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James D. Heffelfinger

National Center for Infectious Diseases

Jacob L. Kool

National Center for Infectious Diseases

Scott Fridkin

National Center for Infectious Diseases

Victoria J. Fraser

Washington University School of Medicine in St. Louis

Jeffrey Hageman

National Center for Infectious Diseases

See next page for additional authors

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Authors

James D. Heffelfinger, Jacob L. Kool, Scott Fridkin, Victoria J. Fraser, Jeffrey Hageman, Joseph Carpenter, and
Cynthia G. Whitney



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Author(s): James D. Heffelfinger , MD, MPH, Jacob L. Kool , MD, PhD, Scott Fridkin , MD, Victoria J. Fraser , MD, Jeffrey Hageman , MHS, Joseph Carpenter , PE, Cynthia G. Whitney , MD, MPH

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RISK OF HOSPITAL-ACQUIRED LEGIONNAIRES' DISEASE IN CITIES USING MONOCHLORAMINE VERSUS OTHER WATER DISINFECTANTS

James D. Heffelfinger, MD, MPH; Jacob L. Kool, MD, PhD; Scott Fridkin, MD; Victoria J. Fraser, MD; Jeffrey Hageman, MHS; Joseph Carpenter, PE; Cynthia G. Whitney, MD, MPH; Society for Healthcare Epidemiology of America

ABSTRACT

OBJECTIVE: To measure the association between the disinfection of municipal drinking water with monochloramine and the occurrence of hospital-acquired legionnaires' disease (LD).

SETTING: One hundred sixty-six U.S. hospitals.

DESIGN: Survey of 459 members of the Society for Healthcare Epidemiology of America (SHEA) for hospital features; endemic- and outbreak-related, hospital-acquired LD; the source of the hospital water supply; and the methods of disinfection used by the hospitals and municipal water treatment plants.

RESULTS: SHEA members representing 166 (36%) of 459 hospitals responded; 33 (20%) reported one or more episodes of hospital-acquired LD during the period from 1994 to 1998 and 23 (14%) reported an outbreak of hospital-acquired LD during the period from 1989 to 1998. Hospitals with an occurrence of hospital-acquired LD had a higher census (median, 319 vs 221; $P =$

.03), more acute care beds (median, 500 vs 376; $P = .04$), and more intensive care unit beds (median, 42 vs 24; $P = .009$) than did other hospitals. They were also more likely to have a transplant service (74% vs 42%; $P = .001$) and to perform surveillance for hospital-acquired disease (92% vs 61%; $P = .001$). After adjustment for the presence of a transplant program and surveillance for legionnaires' disease, hospitals supplied with drinking water disinfected with monochloramine by municipal plants were less likely to have sporadic cases or outbreaks of hospital-acquired LD (odds ratio, 0.20; 95% confidence interval, 0.07 to 0.56) than were other hospitals.

CONCLUSION: Water disinfection with monochloramine by municipal water treatment plants significantly reduces the risk of hospital-acquired LD (*Infect Control Hosp Epidemiol* 2003;24:569-574).

Approximately 8,000 to 18,000 cases of legionnaires' disease occur in the United States each year.¹ Of these cases, 80% to 90% are sporadic, whereas 10% to 20% occur as part of an outbreak.²⁻⁴ Thirty-five percent of the cases reported to the Centers for Disease Control and Prevention during the period from 1980 to 1998 were acquired in hospitals, and approximately 30% of these cases were associated with an outbreak.⁵ The overall fatality rate for cases of legionnaires' disease reported to the Centers for Disease Control and Prevention was 20% and the fatality rate for reported cases of hospital-acquired legionnaires' disease was 28%.⁵

