ORIGINAL ARTICLE

Role of Environmental Surveillance in Determining the Risk of Hospital-Acquired Legionellosis: A National Surveillance Study With Clinical Correlations

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OBJECTIVE. Hospital-acquired *Legionella* pneumonia has a fatality rate of 28%, and the source is the water distribution system. Two prevention strategies have been advocated. One approach to prevention is clinical surveillance for disease without routine environmental monitoring. Another approach recommends environmental monitoring even in the absence of known cases of *Legionella* pneumonia. We determined the *Legionella* colonization status of water systems in hospitals to establish whether the results of environmental surveillance correlated with discovery of disease. None of these hospitals had previously experienced endemic hospital-acquired *Legionella* pneumonia.

DESIGN. Cohort study.

SETTING. Twenty US hospitals in 13 states.

INTERVENTIONS. Hospitals performed clinical and environmental surveillance for *Legionella* from 2000 through 2002. All specimens were shipped to the Special Pathogens Laboratory at the Veterans Affairs Pittsburgh Medical Center.

RESULTS. *Legionella pneumophila* and *Legionella anisa* were isolated from 14 (70%) of 20 hospital water systems. Of 676 environmental samples, 198 (29%) were positive for *Legionella* species. High-level colonization of the water system (30% or more of the distal outlets were positive for *L. pneumophila*) was demonstrated for 6 (43%) of the 14 hospitals with positive findings. *L. pneumophila* serogroup 1 was detected in 5 of these 6 hospitals, whereas 1 hospital was colonized with *L. pneumophila* serogroup 5. A total of 633 patients were evaluated for *Legionella* pneumonia from 12 (60%) of the 20 hospitals: 377 by urinary antigen testing and 577 by sputum culture. Hospital-acquired *Legionella* pneumonia was identified in 4 hospitals, all of which were hospitals with *L. pneumophila* serogroup 1 found in 30% or more of the distal outlets. No cases of disease due to other serogroups or species (*L. anisa*) were identified.

CONCLUSION. Environmental monitoring followed by clinical surveillance was successful in uncovering previously unrecognized cases of hospital-acquired *Legionella* pneumonia.

Infect Control Hosp Epidemiol 2007; 28:818-824

Among cases of *Legionella* pneumonia that were reported to the Centers for Disease Control and Prevention (CDC) from 1980 to 1998, the percentage of cases identified as hospital-acquired ranged from 25% to 45%.[1] The hospital water system was identified as the source of these cases of *Legionella* pneumonia, most of which were caused by *Legionella pneumophila*.[2,3] Mortality associated with hospital-acquired *Legionella* pneumonia (28%) is approximately double the mortality for community-acquired cases (14%).[1]

The diagnosis of *Legionella* pneumonia cannot be made by

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Received August 29, 2006; accepted December 21, 2006; electronically published June 5, 2007.

 0899-823X/2007/2807-0008$15.00. DOI: 10.1086/518754

clinical criteria alone.[4] Prevention of this disease is possible if *Legionella* diagnostic testing is performed and if the source is identified. Two different strategies for the prevention of hospital-acquired *Legionella* pneumonia have been advocated. One strategy is presented in *The Guideline for Prevention of Nosocomial Legionellosis,* published by the Allegheny County Health Department (Pittsburgh, Pennsylvania).[5] This approach emphasizes environmental monitoring for *Legionella* species. The presence of *Legionella* species in the hospital water supply suggests that patients in the hospital may be at risk for hospital-acquired *Legionella* pneumonia and triggers the routine implementation of *Legionella* diagnostic tests for patients with hospital-acquired pneumonia. Adoption of this approach by Allegheny County hospitals resulted in a significant decrease in hospital-acquired *Legionella* pneumonia in western Pennsylvania.[4]

An alternative strategy proposed by the CDC advocates intensive clinical surveillance without routine environmental surveillance. The CDC does not recommend routine environmental surveillance for *Legionella* species in the absence of recognized disease, with the exception of transplant units.[6] Thus, the utility of environmental monitoring for *Legionella* species continues to be debated.[7]

We believed that an evidence-based approach to resolving this issue would be to perform a prospective, multicenter, observational study.[8,9] Our study objectives were (1) to determine the prevalence of *Legionella* colonization in the water systems of 20 US hospitals not known to have experienced outbreaks of hospital-acquired *Legionella* pneumonia, (2) to determine whether clinical surveillance after introduction of specialized *Legionella* diagnostic tests would uncover unrecognized cases of hospital-acquired *Legionella* pneumonia in colonized hospitals, and (3) to determine whether the prevalence of contaminated sites of environmental surveillance correlated with occurrence of disease.

