

## Nosocomial Legionnaires' Disease: Aspiration as a Primary Mode of Disease Acquisition

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**PURPOSE:** Nosocomial Legionnaires' disease remains a significant problem with many unresolved questions regarding transmission of legionella organisms to patients. We performed a case-control and environmental study to identify risk factors and modes of transmission of *Legionella* infection during an outbreak of nosocomial Legionnaires' disease in a military medical center.

**PATIENTS AND METHODS:** During the calendar year 1989, 14 cases of nosocomial Legionnaires' disease were identified by active surveillance following the discovery of 2 culture-proven cases among organ transplant recipients. Four control patients were matched to each case by age, sex, and date of admission. Cases and controls were compared with respect to past medical history and hospital exposure variables. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for matched variables. Environmental culturing of air and water supplies in and around the medical center was also performed.

**RESULTS:** The case-control study revealed the following significant risk factors for the acquisition of nosocomial Legionnaires' disease: immunosuppressive therapy (OR = 32.7, CI = 4.5 to 302.6), nasogastric tube use (OR = 18.4, CI = 2.6 to 166.2), bedbathing (OR = 10.7, CI = 2.2 to 59.0), and antibiotic therapy (OR = 14.6, CI = 2.9 to 84.4). Shower use (OR = 0.1, CI = 0 to 0.4) appeared to be a negative risk factor. Water cultures revealed *Legionella pneumophila* serogroup 1, monoclonal antibody subtype Philadelphia (identical to all patient isolates) in

the ground-water supply to the hospital, 1 hot-water tank, and 15% of 85 potable water sites tested. Air sampling of cooling towers, hospital air intakes, and medical air and oxygen supplies were negative for *Legionella* organisms.

**CONCLUSIONS:** This study confirms the importance of potable water in transmitting nosocomial Legionnaires' disease and suggests that the organism gains access to the hospital via external water supplies. The risk factors identified in this case-control study provide evidence that Legionnaires' disease may act as a superinfection in a nosocomial setting and is likely acquired by aspiration, similar to other nosocomial pneumonias.

Since the original description of Legionnaires' disease in Philadelphia in 1976, and the subsequent characterization of the etiologic agent, *Legionella pneumophila*, significant progress has been made in defining the epidemiology and clinical significance of infection with this agent [1,2]. Nevertheless, many questions remain regarding the role of *Legionella* in acute infection of the lower respiratory tract [3]. In particular, the mode of transmission of *Legionella* organisms from environmental sites into humans continues to be controversial [4]. Environmental sources implicated in previous outbreaks of Legionnaires' disease have included potable water, cooling systems, respiratory therapy devices, industrial coolants, and whirlpool spas [5]. Of these sources, potable water has been identified most frequently as the culprit in nosocomial outbreaks of legionellosis [6-20]. Two potential mechanisms by which *Legionella* organisms gain access to the respiratory tract include aerosolization directly from potable water sources and colonization of the oropharynx with subsequent aspiration. A recent study has shown, for the first time, an epidemiologic link between shower use and acquisition of Legionnaires' disease, suggesting aerosolization as the likely mode of acquisition in that study [15]. Circumstantial evidence from other studies, however, suggests that colonization with aspiration may also be a likely mode of organism transfer [4,6,11,18,20].

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Investigation of a nosocomial outbreak of legionellosis associated with our hospital potable water supply provided an opportunity to address this issue with a 1-year case-control study.

## PATIENTS AND METHODS

### Hospital

Wilford Hall USAF Medical Center is a 1,000-bed multi-specialty hospital that delivers primary and tertiary care to the military population of San Antonio, Texas, and maintains active programs in solid organ and bone marrow transplantation. The hospital is composed of a single building built in 1958 with a clinic attachment added in 1981. Water for the hospital system originates from ground-water wells located on the hospital grounds. Water is chlorinated at the well head and then pumped to an energy plant where it is instantaneously heated then delivered to the hospital, where it is stored in the basement in two hot-water tanks. The hot water from these tanks is then mixed and distributed throughout the hospital potable water system.

The entire hospital is supplied by central air conditioning; windows are locked in the closed position. Cooling towers for the hospital are located 200 yards to the north of the hospital and prevailing winds blow to the northeast, away from the hospital.