Legionnaires' disease is caused by numerous species of *Legionella*, bacteria that are ubiquitous in natural and man-made aquatic environments.⁶ Acquisition of legionnaires' disease usually occurs following the aspiration or inhalation of aerosols from contaminated potable water or cooling towers.⁷⁻¹⁴ Most hospital-acquired outbreaks of legionnaires' disease have been associated with the contamination of hospital drinking water with *Legionella* species.¹⁵ Efforts to prevent hospital-acquired

legionnaires' disease have focused on increasing the temperature of hot water and the supplemental chlorination of drinking water.¹⁶⁻¹⁸ Although these measures may be effective in controlling the growth of *Legionella* species in drinking water systems, high water temperatures may result in scalding injuries and supplemental chlorination may hasten the development of corrosion and leaks in plumbing systems.¹⁹ The long-term efficacy of alternative methods for controlling and eradicating legionellae in hospital water systems (eg, ozone, ultraviolet light, and copper-silver ionization) has not been determined. Therefore, guidelines of the Healthcare Infection Control Practices Advisory Committee recommend performing surveillance for legionnaires' disease among patients and eliminating potential sources if hospital-acquired disease is suspected.¹⁶

Disinfection of municipal drinking water is accomplished in two stages. The goal of primary disinfection is to eradicate microorganisms from raw water entering the treatment plants and the goal of secondary (residual) disinfection is to prevent subsequent new growth of

Drs. Heffelfinger, Kool, and Whitney are from the Respiratory Diseases Branch, Division of Bacterial and Mycotic Diseases; and Dr. Fridkin, Mr. Hageman, and Mr. Carpenter are from the Division of Healthcare Quality Promotion, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia. Dr. Fraser is from the Division of Infectious Diseases, Department of Medicine, Washington University Medical Center, St. Louis, Missouri.

Address reprint requests to Cynthia G. Whitney, MD, MPH, Centers for Disease Control and Prevention, 1600 Clifton Road, MS C-02, Atlanta, GA 30333.

microorganisms in the water distribution systems. Monochloramine, formed when ammonia and free chlorine are combined in water, has been used as a residual disinfectant for drinking water since 1916.^{20,21} Monochloramine is an effective residual disinfectant because it is more stable than free chlorine,²¹ allowing active concentrations to be maintained throughout larger areas of water system distribution at a decreased cost; monochloramine also has better penetration into the biofilm that harbors microorganisms, including *Legionella*.^{22,23} Two previous studies suggest that residual disinfection with monochloramine by municipal water treatment plants may have a protective effect against outbreaks of hospital-acquired legionnaires' disease.^{24,25}

The aim of this study was to quantify the association between the residual disinfection of municipal water with monochloramine and the occurrence of either endemic or outbreak-related, hospital-acquired legionnaires' disease among a representative sample of hospitals in the United States.

METHODS

We conducted a retrospective cohort study involving the hospitals of members of the Society for Healthcare Epidemiology of America (SHEA). The most senior SHEA member with infection control responsibilities on record at each acute care inpatient facility was eligible to be enrolled.

Standardized questionnaires and requests to participate were sent to 459 eligible members in January 1999. Information was requested concerning episodes of hospital-acquired legionnaires' disease during the preceding 5 years (1994 to 1998), outbreaks of hospital-acquired legionnaires' disease during the previous 10 years (1989 to 1998), determination of the probable source of any such infections, hospital demographics, the nature of surveillance done by the hospital to detect hospital-acquired legionnaires' disease, the source of the hospital's water supply, the type of disinfection used by the municipal water plant supplying water to the hospital, and any additional treatment of drinking water performed at the hospital. Following the initial mailing, participants were sent two reminders by mail and a third reminder by either facsimile or e-mail. Surveys with ambiguous or incomplete information were clarified by contacting SHEA members, municipal water treatment plants, or both, by telephone.

Legionnaires' disease was defined as a clinical diagnosis of pneumonia confirmed by chest radiograph in an individual with at least one of the following: (1) isolation of *Legionella* from respiratory secretions or lung tissue; (2) detection of *L. pneumophila* serogroup 1 antigen in urine; (3) detection of *Legionella* in respiratory secretions or lung tissue by direct fluorescent antibody; or (4) detection of a fourfold or greater rise in titers of antibodies against *L. pneumophila* in acute- and convalescent-phase serum, to a value of 1:128 or higher. Definite hospital-acquired legionnaires' disease was defined as legion-

