AN OUTBREAK INVESTIGATION OF NOSOCOMIAL LEGIONELLOSIS

BACKGROUND

On March 6, 2002, the Infection Control Practitioner (ICP) at a local hospital consulted with ACDC regarding two hospital-acquired cases of legionellosis (LD) occurring in patients at their facility. The hospital had previously reported these cases using the standard Confidential Morbidity Report and was concerned once the second case was identified. Additionally, the hospital had contracted a private environmental testing company to test its water supply, which was completed on March 11. ACDC advised the hospital to begin a laboratory review for missed positive laboratory specimens indicating LD cases and to conduct a six-month retrospective review of hospitalized patients looking for nosocomial pneumonia cases that might have been due to LD. At this point, no new LD cases were identified and the hospital water samples were negative for *Legionella*.

Due to the heightened awareness, a third case of LD was diagnosed, but this case was determined by ACDC to be community-acquired. After a fourth LD case was reported on March 17, the hospital took the initiative to test the shower hoses of 3 case-patient rooms, as well as remove the shower handles from showers on one ward of the 4th floor. This location was selected because all case-patients had spent time on this ward prior to becoming ill.

On March 20, ACDC gave recommendations to the hospital to initiate active prospective LD surveillance. Additional testing of the water supply of patient rooms was conducted by the same private environmental testing company. This was completed on March 22. In addition, ACDC sent a second set of recommendations to the hospital on March 28. At that time, the hospital removed the shower handles from the other 4th floor ward.

In consultation with the California State Department of Health Services, ACDC initiated an investigation of this cluster of Legionnaires' disease on March 29.

METHODS

An initial site visit was conducted to review case-patient charts, evaluate the hospital plumbing system, and collect water samples for testing by the LAC Public Health Laboratory (PHL). Additionally, consultants from the CDC, the Los Angeles City Department of Water and Power (DWP), LAC Health Facilities, the PHL, and other *Legionella* experts were contacted for technical advice.

Recommendations made in the previously mentioned letters (dated March 20, March 22, and March 28) were augmented with additional letters sent on March 31, June 6, and June 19. The intent of these recommendations was to reduce risk to patients, find potential cases, and assure adequate treatment.

Active case finding was conducted both prospectively and retrospectively. A retrospective analysis of all nosocomial pneumonia cases diagnosed in the previous 6 months was completed by the hospital ICP and the Director of Medical Records. Charts were then reviewed to identify possible nosocomial pneumonias and to review if any testing was completed and found positive for *Legionella*. Prospectively, the hospital laboratory staff took the lead role. For every respiratory specimen culture ordered in the hospital, they sent a sample to their outside clinical laboratory for Legionella culturing, and performed urine antigen testing as well. Because this was very labor and resource intensive, and the primary interest was to identify nosocomial legionellosis, this level of surveillance was changed on June 19. The hospital then began requesting urine specimens from a patient hospitalized greater than or equal to 48 hours from whom respiratory specimens had been sent to the laboratory. Both legionella urinary antigen testing and cultures

were done for these patients (the urinary antigen testing at the hospital laboratory and the cultures at their outside clinical laboratory).*

Between late March 29 and early April, the CDC EIS Officer collected 53 environmental specimens: 29 swab samples, 22 water samples, and 2 ice samples. The swabs were collected by vigorously swabbing water fixtures (and in the case of showers, into the tubing of the shower hose). On June 10, three additional water specimens were collected from the cooling tower, the operating room air humidifier, and cold water at the point where city water enters the hospital. All specimens were collected in sterile containers and under conditions and specifications recommended by the PHL. All specimens were transported on the day of collection to the PHL and results were reported out as available. Additionally, temperature and pH levels were measured at the time of collection. On June 6, a representative from the LAC Environmental Health Division (EH) visited the hospital with ACDC to test chlorine levels in the water supply.

Hospital building plans were reviewed with the hospital Director of Engineering, ACDC, and EH to look for potential sources of water pooling which would allow *Legionella* to propagate. Repair records were reviewed to determine if any work had been done which may have altered the hospital water supply. A walk-through of hospital wards, operating rooms, and the power plant was done.

A floor map was used to visualize the rooms of patients who were housed primarily on the 4th floor. The distal rooms were defined as the last four rooms at the end of each hall on the ward—a total of 24 rooms met this definition. The 5th floor patient census data was also reviewed. These patients (hematology/oncology and pulmonary patients) were presumed to be at an increased risk for developing LD. ACDC staff reviewed respiratory therapy and ventilation techniques with the hospital's Director of Respiratory Therapy Services.