### Case Definition

A case of Legionnaires' disease was defined as a radiographically documented pneumonia in association with one or more of the following test results: a fourfold or greater increase in titer (specimens separated in time by at least 14 days) of indirect immunofluorescent antibodies (IFA) to a titer of greater than or equal to 1:128 using a polyvalent antigen battery consisting of *L. pneumophila* serogroups 1 to 4 (Zeus Scientific Inc., Raritan, NJ); a positive result of a direct immunofluorescent antibody (DFA) test of respiratory secretions or tissue using a monoclonal antibody directed against all known serogroups of *L. pneumophila* (Genetic Systems, Seattle, WA); or isolation of *L. pneumophila* from respiratory secretions or tissue. A case was defined as nosocomial if infection occurred 2 or more days after admission or within 10 days of hospital discharge.

### Disease Surveillance and Case Finding

In April 1989, two culture-proven cases of *Legionella* pneumonia were identified in transplant patients on different units. After these cases, active surveillance for the disease was initiated by education of house staff and nurses as to the appropriate diagnostic tests to order. In addition, preprinted order forms for these tests were distributed to pa-

tient wards to be used for cases of nosocomial pneumonia. A retrospective review for positive *Legionella* IFA and DFA results for the calendar year 1989 was also performed. Cases of pneumonia were identified in a prospective fashion by the ongoing twice-weekly surveillance of all inpatients performed by the Infection Control Service. When a case was identified, the Infectious Disease consult service was notified and appropriate diagnostic studies were obtained.

### Environmental Sampling and Microbiologic Methods

Clinical samples were placed on buffered charcoal yeast extract (BCYE) and two selective media as previously described (Remel, Lenexa, KS) [21]. Sputum samples were pretreated with an acid wash procedure during the final 2 months of the study [21]. Samples of tissue and bronchoscopy specimens were plated directly. Environmental samples were obtained by swabbing faucets and shower heads with sterile rayon swabs and inoculating these directly onto BCYE media supplemented with dyes, glycine, vancomycin, and polymyxin B (DGVP media) [21]. Water samples from the hot-water tanks were collected in two 1.0-L aliquots and filtered through nitrocellulose filters. Scrapings from these filters were then placed onto DGVP media. In addition, quantitative analysis of *Legionella* colonization was performed by inoculating 0.1-mL samples of potable water directly onto DGVP media as well as filtering 100-mL samples through nitrocellulose filters and plating these on DGVP media. Air samples were obtained using a two-stage microbial air sampler (Anderson Samplers, Atlanta, GA) from sites around the base of the cooling tower, at air intakes of the hospital, and from the hospital medical air and oxygen systems. The sampler was connected to a portable vacuum pump and flow meter. The two-stage sampler separates particles into nonrespirable (greater than 8.0  $\mu\text{m}$ ) and respirable droplet sizes [22]. Petri dishes containing BCYE media were placed on each stage and sampling was performed for 15 minutes at each site.

Clinical and environmental cultures were examined daily for 14 days. All colonies compatible with *Legionella* organisms were studied by a monoclonal antibody directed against all known serogroups of *L. pneumophila* (Genetic Systems). Serogrouping of *L. pneumophila* isolates was performed by the Special Pathogens Laboratory at the Pittsburgh Veterans Administration Hospital (Richard M. Vickers). Monoclonal antibody subtyping of *L. pneumophila* serogroup 1 isolates was performed by Dr. Jean R. Joly [23].

### Case-Control Study

Control patients without pneumonia were select-

TABLE I

*Legionella* Diagnostic Studies in Case Patients

Test	No. Positive/No. With Test Performed (%)
DFA	12/14 (86)
IFA	3/9 (33)
Culture	3/12 (25)
DFA + culture	2/12 (17)
DFA + IFA	1/9 (11)
DFA + IFA + culture	1/9 (11)

DFA = direct fluorescent antibody test; IFA = fourfold rise in indirect fluorescent antibody titer of specimens separated by at least 14 days.

ed and matched by age ( $\pm 5$  years), sex, and date of admission to each case patient in a ratio of 4:1. Thorough medical record reviews, including review of nursing notes and respiratory therapy records, were conducted to determine potential risk factors for acquisition of *Legionella* infection. Past medical history variables present prior to and during hospitalization included: history of cancer, cardiovascular disease, chronic obstructive pulmonary disease, asthma, chronic renal failure, use of steroids, immunosuppressive therapy or antacids/antihistamines ( $H_2$  blockers), smoking, and alcohol use. Hospital exposure variables studied for the 10 days prior to onset of pneumonia were oxygen therapy, intravenous antibiotics, nebulizer use, showering, bed-bathing, radiology procedures, endoscopy, presence of a nasogastric tube, physical therapy, bronchoscopy, surgery, general anesthesia, emergency room admission, endotracheal intubation, pulmonary function testing, and ambulation.