naires' disease occurring in an individual who had been hospitalized continuously for the entire period of 2 to 10 days before the onset of disease. Probable hospital-acquired legionnaires' disease was defined as legionnaires' disease occurring in an individual who had been hospitalized during part of the period from 2 to 10 days prior to the onset of disease. An outbreak of hospital-acquired legionnaires' disease was defined as 2 or more cases of definite hospital-acquired legionnaires' disease occurring in a hospital within a 6-month period. A combination of either definite cases of hospital-acquired legionnaires' disease occurring during the preceding 5 years or outbreaks of hospital-acquired legionnaires' disease occurring during the preceding 10 years was the primary outcome variable (ie, case-hospital) used in the analysis.

We used data from the 1997 American Hospital Association survey to compare the characteristics of hospitals among responders and nonresponders to the survey regarding hospital census, the number of beds in the acute and intensive care units, metropolitan size, academic affiliation, and the presence of oncology and transplant services.

Statistical testing for differences between the two groups was performed using the chi-square or Fisher's exact test as appropriate. Continuous variables were evaluated by the Wilcoxon rank sum test or Student's *t* test. Data were analyzed using Stata software (version 6.0; Stata Corp., Corpus Christi, TX). We used stepwise multivariable logistic regression to assess potential interaction and confounding by factors known to be associated with hospital-acquired legionnaires' disease or those that were significant at a *P* value of .1 or less on univariate analysis. Hospitals reporting only probable hospital-acquired legionnaires' disease (*n* = 10) and those supplied by municipal water plants that changed the method of residual disinfection of drinking water from a chlorine-based system to monochloramine during the study period (*n* = 4) were excluded from multivariable analyses. No hospitals were supplied by municipal water plants that changed their method of residual disinfection of drinking water from monochloramine to a chlorine-based system during the study period.

Potential confounding factors examined in the modeling process included the number of beds in the intensive care unit, hospital census, water temperature, the presence of a transplant service (bone marrow, solid organ, or both), the performance of patient-based surveillance for hospital-acquired legionnaires' disease (ie, passive reporting, active laboratory surveillance, or active surveillance for legionnaires' disease on hospital wards), and testing of the drinking water for *Legionella* species. Supplemental disinfection of the drinking water by hospitals was not included in logistic regression models because we did not have information about the timing of the implementation of supplemental disinfection by hospitals reporting hospital-acquired legionnaires' disease. Facilities with hospital-acquired disease that used additional methods to disinfect their drinking water may have

TABLE 1
HOSPITAL CHARACTERISTICS OF RESPONDING AND
NONRESPONDING SOCIETY FOR HEALTHCARE EPIDEMIOLOGY OF
AMERICA (SHEA) MEMBERS, REPORTED TO THE 1997 AMERICAN
HOSPITAL ASSOCIATION SURVEY

Characteristic	Returned Survey		P
	Yes (n = 154)	No (n = 215)	
Median average daily census (range)	258.5 (20-1,317)	260 (8-1,420)	.41
Median metropolitan size (range)	1-2 million (0-6 million)	1-2 million (0-6 million)	.91
No. with academic affiliation (%)	122 (79)	157 (73)	.17
Median no. of acute care beds (range)*	271 (0-914)	236.5 (0-1,169)	.1
Median no. of intensive care unit beds (range)*	34 (0-153)	32 (0-160)	.23
No. with a trans- plant service* (%)	66 (49)	78 (41)	.14
No. with an oncology service* (%)	123 (92)	170 (89)	.49

*Information for these variables was available for 134 hospitals of the responding SHEA members and 190 hospitals of the nonresponding SHEA members included in the 1997 American Hospital Association survey.

implemented these measures in response to cases or outbreaks of hospital-acquired legionnaires' disease. Factors were eliminated on the basis of their significance as confounders or effect modifiers and their effect on the precision of the estimated odds ratio of the main exposure variable. In the final model, associations with a *P* value of .05 or less were considered statistically significant.