A case-control study was undertaken. A confirmed case of legionellosis was defined as having a compatible clinical history and one of the following laboratory criteria: 1) isolation of *Legionella* species from lung tissue, respiratory secretions, pleural fluid, blood, or other sterile site, 2) demonstration of Legionella species in lung tissue, respiratory secretions, or pleural fluid by direct fluorescent antibody testing, 3) fourfold or greater rise in immunoflourescent antibody titer to Legionella species (to 128 or greater), and 4) detection *of L. pneumophila* serogroup 1 antigen in urine.

A *community-acquired case* was defined as a patient admitted with symptoms compatible with legionellosis or who developed such symptoms within 48 hours of admission. A *probable case* was defined as a patient admitted for a portion of the incubation period prior to onset of illness, including patients who were discharged and re-admitted within the incubation period. A *definite case* was defined as a patient admitted for at least 10 days prior to onset of illness.

* The diagnosis of legionellosis can be made using a number of laboratory tests, each of which has advantages and disadvantages. A detailed description of all testing methods is available in the review article by Fields, Benson, and Besser, *Legionella* and Legionnaires' disease: 25 Years of Investigation, Clinical Microbiology Reviews, July 2002, p 506-526. In summary:

1. Culture remains the "gold standard" for diagnosis. Legionellae can be isolated from a number of specimens, though respiratory secretions (sputum, bronchial alveolar lavage, and bronchial aspirate) are considered the specimens of choice. The sensitivity of culture can be affected by many factors such as laboratory experience, inadequate samples, and delay of testing.
2. Microscopic examination of specimens using direct fluorescent antibody (DFA) staining provides a rapid method of identifying *Legionella*; immunofluorescent microscopy is technically demanding and should be performed by experienced laboratory personnel.
3. Serologic tests to detect antibodies to *Legionella* have important limitations. Indirect immunofluorescent assay (IFA) is the most common test used to detect antibodies. Even in cases of culture-confirmed Legionnaires' disease, a fourfold rise in antibody by IFA can be documented for only 70 to 80% of patients, and seroconversion following legionellosis may not occur for up to 2 months after illness onset.

Urinary antigen testing uses an antibody specific for *L. pneumophila* serogroup 1, and therefore may miss cases of legionellosis caused by other serogroups and species. Most patients will test positive for 4 to 14 days after exposure, though positive results have been shown to persist for up to 300 days. This test works best when combined with culture.

A chart abstraction form was developed. Three controls were chosen per case and were matched on +/- 2 days of the date of admission, were greater than 50 years old, and were admitted with a cardiac diagnosis. Data were analyzed using Epi Info 2000, Epi Info 6.0, and SAS. Matched analysis was performed on bivariate variables only.

RESULTS

Environmental Findings: Review of hospital plumbing indicated that city water enters the hospital pump room via two sources. It then divides into a supply for the fire control system and for potable water. The potable water passes through a water softening process, which uses a constant flow system. It then divides into cold and hot water supplies, one which serves the basement through 3rd floor (loop 1) and one which serves floors 4 through 8 (loop 2). There are two flash steam hot water heaters, one for each loop. Hot water is constantly recirculated through the system. The only potential for a "dead leg" in the system is if the distal areas do not utilize hot water. There were no indications of differences between floors or loops, and no obvious physical plant abnormalities which would allow *Legionella* to propagate were noted on the walk-through of the facility.

No recent plumbing repairs were noted in the hospital logs or DWP's review of records for the area around the hospital.

The environmental testing performed by the hospital's own clinical laboratory was reported as 1/3 (33%) positive for *Legionella pneumophila* serotype 1. These results were the first indication that the hospital water supply was contaminated with *Legionella*. Once these results were available, hospital administration decided to replace all spa-type showers with shower heads that prevent pooling of water behind the faucet. The only exception was some spa-type showers kept in the labor and delivery unit to facilitate bathing of an extremely low risk patient group.

The second set of environmental tests collected by the hospital's privately contracted environmental testing company was negative for *Legionella*.

In contrast, 25 of 56 (45%) hospital plumbing sites tested by the PHL were positive for *Legionella pneumophila* serotype 1, including one ice sample. Based on these results, the hospital water supply was super-heated by increasing the water temperature to ≥140º F and flushing the distal faucets for 15 minutes. Patients and staff were notified to prevent scalding and staff were posted at sites while the flushing was being done. One staff member suffered a mild burn injury during this procedure.