Odds ratios (ORs) and Cornfield 95% confidence intervals (95% CIs) for matched variables were calculated using EPI INFO 5 computer software (USD Inc., Stone Mountain, GA). In order to identify confounding among variables, a series of stratified  $2 \times 2$  tables were performed in which each significant variable from the univariate analysis was stratified against each other significant variable in a sequential bivariate analysis (Mantel-Haenszel stratified analysis) [24].

## RESULTS

From January 1 through December 31, 1989, 14 cases of nosocomial pneumonia were identified that met the case definition for Legionnaires' disease. The mean age of these cases was 46.7 (standard deviation [SD]  $\pm 19.7$ ) years; the sex distribution was equal. Thirteen of the 14 patients (93%) were white. The mean duration of hospitalization prior to onset of pneumonia was 20.5 (SD  $\pm 15.5$ ) days. The case-fatality rate was 43%. During this time

TABLE II

## Univariate Analysis of Past Medical History Variables Evaluated in the Case-Control Study

Risk	No. of Cases (%)	No. of Controls (%)	Odds Ratio	95% Confidence Intervals
Immunosuppression*	8 (57)	2 (4)	32.7	4.5-302.6
Steroid use	8 (57)	4 (8)	15.7	2.9-93.1
Chronic renal failure	4 (29)	1 (2)	20.0	1.7-534.8
$H_2$ -blocker use	8 (57)	10 (20)	5.3	1.3-23.3
Diabetes	1 (7)	1 (2)	3.8	0-156.2
Cancer	4 (29)	11 (22)	1.5	0.3-6.6
Dialysis	1 (7)	None	Undefined	Undefined
Cardiovascular disease	5 (36)	16 (31)	1.2	0.3-4.9
Chronic obstructive pulmonary disease	1 (7)	7 (14)	0.5	0-4.7

\* $p < 0.05$  by sequential bivariate analysis of variables found to be significant in the univariate analysis.

period, there was no increase noted in the overall nosocomial pneumonia rate in our hospital compared with historical norms. Major underlying conditions for case patients included allogeneic bone marrow transplantation in three (21%), renal transplantation in two (14%), neurologic disease in two (14%), coronary artery disease in two (14%), and one case each of acute leukemia, solid tumor, ulcerative colitis, diabetes mellitus with renal failure, and surgery for a thyroidectomy.

The diagnostic studies used to confirm the diagnosis of *Legionella* pneumonia are shown in Table I. Culture-negative cases were significantly more likely to have been treated with third-generation cephalosporins, doxycycline, or erythromycin in the 10 days prior to disease onset compared with culture-positive cases ( $p = 0.03$ , Fisher exact test). All patient isolates were shown to be *L. pneumophila* serogroup 1, subtype Philadelphia, by monoclonal antibody subtyping [23]. All 14 of the nosocomial cases had at least 1 DFA test performed (mean: 2.5 per patient), and 12 patients (86%) had at least 1 positive test result. In addition, of the 35 specimens submitted for DFA testing on our 14 cases, 20 (57%) were positive, or 1.7 per case.

## Case-Control Study

Fifty-one control patients (mean of 3.6 per case) were matched to the 14 case patients as described above. The mean age of controls was 46.7 years (identical to cases) and the mean duration of hospitalization for controls was 5.9 days (SD  $\pm 6.5$  days). Table II shows the results of a univariate analysis of the past medical history variables evaluated in this study. When adjustment was made for variables found to be statistically significant in the univariate analysis, only immunosuppressive therapy remained a statistically significant ( $p < 0.05$  by sequential bivariate analysis) medical history risk factor for the acquisition of *Legionella* infection.

Table III shows a univariate analysis of the hos-

pital exposure variables studied in this outbreak as potential risk factors for the acquisition of Legionnaires' disease. Of these variables, only the presence of a nasogastric tube, antibiotic use, and bedbathing remained statistically significant ( $p < 0.05$ ) after controlling for significant hospital exposure variables from the univariate analysis.