METHODS

Institutions that participated in the study were hospitals in which outbreaks of legionellosis had not been identified. These hospitals instituted prospective clinical and environmental testing for *Legionella* species. Twenty hospitals in 14 states participated in the study. The study was performed between October 2000 and November 2002.

A coinvestigator at each hospital performed an environmental survey of the hospital water system as described in the Allegheny County Health Department guidelines.[5] Swab and water samples were collected from distal outlets, and water samples of 50-100 mL were collected from hot water tanks. A minimum of 10 samples was collected at each institution during each cycle. All environmental samples were sent to the Special Pathogens Laboratory at the Veterans Affairs Pittsburgh Healthcare System for culture. Culture for *Legionella* species was performed as described elsewhere.[10] Monoclonal antibody subtype was determined by direct fluorescent antibody staining of select isolates (Monoclonal Technologies). We defined high level colonization as 30% or more of distal sites testing positive for *Legionella* species.[5]

A case of pneumonia was considered hospital-acquired if the patient was hospitalized during the period from 2-10 days before the onset of symptoms. A case of hospital-acquired *Legionella* pneumonia was defined by the onset of a new infiltrate seen on chest radiograph plus a culture positive for the organism and/or a positive test result for *Legionella* urinary antigen. Urine and sputum specimens were sent to the Special Pathogens Laboratory for *Legionella* testing. Urine was tested using the *Legionella* Urine Antigen Enzyme Immunoassay test (Wampole, Carter-Wallace). Culture for *Legionella* species was performed after treatment with acid buffer and after plating 0.1 mL onto agar plates of nonselective buffered charcoal yeast extract and selective agar plates with polymyxin, anisomycin, and vancomycin and with polymyxin, anisomycin, and cefamandole (Remel). Isolates of *L. pneumophila* from 2 patients and from hospital water systems were subtyped by serogroup, followed by pulsed-field gel electrophoresis (PFGE) peformed using the restriction enzyme *Sfi*I.[11] The study was approved by the local institutional review boards of all participating hospitals and by the institutional review board of the VA Pittsburgh Healthcare System.

RESULTS

A total of 676 environmental samples were tested from the 20 hospitals. All hospitals obtained at least 10 samples per cycle, except for 1 hospital that collected 9 samples for 1 of the 5 cycles. *L. pneumophila* was isolated from 14 (70%) of the 20 hospital water systems (Table 1). *L. pneumophila* serogroup 1 was isolated from 11 (55%) of the hospital water systems (Table 1). Other serogroups of *L. pneumophila* (serogroups 3, 4, 5, or 6, or a serogroup other than 1-6) were recovered from 6 (30%) of the hospital water systems. Five (25%) of the hospital water systems tested negative for *Legionella* species. Nine (45%) of the hospital water systems tested positive for *Legionella anisa.* The percentages total more than 100% because multiple serogroups or species of *Legionella* were recovered from 9 (45%) of the hospitals and from the same culture.

More than 30% of distal water outlets were positive for *L. pneumophila* in 6 (43%) of the 14 hospitals with positive findings (Table 1). *L. pneumophila* serogroup 1 was detected in 5 of these 6 hospitals, whereas 1 hospital was colonized with *L. pneumophila* serogroup 5. Among the hospitals colonized with any *Legionella* species or serogroup, the total percentage of distal outlets positive for *Legionella* species across multiple test cycles was 38% (range, 5%-83%). Among hospitals colonized with *L. pneumophila* serogroup 1, the distal-site positivity rate was 42% (range, 9%-100%).