RESULTS

We obtained complete data about hospital-acquired legionnaires' disease and municipal water disinfection practices from 166 (36%) of the 459 eligible SHEA members. We were able to identify 154 (93%) of the 166 hospitals of the responding SHEA members and 215 (73%) of the 293 hospitals of the nonresponding SHEA members in the 1997 American Hospital Association data set. Responding hospitals were similar to nonresponding hospitals in average daily census, metropolitan size, the number of acute care beds, the number of intensive care unit beds, the presence of oncology and transplant services, and academic affiliation (Table 1). The 166 respondents were from 40 states and the District of Columbia (Figure). Forty-one (25%) reported definite cases during the previous 5 years or outbreaks of hospital-acquired legionnaires' disease during the preceding 10 years, 33 (20%) reported definite cases of hospital-acquired legionnaires' disease during the preceding 5 years, and 23 (14%) reported an outbreak of hospital-acquired disease during the preceding 10 years. Ten (6%) of the hospitals that reported only probable cases of hospi-

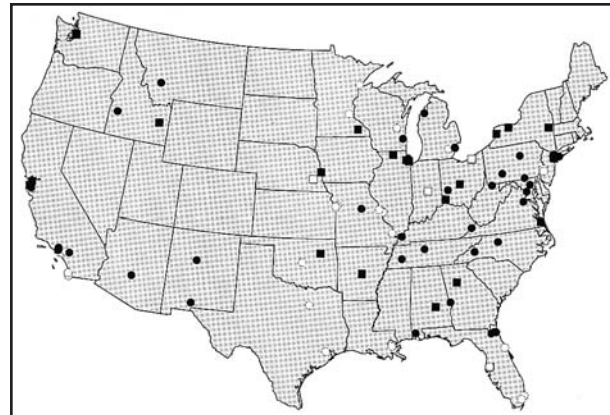


FIGURE. Distribution of the participating hospitals of members of the Society for Healthcare Epidemiology of America. Squares represent hospitals reporting hospital-acquired legionnaires' disease (ie, definite cases or outbreaks of hospital-acquired legionnaires' disease; n = 38) and circles represent hospitals reporting no hospital-acquired legionnaires' disease (n = 114). White symbols represent hospitals in municipalities that use monochloramine as a residual disinfectant and black symbols represent hospitals in municipalities that do not use monochloramine as a residual disinfectant.

tal-acquired legionnaires' disease were excluded from further analyses. Four additional hospitals (2%) were excluded from further analyses because they were supplied by municipal water plants that changed the method of residual disinfection of drinking water from a chlorine-based system to monochloramine during the study period. Of the 152 responding hospitals with complete data for exposure and primary outcome, 38 (25%) reported definite cases in the previous 5 years or outbreaks of hospital-acquired legionnaires' disease in the preceding 10 years, and were thus considered case-hospitals.

Case-hospitals were larger, had more beds in intensive care units, and were more likely to have transplant programs, perform patient-based surveillance for legionnaires' disease, use additional disinfection methods to treat their water supply, and maintain hot water at a higher temperature than were other hospitals (Table 2). Hospitals were similar regarding their use of urinary antigen testing for the diagnosis of legionnaires' disease. Residual disinfection methods for drinking water used by municipal water plants included free chlorine for 89 (59%) of the hospitals, monochloramine for 58 (38%) of the hospitals, and other methods for 5 (3%) of the hospitals. Eighteen (47%) of the 38 case-hospitals identified drinking water as the only source of transmission of disease, 2 (5%) of the case-hospitals identified drinking water and contaminated water in cooling towers as the source of transmission, 4 (11%) of the case-hospitals identified contaminated water in cooling towers or an air conditioning unit as the sole source of transmission, and 14 (37%) of the case-hospitals did not identify the source of transmission.

