents	No. Reporting Watery Diarrhea	Attack Rate (%)
Total	1663	436	26
Sex			
Male	783	193	25
Female	877	243	28
Unknown	3	0	
Age (yr)			
≤9	255	49	19
10–19	240	63	26
20–29	202	61	30
30–39	308	104	34
40–49	228	74	32
50–59	149	37	25
60–69	106	24	23
≥70	155	22	14
Unknown	20	2	10
Water Works region			
MWW	790	309	39
Southern	359	186	52
Middle zone	129	42	33
Northern	312	81	26
Non-MWW	873	127	15

break, whereas among nursing home residents in the southern region, there was a marked increase in the prevalence of diarrhea (unpublished data).

Our findings demonstrate a wide range in the duration and severity of illness caused by cryptosporidium infection. As expected, people with laboratory-confirmed cryptosporidiosis had diarrhea of significantly longer duration and more frequent bowel movements, vomiting, fever, and fatigue than those with clinical cryptosporidiosis who were identified through the telephone survey. The epidemiologic features and dates of onset of illness among the people with laboratory-confirmed cryptosporidium infection were similar to those among the people interviewed by telephone who reported having watery diarrhea, supporting our hypothesis that the latter group had clinical cryptosporidiosis.

Despite communitywide increases in diarrheal illness in Milwaukee, the recognition of cryptosporidium infection as the cause of this outbreak was delayed for several reasons. The constellation of gastrointestinal symptoms (e.g., diarrhea, abdominal cramping, and nausea) and constitutional signs and symptoms (e.g., fatigue, low-grade fever, muscle aches, and headaches) reported by Milwaukee-area residents led many physicians to diagnose viral gastroenteritis or "intestinal flu," without further investigation. Our findings suggest that people with diarrhea seek health care infrequently, do so only when the illness is severe or prolonged, and are unlikely to be tested for cryptosporidium infection. Unlike the detection of other intestinal parasites, which are identified by means of a standard examination for ova and parasites, the detection of cryptosporidium requires special testing. Infrequent testing for cryptosporidium in patients with diarrhea may be due to misconceptions about the incidence and severity of this infection among immunocompetent patients. A large, multicenter, laboratory-based study of patients with acute infectious diarrhea in England found that infection with cryptosporidium was almost as common as salmonella infection and nearly three times more common than shigella infection.[23] Although clinicians may question the value of testing when infection is self-limited in immunocompetent hosts and no effective treatment is available, testing allows the education of patients, facilitates the recognition of an outbreak, and may lead to the institution of measures to prevent the spread of infection.[15,16,24]

In the Milwaukee outbreak, cryptosporidium oocysts in untreated water from Lake Michigan apparently entered the southern water-treatment plant and were then inadequately removed by the coagulation and filtration process. Cryptosporidium oocysts have often been found in untreated surface water used for public water supplies in the United States.[25,26] The source of the oocysts leading to the outbreak in Milwaukee and the timing of their entrance into Lake Michigan remain speculative. Possible sources include cattle along two rivers that flow into the Milwaukee harbor, slaughterhouses, and human sewage. Rivers that were swelled by spring rains and snow runoff may have transported oocysts into Lake Michigan and from there to the intake of the MWW southern plant.

As in previous cryptosporidium outbreaks in the United States associated with filtered water supplies, water-quality measurements at the MWW southern plant were within the required limits; however, unlike the plants involved in the previous outbreaks, the MWW plant had no evident mechanical breakdown of its flocculators or filters.[14,27] The reason for the plant's failure to maintain treated water at low turbidity is unclear and continues to be investigated. Difficulty in determining the appropriate amounts of polyaluminum chloride and alum may have been a contributing factor in the failure to maintain low turbidity; the MWW has correctly reinstalled the streaming-current monitor, which now aids in determining the amount of coagulant. The recycling of filter backwash water may increase the concentration of oocysts in water passing through filters; therefore, this practice has been discontinued. Decreased turbidity and removal of particles under 15 μm in diameter from water have been shown to correlate significantly with the detection of cryptosporidium in water.[28] The MWW therefore has installed continuous turbidity monitors on each filter bed, with an alarm sounded and the system automatically shut down if the turbidity of filtered water exceeds 0.3 NTU, and has instituted frequent measurement of particles in untreated and treated water.