Environmental testing was performed in all 20 hospitals at least once. There were 5 environmental testing cycles: cycle 1 was performed between October 2000 and February 2001,

TABLE 1. Detection of Legionellosis and Colonization of Hospital Water Supplies by *Legionella pneumophila*

	Hospital characteristics			Percent (proportion[a]) of environmental sites positive for *Legionella*		
Hospital	Location	Cases of legionellosis identified	⩾30% of distal water outlets positive for *L. pneumophila*	*L. pneumophila* serogroup 1	*L. pneumophila* serogroups 2-14	*L. anisa*
1	CA	Yes	Yes	47 (7/15)	0 (0/15)	13 (2/15)
2	PA	Yes	Yes	30 (12/40)	25 (10/40)	0 (0/40)
3	NY	Yes	Yes	36 (8/22)	0 (0/22)	0 (0/22)
4	IA	Yes	Yes	35 (19/55)	0 (0/55))	0 (0/55)
5	NE	No	Yes	83 (58/70)	0 (0/70)	24 (17/70)
6	OH	No	No	25 (11/44)	0 (0/44)	0 (0/44)
7	AZ	No	No	20 (10/49)	12 (6/49)	16 (8/49)
8	MI	No	No	5 (2/44)	14 (6/44)	7 (3/44)
9	FL	No	No	17 (2/12)	0 (0/12)	8 (1/2)
10	WV	No	No	12 (7/58)	0 (0/58)	12 (7/58)
11	CA	No	No	7 (3/42)	0 (0/58)	0 (0/58)
12	OH	No	No	0 (0/57)	67 (38/57)	28 (16/57)
13	TN	No	No	0 (0/28)	7 (2/28)	4 (1/28)
14	MA	No	No	0 (0/20)	5 (1/20)	0 (0/20)
15	KY	No	No	0 (0/11)	0 (0/10)	0 (0/10)
16	MI	No	No	0 (0/44)	0 (0/44)	0 (0/44)
17	DE	No	No	0 (0/23)	0 (0/23)	9 (2/23)
18	NY	No	No	0 (0/12)	0 (0/12)	0 (0/12)
19	NY	No	No	0 (0/13)	0 (0/13)	0 (0/13)
20	MI	No	No	0 (0/10)	0 (0/10)	0 (0/10)

[a] Proportions are given as the number of sites that tested positive / total number of sites tested.

cycle 2 between May 2001 and June 2001, cycle 3 between October 2001 and December 2001, cycle 4 between April 2002 and August 2002, and cycle 5 between September 2002 and November 2002. Nine hospitals performed 4-5 cycles of testing, whereas 11 completed 1-2 cycles of testing. Some variation in the distal-site positivity rate was seen across the 5 cycles. In 2 hospitals (hospitals 8 and 11), one test cycle showed 0% positivity but other test cycles showed a higher positivity (20% and 55%) (Table A, in the Appendix, and Figure).

After the first environmental test cycle, 8 of the 20 hospitals did not perform any further testing of either patient or environmental samples. For 2 of these 8 hospitals, cases of *Legionella* pneumonia were detected by clinical surveillance; this prompted their withdrawal from the study. These hospitals performed active disinfection of the hot-water system. Six hospitals withdrew from the study because environmental culture results were negative. During this 2-year study, 633 patients were evaluated for *Legionella* pneumonia from 12 hospitals that submitted clinical samples (Table 1). A total of 377 urine specimens and 577 respiratory tract specimens from the 12 healthcare facilities were submitted for diagnostic testing. The mean number of urine specimens per facility was 31 (range, 1-240), and the mean number of respiratory tract specimens per facility was 48 (range, 0-251).

Of 12 hospitals that submitted respiratory tract specimens, 10 also had *L. pneumophila* in the hospital water system. Of these 10 hospitals, 4 (40%) subsequently identified cases of nosocomial *Legionella* pneumonia (Table 1). Of the 5 hospitals that had distal-site positivity rates of 30% or more for *L. pneumophila* and were colonized by *L. pneumophila* serogroup 1, 4 identified cases of hospital-acquired *Legionella* pneumonia (Table 2).