Ice machines were disassembled and disinfected and were not to be re-installed until the water supply was determined to be safe.

Follow-up environmental testing was performed by a different outside laboratory contracted by the hospital and the results of this testing showed all sites (15 of 15, 100%) positive for *Legionella* species (Table 1).

Table 1: Laboratory Final Report Following Super-Heating, 06/24/02

Sample	CFU*	Legionella Species/Serogroup
1	20	*L. pneumophila* serogroup 1, *L. bozemanii*
2	1	*L. pneumophila* serogroup 1
3	5	*L. pneumophila* serogroup 1, *L. bozemanii*
4	1	*L. pneumophila* serogroup 1
5	<1	*L. pneumophila* serogroup 1, *L. bozemanii*
6	<1	*L. pneumophila* serogroup 1
7	10	*L. pneumophila* serogroup 1
8	1	*L. pneumophila* serogroup 1
9	20	*L. pneumophila* serogroup 1
10	2	*L. pneumophila* serogroup 1
11	2	*L. pneumophila* serogroup 1, *L. bozemanii*
12	2	*L. pneumophila* serogroup 1
13	<1	*L. pneumophila* serogroup 1
14	10	*L. pneumophila* serogroup 1, *L. bozemanii*
15	60	*L. pneumophila* serogroup 1

* Colony forming units of *Legionella* per milliliter sample.

DWP indicated that the area in which the hospital is located is in a part of the city that does not draw any water from a monochloraminated source. DWP collected samples on June 10, from a site near the hospital input. Results of DWP testing of municipal water are summarized in Table 2.

Table 2: DWP Laboratory Results of Municipal Water

Analysis	Result
Temperature	22º C (71.6º F)
pH	7.17
Chlorine, free	1.22 mg/L
Chlorine, total	1.52 mg/L
Coliform, total	<1 NUM/100 ml
E. coli	<1 NUM/100 ml
Legionella pneumophila culture	0 CFU/ml

The hospital then discussed further decontamination procedures with its environmental hygiene consultant and based on his recommendations (consistent with CDC guidelines), decided to super-chlorinate the water supply (July 9–July 10). The second set of follow-up testing, collected on July 15, showed 7 of 12 (58%) sites positive for *Legionella pneumophila* serogroup 1 or *L. bozemanii* (Table 3).

Table 3: Laboratory Final Results Following Hyper-Chlorination,

Sample	Concentration*	Legionella Species/Serogroup
1	<1	*L. pneumophila* serogroup 1
2	1	*L. pneumophila* serogroup 1, *L. bozemanii*
3	1	*L. pneumophila* serogroup 1, *L. bozemanii*
4	Not detected	
5	Not detected	
6	Not detected	
7	Not detected	
8	Not detected	
9	<1	*L. bozemanii*
10	<1	*L. bozemanii*
11	<1	*L. pneumophila* serogroup 1, *L. bozemanii*
12	<1	*L. bozemanii*

* Colony forming units of *Legionella* per milliliter sample.

Water temperature at 20 distal hot water sites (measured on May 30) showed a mean of 101.5º F (range 91.4–118.2º F). Because several temperature readings were lower than the recommended 105–120º F, overall hospital hot water temperature was increased and a daily temperature log was to be kept. Subsequent temperature ranges taken at 34 sites showed a mean of 113º F (range 105–120º F). Additionally, booster pumps were increased to re-circulate the hot water through the system faster.

Water pH levels at 22 distal sites ranged from 7.3–8.0. Free chlorine levels were recorded at 9 distal sites. Hot water free chlorinelevels were all 0.0–0.2 ppm; 4 cold water levels were 0.0–0.2 ppm, 2 were 1.2 ppm, 1 was 1.3 ppm, and 2 were 1.5 ppm. The 0.0– 0.2 ppm cold water levels were all found in the basement or power plant, closer to the city water supply than patient rooms, where other levels were measured.

A review of the 5th floor oncology ward for 5 days in May and June 2002, showed that the majority of patients admitted to the ward are general medicine patients and no patients were noted to be on high-dose chemotherapy, which would confer the greatest risk for developing legionellosis.

A thorough look at the pre-operative, intra-operative, and post-operative procedures indicated no commonalities between those patients who had different procedures.

All respiratory therapy (including ventilators) utilizes sterile water, as well as self-humidifying systems when possible. No breaches in this system were identified.

On August 1, water samples from 10 sites throughout the hospital were tested again; all samples were negative for *Legionella*.