Because some visitors to the MWW service area who drank very small amounts of water ($\leq$240 ml [8 oz]) had laboratory-confirmed cryptosporidiosis (unpublished data), the peak concentration of oocysts in the water probably far exceeded one oocyst per liter. Thus, we believe the concentration of cryptosporidium oocysts found in the tested ice vastly underestimates the peak level in water from the southern plant. The lower-than-expected concentration of oocysts may have been due in part to the timing of the specimen collection (i.e., the freezing of ice blocks), losses during the freeze–thaw process, and insensitivity of testing procedures.[29]

The number of both laboratory-confirmed and clinically defined cases of cryptosporidium infection with an onset of illness before March 23, when the turbidity of treated water increased, was higher than expected, suggesting that cryptosporidium oocysts had entered the water supply before the increase in turbidity was apparent. This occurrence would not be without precedent. In England a waterborne outbreak of cryptosporidium infection associated with a filtered water supply occurred while the turbidity of treated water remained less than 0.5 NTU.[30] Surveillance in the United Kingdom has uncovered sudden, irregular, communitywide increases in cryptosporidiosis that were unlikely to have been transmitted by the fecal–oral route, suggesting that some sporadic cases of cryptosporidiosis may be waterborne.[23]

Cryptosporidiosis is an underdiagnosed condition, and outbreaks are likely to be underrecognized.[8,18] Our findings have implications for standards of water quality, public health surveillance, and recognition of cryptosporidium outbreaks in the United States. Until an inexpensive, rapid, and sensitive means of detecting and quantifying cryptosporidium in treated water is available, we believe that water-treatment plants should consider instituting continuous monitoring of treated water for turbidity, particularly of filter effluent, and particle size. Plant design and water-treatment procedures should be improved to maintain the qaulity of treated water at a level that will make the presence of oocysts unlikely (e.g., a goal of turbidity ≤0.1 NTU). We recommend that clinicians and laboratories consider performing routine stool tests for cryptosporidium in people with watery diarrhea and that public health officials make cryptosporidium infection a reportable condition. In the United Kingdom, water and health officials have already developed an extensive strategy to investigate the clinical importance of cryptosporidium found in water supplies.[31] Intensive efforts and cooperation between the medical community and those who provide and regulate drinking water in the United States will be required to prevent future waterborne outbreaks caused by this emerging pathogen and ensure the safety of drinking water for all citizens.

We are indebted to the following people for their contributions to this study: Walter Powers, A.J. Henry, and Richard R. Regent, Milwaukee Water Works; the infection-control practitioners at participating nursing homes and hospitals in the Milwaukee area; the directors and parasitologists at the 14 participating clinical laboratories in the Milwaukee vicinity; Hon. John Norquist, mayor of the City of Milwaukee; Paul Nannis, director, Thomas Schlenker, M.D., and the staff of public health nurses and administrators, Milwaukee Health Department; Wendy L. Schell, M.A., Helen North, R.N., Jackie Kowalski, R.N., John Chapin, Ivan Imm, and Ann Haney, Wisconsin Division of Health; Ron Tursky and the staff of the Milwaukee STD Program; Carol Graham, R.N., and the volunteer public health nurses of the Greater Milwaukee area; Gerald Sedmak, Ph.D., Ajaib Singh, Ph.D., and the staff of the Milwaukee Bureau of Laboratories; Paul Biedrzycki and the staff of the Environmental Health Section, Milwaukee Health Department; Dennis Juranek, D.V.M., Division of Parasitic Diseases, Center for Infectious Diseases; Roger Glass, M.D., M.P.H., Ph.D., Stephan S. Monroe, Ph.D., Charles Humphries, Ph.D., and Sara Stine, Centers for Disease Control and Prevention (CDC) Viral Gastroenterology Laboratory; Margaret Hurd and the staff of the CDC Parasitology Laboratory; the staff of the Wisconsin State Laboratory of Hygiene; the staff of the Survey Research Laboratory, University of Wisconsin Extension; Darren Lytle, P.E., U.S. Environmental Protection Agency; and Ava Navin, Epidemiology Program Office, CDC.

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