A total of 6 patients received a diagnosis of *Legionella* pneumonia in those 4 hospitals: 3 patients were in a long-term care facility and 1 patient was in each of the remaining 3 hospitals (Table 2). Four diagnoses were made by urinary antigen testing only, and 2 were made by culture and urinary antigen testing. All 6 patients had pneumonia due to *L. pneumophila* serogroup 1. Of the 6 patients, 3 (50%) died. All patients had underlying illnesses that would increase their risk of *Legionella* pneumonia (Table 2). For all 6 patients, the same serogroup of *L. pneumophila* that infected the patient was also recovered from the water system of the hospital in which they stayed. PFGE was performed on the *L. pneumo-*

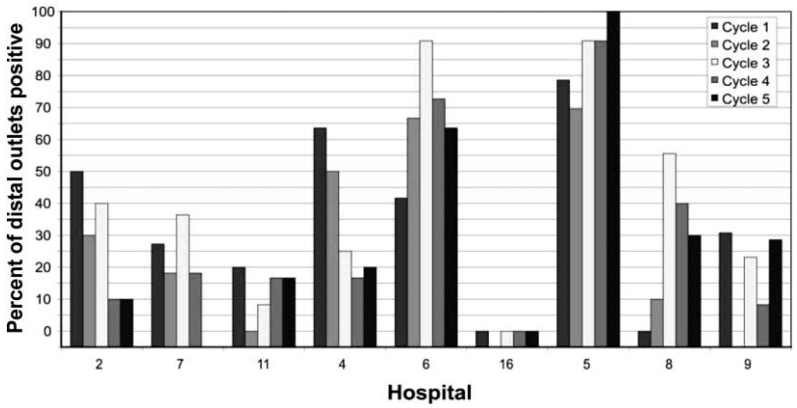

FIGURE. Percentage of distal water outlets that tested positive for *Legionella* species during cycles 1-5 in 9 hospitals. Hospitals 9 and 16 did not perform testing during cycle 2.

phila serogroup 1 isolates obtained from the patients and the isolates obtained from 2 hospital water systems; the PFGE patterns of the patient strains were identical to the environmental strains (Table 2). Nine (45%) of 20 hospital water systems were positive for *L. anisa*. No cases of hospital-acquired pneumonia due to *L. anisa* were identified. No cases of hospital-acquired *Legionella* pneumonia were identified for hospital 5, despite the fact that it was heavily colonized (more than 30% of outlets were positive for *L. pneumophila* serogroup 1) (Table 1). Monoclonal antibody subtyping of the environmental isolates was performed and showed that the isolates were negative for monoclonal antibody 2. Clinical surveillance was performed at this hospital (Table 1). Disinfection of the hospital water system was initiated in 3 of the 4 hospitals after the diagnosis of hospital-acquired *Legionella* pneumonia.

DISCUSSION

A powerful argument against routine environmental surveillance for *Legionella* has been the supposedly ill-defined relationship between the presence of *Legionella* species in hospital water systems and the risk for legionellosis. Our study confirms and defines the relationship between the colonization of a hospital water supply with *L. pneumophila* and the occurrence of hospital-acquired *Legionella* pneumonia. Hospital-acquired pneumonia due to *L. pneumophila* serogroup 1 occurred in 4 of the 20 study hospitals. The potable water supply of all 4 hospitals was found to be extensively colonized with *L. pneumophila* serogroup 1; that is, the distal-site positivity rate was 30% or more (Table 1).

The extent of *Legionella* colonization of a hospital water system (the percentage of water sites testing positive) has been found to be a better indicator of the risk of hospital-acquired legionellosis than is the quantitative concentration of *Legionella* species recovered from the site.[12,13] The 30% cutoff for the positivity rate was empirically derived from our 1983 study, which showed that, when the percentage of water outlets positive for *L. pneumophila* serogroup 1 exceeded 30%, cases of hospital-acquired *Legionella* pneumonia occurred.[13] This association has been confirmed by other investigators.[12,14,15]

TABLE 2. Clinical Characteristics of 6 Patients with Hospital-Acquired Legionellosis Identified in Hospitals With 30% or More of the Distal Water Outlets Colonized with *Legionella pneumophila* Serogroup 1

Patient	Age, years	Underlying disease(s) (medication received)	Method of diagnosis	Outcome	Hospital	Hospital *L. pneumophila* positivity rate,[a] %	PFGE[b] match
1	46	Cirrhosis (prednisone)	Urinary antigen	Died	1	47	NA
2	74	COPD	Urinary antigen	Lived	2	43	NA
3	87	COPD, dementia	Urinary antigen	Lived	2	43	NA
4	87	Diabetes, seizures, lymphoma	Urinary antigen and culture	Died	2	43	Yes
5	57	Lymphoma (corticosteroids)	Urinary antigen and culture	Died	3	36	Yes
6	61	Renal insufficiency, heart failure	Urinary antigen	Lived	4	35	NA

NOTE. COPD, chronic obstructive pulmonary disease; NA, not applicable because an isolate was not available for testing; PFGE, pulsed-field gel electrophoresis.