On multivariable analysis, census, the number of acute care beds, the number of intensive care unit beds,

TABLE 2
COMPARISON OF HOSPITAL CHARACTERISTICS BY STATUS OF HOSPITAL-ACQUIRED LEGIONNAIRES' DISEASE* AMONG 152 SURVEYED MEMBERS OF THE SOCIETY FOR HEALTHCARE EPIDEMIOLOGY OF AMERICA, 1989 TO 1998

Characteristic	Reported Hospital-Acquired Legionnaires' Disease		P
	Yes (n = 38)	No (n = 114)	
Median census (range)	319 (80-665)	221 (18-999)	.03
Median no. of acute care beds (range)	500 (120-1,157)	376 (50-1,700)	.04
Median no. of intensive care unit beds (range)	42 (6-145)	24 (0-156)	.009
No. with a transplant service† (%)	28 (74)	48 (42)	.001
No. with patient-based surveillance for legionnaires' disease‡ (%)	35 (92)	69 (61)	.001
No. using urine antigen for the diagnosis of legionnaires' disease (%)	37 (97)	107 (94)	.41
No. with supplemental hospital-based disinfection of drinking water (%)	13 (34)	5 (4)	< .001
Median water temperature, °F (range)	120 (100-170)	120 (95-160)	.01
No. with municipal disinfection of drinking water with monochloramine (%)	6 (16)	52 (46)	.001

*Definite cases during 1994 to 1998 or outbreaks during 1989 to 1998.

†Solid organ, bone marrow, or both transplant services.

‡Passive reporting, active laboratory surveillance, or active surveillance on hospital wards for legionnaires' disease.

and the hot water temperature did not affect the association of hospital-acquired legionnaires' disease with the method of residual disinfection of the drinking water or change the risk of hospital-acquired legionnaires' disease associated with other factors to an important degree; these variables were not included in the final multivariable model. When adjustment was made for the presence of a transplant service and patient-based surveillance for legionnaires' disease, hospitals supplied by municipal water plants using monochloramine as a residual disinfectant were less likely to have definite cases or outbreaks of hospital-acquired legionnaires' disease than were hospitals supplied with drinking water with another residual disinfectant (adjusted odds ratio [OR], 0.20; 95% confidence interval [CI]₉₅], 0.07 to 0.56) (Table 3). When we excluded 18 hospitals that did not identify drinking water as a source of transmission from the analysis, residual disinfection with monochloramine was associated with a greater reduction of the risk of hospital-acquired legionnaires' disease (adjusted OR, 0.05; CI₉₅, 0.007 to 0.45).

DISCUSSION

We determined that municipal disinfection of drinking water with monochloramine was associated with a large reduction in the risk of sporadic cases and outbreaks of hospital-acquired legionnaires' disease. Evidence that residual disinfection of municipal water with monochloramine may have an impact on hospital-acquired legionnaires' disease has been accumulating. In an outbreak investigation of hospital-acquired legionnaires' disease in Texas, investigators did not recover *Legionella* species from the hot water systems of 4 participating hospitals located in municipalities that used monochloramine for residual drinking water disinfection, whereas they found *Legionella* species in all of the 11 participating hospitals located in a municipality using free chlorine as the residual disinfectant.²⁴ A follow-up study comparing the municipal water treatment systems at hospitals with reported outbreaks of hospital-acquired legionnaires' disease with those from a sample of other hospitals also demonstrated the protective effect of monochloramine.²⁵ Laboratory studies support this association as well. An in vitro experiment that measured the effect of several disinfectants on *Legionella* growth in a model water system showed that monochloramine was a more effective disinfectant than free chlorine at killing *Legionella* in biofilm.²⁶ Furthermore, a pilot study of supplemental disinfection of one hospital's water system using monochloramine generated on site suggested that this method might lead to rapid and sustained reduction of *Legionella* growth in the hospital's water system.²⁷ However, our study is the first to assess the effect of the disinfection of municipal water with monochloramine on the risk of endemic hospital-acquired legionnaires' disease in a representative sample of hospitals in the United States.

The hospitals that reported hospital-acquired legionnaires' disease tended to be larger than those without hospital-acquired disease, in part because immunocompromised individuals (eg, patients admitted to transplant or oncology services) are more likely to be treated at larger hospitals. Also, hospitals reporting legionnaires' disease were more likely to test their water for *Legionella* and to have used supplemental disinfection methods beyond those used by municipal water plants. We suspect that testing and supplemental disinfection followed the identification of hospital-acquired disease at many hospitals. Most hospitals do not implement supplemental disinfection unless they identify transmission of hospital-acquired *Legionella* or widespread contamination of their water systems with *Legionella*.