Because of the difference in duration of hospitalization prior to the onset of *Legionella* infection for cases versus controls, we performed a subset analysis on 10 cases and 25 controls that were additionally matched on length of stay ( $\pm 7$  days, case median = 10 days [range: 2 to 36 days], control median = 7 days [range: 1 to 32 days]). The only difference between this subset analysis and the full cohort analysis was that exposure to H<sub>2</sub> blockers did not remain a statistically significant past medical history risk factor ( $p = 0.11$ , Fisher exact test). All other medical history and hospital exposure risk factors were unchanged.

Analysis of hospital ward as a risk factor for *Legionella* infection was hampered by an inadequate number of suitable controls in the bone marrow transplant and intensive care units. Of note, however, is the observation that all case patients were hospitalized on the bone marrow transplant, renal transplant, or intensive care units at some time during the 10 days prior to disease onset.

### Environmental Culturing

Despite the initial recognition of *Legionella* cases in April 1989, testing of environmental sites did not begin until December 1989. A number of factors led to this decision, including concerns about the specificity of diagnosis in the cases identified by DFA alone, as well as the possibility of finding *Legionella* in the environment without adequately documenting a sustained outbreak in our patient population. However, after documenting a third culture-proven case of *Legionella* pneumonia in November 1989, it became clear that we were experiencing a persistent problem and environmental testing for *Legionella* was initiated.

Air sampling was performed from 4 sites around the cooling towers, 18 air intakes for the hospital, and the hospital medical air and oxygen systems. In addition, water mist samples were obtained from patient bathrooms with a settle plate technique while the shower was running in an attempt to isolate aerosolized organisms. We were unable to isolate any *Legionella* species from these air and water mist samples.

Water sampling outside the hospital was performed from the ground-water well on the hospital grounds, from the chlorinator at the well head, and from the energy plant. Within the hospital, water samples and swabs were obtained from both hot-

TABLE III

Univariate Analysis of Hospital Exposure Variables Present in the 10 Days Prior to Legionnaires' Disease Onset

Exposure	No. of Cases (%)	No. of Controls (%)	Odds Ratio	95% Confidence Intervals
Nasogastric tube*	6 (43)	2 (4)	18.4	2.6-166.2
Bedbathing*	11 (78)	13 (25)	10.7	2.2-59.0
Antibiotic use*	11 (78)	10 (20)	14.6	2.9-84.4
Nebulizer use	4 (29)	1 (2)	20.0	1.7-534.8
Oxygen use	6 (43)	6 (12)	5.6	1.2-27.7
Radiology	8 (57)	14 (27)	3.5	0.8-14.5
Endoscopy	1 (7)	2 (4)	1.8	0-30.7
Bronchoscopy	1 (7)	None	Undefined	Undefined
Pulmonary function tests	1 (7)	1 (2)	3.8	0-156.2
Endotracheal tube	6 (43)	13 (25)	2.2	0.5-8.9
Surgery	5 (36)	24 (47)	0.6	0.1-2.5
Emergency room admission	1 (7)	6 (12)	0.6	0-5.8
Ambulation	5 (36)	44 (86)	0.1	0-0.4
Showering	5 (36)	27 (53)	0.1	0-0.4

\* $p < 0.05$  by sequential bivariate analysis of variables found to be significant in the univariate analysis.

water tanks in the basement, and swab cultures were performed on 85 sites from patient care areas, including faucets and shower heads in patient rooms, intensive care units, and operating rooms, as well as from fountains located on the first floor of the hospital. In addition, the water traps from 17 ventilators were cultured for *Legionella*. *L. pneumophila* was isolated from the ground water at the well head, from both hot-water tanks in the hospital, from 1 of the 2 fountains, and from 24 (28%) of the patient care areas on high-risk wards where *Legionella* cases had been housed. None of the ventilators tested were found to harbor *Legionella*.

Serogrouping and monoclonal antibody subtyping revealed that the organisms isolated from the ground-water well, 1 of the hot-water tanks, and 13 patient care areas were *L. pneumophila* serogroup 1, subtype Philadelphia, identical to our patient isolates. The other hot-water tank and 11 patient care sites contained *L. pneumophila* serogroup 3. The fountain isolate was an *L. pneumophila* serogroup other than 1 through 6. Quantitative analysis for the number of organisms present in potable water demonstrated 3 to 80 colonies of *Legionella* organisms per plate, by direct plating of 0.1 mL of tap water, and greater than 100 colonies per plate when filtering a 100-mL aliquot of water. These results suggest that our patients were exposed to an organism burden on the order of  $10^4$  to  $10^6$  colony-forming units per liter (cfu/L) in the potable water supply.