[a] Positivity rate for distal water outlets.

[b] Comparison by PFGE was performed on isolates of *L. pneumophila* serogroup 1 obtained from the patient and environmental samples.

If routine environmental surveillance is performed, how often should it be done, to ascertain risk? We performed tests multiple times during the 2-year period. We found that *Legionella* colonization varied over time. Two hospitals experienced a 0% positivity rate in a single cycle, but their mean positivity rates (ie, the mean of the positivity rates for cycles 1, 2, 3, 4, and 5) were 12% and 27% (Appendix and Figure). Therefore, multiple cycles of environmental surveillance may be necessary to ascertain risk. In 3 of the 4 hospitals with identified cases of *Legionella* pneumonia, the cases occurred after testing cycles in which the site positivity rate exceeded 30% (range, 40%-86%). In the remaining hospital, the first identified case occurred after a testing cycle in which the site positivity rate was 25%, although the mean of the positivity rates for cycles 1-5 for this hospital was 35%.

The majority of cases of hospital-acquired *Legionella* pneumonia are caused by *L. pneumophila* serogroup 1.[16-20] Other serogroups and species are unusual causes of pneumonia despite their presence in the water supplies of hospitals.[21,22] In our study, other *Legionella* species (*L. anisa*) were recovered from the water systems of 5 hospitals, but no cases of *Legionella* infection due to this species were identified. Hospital 6 had *L. pneumophila* serogroup 5 identified in more than 30% of water outlets, but no cases of hospital-acquired *Legionella* pneumonia were identified in this hospital (Table 1 and Figure).

The CDC advocates clinical surveillance,[2,23] emphasizing that physicians should order *Legionella* diagnostic tests for patients with hospital-acquired pneumonia. This approach has drawbacks. First, few hospitals have *Legionella* diagnostic tests available within the hospital. A CDC survey showed that 40% of National Nosocomial Infections Surveillance System hospitals sent all samples for *Legionella* diagnostic testing offsite.[24] Hospitals with *Legionella* diagnostic testing available in the hospital were more likely to make a diagnosis of *Legionella* pneumonia.[24] Second, hospital-acquired legionnaires disease has not been reported by hospitals in which the water supply was not colonized with *L. pneumophila.*[4,7,12] In this study, 5 hospitals were free of *Legionella* species in their water supplies, and no cases of *Legionella* pneumonia were found in these hospitals despite active surveillance. Thus, precious resources may be wasted on such diagnostic testing in a hospital that has no *Legionella* species in the water supply.

The CDC states that environmental sampling is of limited value because *L. pneumophila* is "ubiquitous" in hospital water systems.[23] In published surveys of the prevalence of colonization among hospital water systems in the United States, Canada, and the United Kingdom, colonization varied from 12% to 70%.[7,25] In our study, 5 (25%) of the 20 hospital water systems showed no colonization with *L. pneumophila.* None of these hospitals had identified cases of *Legionella* pneumonia.

The CDC further states that the main argument against performing routine environmental surveillance for *Legionella* species is that "in the absence of cases, the relationship between the results of water cultures and the risk for legionellosis remains undefined. The bacterium has been frequently present in water systems of buildings, often without being associated with known disease."[2(p117),26] This statement has been refuted by 7 prospective studies in which surveillance for hospital-acquired legionnaires disease was performed after discovery of *Legionella* species in the hospital water supply; in all 7 studies, hospital-acquired legionellosis was subsequently discovered.[7,14,27-32]

One hospital (hospital 5) was colonized in 83% of distal sites by *L. pneumophila* serogroup 1, but no cases of *Legionella* pneumonia were detected. There are several points to consider that could explain this observation. The subtype of *L. pneumophila* serogroup 1 in this hospital was identified as negative for monoclonal antibody 2, a strain known to be less virulent.[33,34] The municipality in which the hospital was located switched from chlorine to monochloramine for water treatment during the study. Monochloramine is active as a disinfectant for *Legionella* colonization of the water supply.[35,36] Environmental testing performed after the last study cycle showed that the site positivity rate had fallen to 0% (data not shown). The lack of identified cases may have been influenced by changes in the degree of colonization of the hospital water system caused by the change in municipal water system.

