APPENDIX T

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.

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

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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.

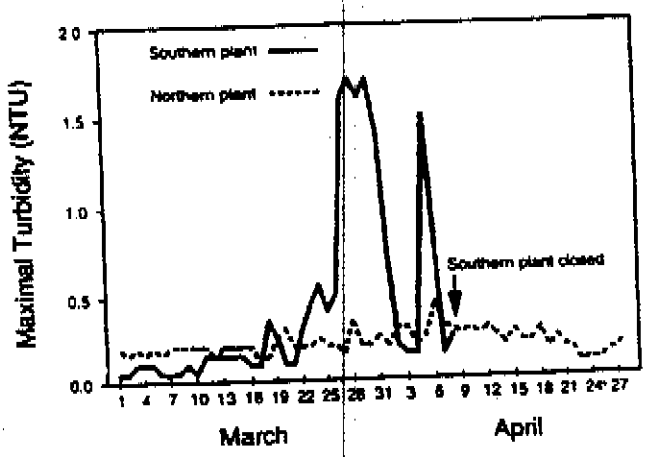

Figure 1. Maximal Turbidity of Treated Water in the Northern and Southern Water-Treatment Plants of the Milwaukee Water Works from March 1 through April 28, 1993.
NTU denotes nephelometric turbidity units.

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

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)

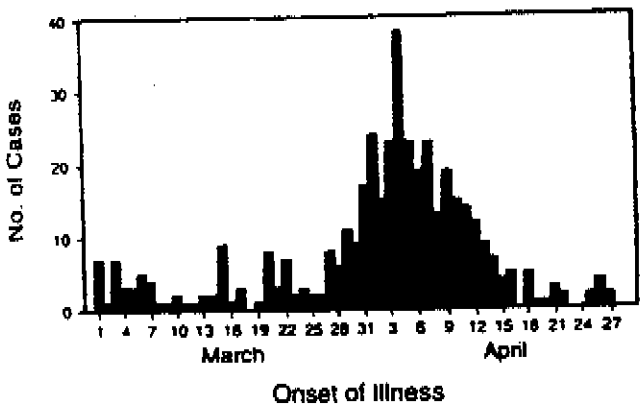

Figure 3. Reported Date of the Onset of Watery Diarrhea during the Period from March 1 through April 28, 1993, in 436 Cases of Infection Identified by a Random-Digit Telephone Survey of the Greater Milwaukee Area.

break (Fig. 3). The attack rate was similar for males and females and was highest among ... aged 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

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 quality 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.

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