Limitations of this study include the low rate of response from SHEA members and the observational design of the study. Although the response rate was low, the characteristics of responding hospitals were similar to those of nonresponding hospitals, and responding hospitals are likely to be representative of the SHEA membership as a whole. Although some hospitals that have had sporadic cases or outbreaks of hospital-acquired legionnaires' disease

TABLE 3

MULTIVARIABLE ANALYSIS MEASURING THE EFFECT OF RESIDUAL DISINFECTION OF DRINKING WATER WITH MONOCHLORAMINE ON HOSPITAL-ACQUIRED LEGIONNAIRES' DISEASE,* SOCIETY FOR HEALTHCARE EPIDEMIOLOGY OF AMERICA AND CENTERS FOR DISEASE CONTROL AND PREVENTION SURVEY, 1999

Exposure Variable	Hospitals With Exposure		Adjusted Odds Ratio	95% Confidence Interval
	With Hospital-Acquired Legionnaires' Disease (n = 38)	Without Hospital-Acquired Legionnaires' Disease (n = 108) [†]		
Municipal monochloramine use [‡]	6 (16)	47 (44)	0.20	0.07–0.56
Presence of a transplant service	28 (74)	45 (42)	5.24	2.13–12.93
Patient-based surveillance for legionnaires' disease [§]	35 (92)	69 (64)	6.85	1.85–25.33

*Definite cases during 1994 to 1998 or outbreaks during 1989 to 1998.

[†]Of 114 hospitals without reported hospital-acquired legionnaires' disease, information was missing from 1 hospital about the presence of a transplant service and from 5 hospitals about whether patient-based surveillance was conducted.

[‡]Residual disinfection of drinking water by municipal water treatment plants.

[§]Passive reporting, active laboratory surveillance, or active surveillance on hospital wards for legionnaires' disease.

naires' disease may have been reluctant to participate in this study, participation was likely independent of the method of municipal water disinfection. In addition, our study likely reflects the experiences of all hospitals in the United States. In our sample, 20% of the hospitals reported at least one definite case of hospital-acquired legionnaires' disease during the previous 5 years and 14% reported an outbreak of hospital-acquired legionnaires' disease during the preceding 10 years. This incidence of disease is comparable to previous estimates.¹⁷ However, any response bias would have led to nondifferential misclassification, reducing our power to detect an association of residual disinfection of drinking water and hospital-acquired legionnaires' disease, leading to an underestimation of the protective effect of monochloramine. Because this was an observational study, there may have been variation in the assessment of the status of hospital-acquired legionnaires' disease because of differences in detecting or reporting cases or outbreaks of disease, and this may also have resulted in nondifferential misclassification and a bias toward the null.

The results of this and previous studies provide further evidence that the use of monochloramine for the residual disinfection of drinking water significantly reduces the risk of hospital-acquired legionnaires' disease. This protective effect may not be restricted to hospitals. Approximately 65% of cases of legionnaires' disease in the United States occur outside of hospitals.⁵ Cooling towers, hotel water systems, and home water systems are thought to be the main sources of community-acquired infection. Widespread use of monochloramine by municipal water treatment plants may reduce the incidence of community-acquired legionnaires' disease due to the latter two sources, and thus it may considerably decrease the overall incidence of this severe disease. Because free chlorine reacts with dissolved organic material in water to

produce trihalomethanes and halo-acetic acids, which are suspected to be carcinogenic,^{28,29} municipal water departments have begun to use monochloramine in place of free chlorine as a residual disinfectant.³⁰ A survey conducted in 1989 of water utilities serving populations greater than 50,000 found that 23% were using monochloramine as a residual disinfectant,²¹ and this proportion likely increased further in recent years. The protective effect of residual disinfection with monochloramine should be further evaluated in prospective studies. Furthermore, decisions by local municipalities on water treatment practices should involve local health departments. The infection control community, as a vital link between local health departments and hospitals, needs to be aware that municipal water treatment may have an impact on disease that occurs within hospitals.

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