This study of *Legionella* colonization of the hospital water supply is unique in the following respects: (1) it included a larger study population representative of a large geographic area (14 states), (2) both *Legionella* sputum culture and urinary antigen tests were made available to all study hospitals, (3) molecular subtyping (PFGE) was included to strengthen epidemiologic associations, and (4) the study was of sufficient duration (2 years) to identify cases of hospital-acquired *Legionella* pneumonia while simultaneously providing data on colonization of the hospital water system over time. This prolonged environmental surveillance also permitted delineation of the fluctuations in *Legionella* colonization.

There are several weaknesses to our study. First, clinical surveillance was variable among the participating institutions. Second, although the extent of *Legionella* colonization at a distal-site positivity rate of 30% or more correlated with the occurrence of disease, a 100% positive predictive value was not seen. Nevertheless, the results of our study provide the strongest evidence to date that determination of the status of *Legionella* colonization is useful in evaluating the risk for hospital-acquired *Legionella* pneumonia. These findings provide strong evidence that environmental surveillance for *Legionella* should be part of a proactive strategy for prevention of hospital-acquired legionnaires disease.

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ACKNOWLEDGMENTS

We gratefully acknowledge Joy A. Watson, IT Specialist, Veterans Affairs Pittsburgh Healthcare System, for developing a program for nosocomial pneumonia screening for this study. We thank Jean Joly, Joseph Plouffe, Miguel Sabria, Luisa Pedro-Botet, and Glen Mayhall for their review of the manuscript.

Financial support. This study was supported by a Veterans Affairs Merit Review grant.

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

APPENDIX

TABLE A. Results of Environmental and Clinical Testing for *Legionella* Species in 20 Hospitals

	Hospital characteristics		No. of cases of hospital-acquired legionellosis	*L. pneumophila* positivity rate, % (proportion) of environmental sites[a]	No. of test cycles	No. of environmental samples positive for *Legionella*			No. of clinical samples positive for *Legionella*/no. tested	
Hospital	Location	No. of beds				*L. pneumophila* serogroup 1	*L. pneumophila* serogroups 2-14	*L. anisa*	Urine	Sputum
1	CA	120	1	47 (7/15)	1[b]	7	0	2	1/1	0
2	PA	199	3	45 (18/40)	3[b]	12	10	0	3/14	1/8
3	NY	152	1	36 (8/22)	2[b]	8	0	0	1/15	1/10
4	IA	93	1	35 (19/55)	5	19	0	0	1/11	0/9
5	NE	108	0	83 (58/70)	5	58	0	17	0/4	0/251
6	OH	120	0	25 (11/44)	4	11	0	0	0/27	0/3
7	AZ	274	0	27 (13/49)	5	10	6	8	0/19	0/17
8	MI	975	0	14 (6/44)	4	2	6	3	0/240	0/240
9	FL	192	0	17 (2/12)	1	2	0	1	0/2	0/2
10	WV	80	0	12 (7/58)	5	7	0	7	0	0
11	CA	350	0	7 (3/42)	2	3	0	0	0/1	0/1
12	OH	213	0	67 (38/57)	5	0	38	16	0/19	0/16
13	TN	238	0	7 (2/28)	1	0	2	1	0	0
14	MA	65	0	5 (1/20)	1	0	1	0	0	0
15	KY	168	0	0 (0/10)	1	0	0	0	0	0
16	MI	94	0	0 (0/44)	4	0	0	0	0	0
17	DE	119	0	0 (0/23)	2	0	0	2	0/19	0/17
18	NY	470	0	0 (0/12)	1	0	0	0	0	0
19	NY	731	0	0 (0/13)	1	0	0	0	0	0
20	MI	172	0	0 (0/10)	1	0	0	0	0	0

[a] Proportions are given as the number of sites that tested positive / total number of sites tested.

[b] The hospital disinfected the water system after identification of cases; only predisinfection results are included.

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