Reviews of maintenance records for the hospital over the course of the year revealed that the potable water chlorine levels, although inadequate for controlling *Legionella* colonization, had been maintained in the acceptable range (0.3 to 0.5 ppm). In

addition, the water temperature in the hot-water tanks had not dropped below 50°C during this time period. Of potential significance, however, was the observation that major renovations were taking place in the water supply to the hospital during 1989. During the time of this outbreak, pipes carrying water from the ground-water wells to the energy plant were being excavated and replaced.

## COMMENTS

This report, describing a 1-year case-control and environmental investigation of 14 cases of nosocomial legionellosis, again implicates the potable water supply as the likely source of infection. This outbreak was first recognized, as in other outbreaks, by the sudden appearance of cases among a transplant population [13,14,25]. These sentinel cases prompted us to increase our surveillance for the disease using multiple diagnostic modalities in other patients with hospital-acquired pneumonia. As other authors have noted, many of these cases may have been missed had we not employed aggressive specialized techniques to confirm the diagnosis [7,11,12].

The relatively low yield from cultures in this series (25%) may be due to several factors. First, we did not routinely use selective BCYE media or acid pretreatment of specimens, both of which have been shown to increase *Legionella* recovery rates [26-28]. In addition, once this outbreak was recognized in our hospital, the physicians caring for immunocompromised patients began the early empiric use of erythromycin or doxycycline for patients with nosocomial pneumonia, frequently prior to obtainment of sputum or bronchoscopic cultures. Furthermore, many of our patients were already receiving broad-spectrum antibiotics at the time they developed their *Legionella* infection, and we occasionally noted overgrowth of the *Legionella* plates with yeast despite acid pretreatment of samples. An antibiotic pretreatment effect in reducing *Legionella* culture rates is supported by our finding that culture-negative cases were significantly more likely to have been treated with broad-spectrum antibiotics or antibiotics effective against *Legionella* compared with culture-positive cases. Other recent nosocomial legionellosis series have shown *Legionella* culture recovery rates of 14% to 35%, similar to our experience [12,15,17]. In addition, the seroconversion rate of 33% noted among our cases compares favorably with other recent series of nosocomial legionellosis in which seroconversion rates of 33% to 47% have been reported [12,14]. The inclusion of bone marrow transplant patients in our series may have also decreased the yield from serologic testing,

since these patients have impaired humoral responses to new antigenic challenge [29].

The case-control portion of our investigation found immunosuppressive, corticosteroid, and H<sub>2</sub>-blocker therapy as well as chronic renal failure to be significant univariate medical history risk factors for the acquisition of Legionnaires' disease in our hospital. After an analysis for confounding variables, however, only the use of immunosuppressive therapy remained significant. Corticosteroid and immunosuppressive therapies have previously been shown to be significant risk factors for developing nosocomial *Legionella* infection in a number of other studies [14,15,30]. Antihistamine (H<sub>2</sub>-blocker) therapy, however, has not previously been associated with the development of Legionnaires' disease. Antihistamine therapy has, however, been shown to predispose to the acquisition of nosocomial pneumonia in general [31,32], presumably by allowing bacteria to colonize the gastrointestinal tract with the subsequent aspiration of these organisms [33]. Although demonstrated only in the univariate analysis, the increased risk for *Legionella* infection in our patients treated with H<sub>2</sub>-blocker therapy suggests that *Legionella* organisms may be acquired in a manner similar to other nosocomial pneumonias.

In the univariate analysis of hospital exposures associated with *Legionella* in this study, the presence of a nasogastric tube, bedbathing, antibiotic treatment, nebulizer use, and oxygen use appeared to be significant variables. After adjustment for confounding, however, only nasogastric tube use, bedbathing, and antibiotic use remained significant. This association between *Legionella* infection and the presence of a nasogastric tube among our cases strongly supports the role of aspiration as a mode of disease acquisition. Marrie *et al* [20] have also recently described nasogastric tubes as a risk factor for nosocomial Legionnaires' disease. They suggest that microaspiration of contaminated potable water used to flush these tubes may be an important mode of disease acquisition. Our study supports this concept and suggests that nasogastric tube use may be a major risk factor for *Legionella* infection in hospitals that have potable water contaminated by *Legionella* organisms.

Previous studies have suggested that patients may acquire *Legionella* infection in the hospital by inhaling aerosolized organisms while showering [15,18]. In the present study, however, showering appeared to be a negative risk factor for the development of legionellosis (Table III). Conversely, patients taking only bed baths were at increased risk of developing the disease in our hospital. This finding also supports the role of aspiration in the acqui-

sition of disease in this study. Patients confined to bed, too ill to take showers, would be expected to have an increased risk for aspiration. Other nosocomial *Legionella* studies have also noted a negative association between cases and showering (or duration of time spent showering) [7,9,19], suggesting that mechanisms other than aerosolization from showers are important in transmitting the organism in a nosocomial setting.

Antibiotic therapy, in a number of previous studies, has been shown to be a significant risk factor for the development of superinfection, in general, and nosocomial pneumonia, in particular [34-36]. Antibiotic therapy has not previously been associated with the development of *Legionella* infection, however. Our finding of antibiotic therapy as a significant risk factor for the development of legionellosis suggests that antibiotics may alter the usual commensal flora, allowing for colonization by *Legionella* organisms.

Although this study reveals an epidemiologic link between our cases and known risk factors for colonization by opportunistic pathogens, we did not demonstrate oropharyngeal colonization by *Legionella* organisms. Two previous studies have suggested, however, that colonization by *Legionella* organisms may occur [37,38]. Further studies in this area are necessary with more sensitive diagnostic methods, such as polymerase chain reaction, in order to document the presence of *Legionella* colonization.

The use of medication nebulizers has recently been shown to be associated with an outbreak of nosocomial Legionnaires' disease [39]. In that outbreak, it was noted that 57% of respiratory therapy personnel rinsed nebulizers in tap water. In the current study, use of nebulizer therapy appeared to be a significant risk factor in the univariate analysis, although only four case patients (28%) were exposed to this variable. In a blind survey of our own respiratory therapy personnel, 66% admitted to rinsing nebulizers in tap water. On the basis of these observations, we would agree with Mastro *et al* [39] that rinsing nebulizers with tap water may be a common practice among respiratory therapy personnel. Although nebulizer therapy did not appear to be the major mode of *Legionella* transmission in this study, it may have been an important risk factor for those case patients exposed to this variable. We concur with the recommendations of Mastro *et al* [39] that nebulizers should not be rinsed or filled with tap water.

Our environmental investigation indicates that the reservoir of *Legionella* in our hospital is the potable water supply. *L. pneumophila* serogroup 1 isolates of the same monoclonal antibody subtype

were isolated from cases and environmental sites, including a hot-water tank supplying patient care areas and multiple sinks and showers on patient wards where cases occurred. We were unable to isolate *Legionella* organisms from air sampling around the hospital cooling towers, from air intakes to the hospital, or from the hospital medical air and oxygen supplies, demonstrating the absence of *Legionella* organisms in aerosols from other potential sources. Also of significance is the finding of an identical subtype of *L. pneumophila* serogroup 1 from the ground water that supplies the hospital system. Previous authors have theorized that *Legionella* organisms gain access to the hospital water system from municipal or reservoir water supplies [40], but this is the first study in which the outbreak-associated strain has been cultured from the ground-water supply to a hospital. The temporal relationship between the excavation and replacement of pipes carrying water from the ground-water wells to the energy plant, and the onset of this outbreak, is intriguing. We speculate that this disturbance of the water supply may have triggered or exacerbated colonization of the hospital potable water system leading to the onset of cases among our patients. Because of this observation, we would recommend increased surveillance for nosocomial Legionnaires' disease, among susceptible patients, during periods of construction or maintenance of hospital water supplies.

In summary, this 1-year case-control and environmental study of nosocomial legionellosis has demonstrated *Legionella* infection in association with known risk factors for colonization by nosocomial pathogens. In addition, we have shown that *Legionella* infection is associated with risk factors for aspiration, suggesting that aspiration may be an important mode of disease acquisition. We have also confirmed that the outbreak-related strain of *Legionella* likely gains access to the hospital via the external water supply. Future studies should focus on quantitating the threshold of *Legionella* colonization that puts patients at risk of acquiring disease, as well as determining optimal methods for decreasing *Legionella* colonization of potable water systems.

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