Retrospective Case Findings: The retrospective examination conducted by the hospital ICP revealed that between October 07, 2001 to March 18, 2002, 9 patients had been tested for Legionella infection. All were negative.

Case-Control Findings: Between January and July 2002, the hospital reported 13 LD cases. Of these, 4 cases were determined to be community-acquired cases, 6 were probable cases, and 3 definite cases. The case-control study considered all nine probable and definite LD cases. All case-patients were admit-

ted to the hospital with a cardiac diagnosis. All case-patients had fever and roentgenographic changes and were diagnosed with legionella urinary antigen testing. *Legionella*species were not recovered by culture from any case-patient isolates.

The mean length of stay of case-patients was 29 days (range 6–69 days), as compared to the controls, who stayed a mean of 6 days (range 1–35) (p = 0.0003). 8/9 case-patients spent time on the 4th floor prior to becoming ill; 7 were housed in distal rooms. Case-patients spent a mean of 3.9 days (range 0–9 days) in distal rooms and controls spent a mean of 1.4 days (range 0–8 days) in distal rooms (p = 0.02). It is common practice on the 4th floor to place (and move) patients to the rooms closest to the nurses' station (i.e., proximal rooms). The mean days that a distal room was open before a patient was placed there was 4.1 days for case-patients and 0.67 days for controls (p = 0.004).

The mean age of case-patients was 69 years (range 53–81 years), compared with the mean age of controls, 71 years (range 54–87 years, p = 0.61); 78% (7/9) of case-patients and 48% (13/27) of controls were male (p = 0.12). While hospitalized, 89% (8/9) of case-patients had at least one cardiac procedure (2 had two procedures), defined as coronary artery bypass graft, pacemaker placement, automatic internal cardiac defibrillator, or cardiac catheterization. Case-patients were more likely than controls to have a cardiac procedure (OR = 5.3, CI = 1.1–433, p = 0.02).

The American Society of Anesthesiologists (ASA) Physical Status Classification System provides a rating based on a patient's pre-operative underlying health status as a range where 1 is less ill and 5 is very ill. The ASA rating was available for 7/9 case-patients, but only 2/27 controls. The mean ASA for case-patients was 4 and for controls it was 3, with no significant difference between the two (p = 0.23). Left ventricular ejection fraction (LVEF) on admission was available for 9/9 case-patients and for 15/27 controls. The mean LVEF of cases was 33% and 49% for controls (p = 0.017).

Table 4 summarizes the evaluation of co-morbid diseases for significance as a risk factor for developing legionellosis. The co-morbid diseases that were statistically significant include congestive heart failure (CHF), diabetes mellitus (DM), chronic renal insufficiency (CRI), and acute renal failure during hospitalization (ARF). Other co-morbid conditions not found to be significant included chronic obstructive pulmonary disease (COPD), chronic renal failure (CRF), hemodialysis, HIV/AIDS, and malignancy.

Table 4: Co-morbid Diseases

Disease	Cases (n = 9)	Controls (n = 27)	OR	CI
COPD	3/9 (33%)	4/27 (15%)	3	0.5–17
DM	5/9 (56%)	4/27 (15%)	7	1.3–39
CHF	6/9 (67%)	5/27 (19%)	9	1.6–48
CRI	3/9 (33%)	1/27 (4%)	13	1.1–148
ARF	3/7 (43%)*	1/26 (4%)*	19	1.5 –228
CRF	1/9 (11%)	0/27 (0%)	Undefined**	
Hemodialysis	2/9 (22%)	1/27 (4%)	7	0.6–94
HIV/AIDS	0/2 (0%)*	1/3 (33%)*	Undefined**	
Malignancy	1/7 (14%)*	2/26 (8%)*	2	0.15–26

* missing data
** because of lack of data (p=>0.25)

When all co-morbid diseases were combined, case-patients were more likely than controls to have at least one co-morbid condition (OR undefined; p = 0.002), though this significance was lost once matched analysis was done (OR = 1.5, CI = 0.21–18, p = 0.67). Additionally, when controlling for each disease, CHF and DM remained significant, but CRI did not.

Other risk factors evaluated (Table 5) included ever having smoked tobacco and alcoholism. Alcoholism did not confer a significant risk; however, case-patients were 3.5 times more likely to have ever having smoked tobacco than controls (CI = 0.69–23, p = 0.07). Table 6 includes data collected on pre-operative Hibiclenz showers, days spent "nothing by mouth" (NPO), days with oxygen supplementation (O2), and number of nebulizer treatments (Nebs) also did not contribute significant risk. Mean days with a nasogastric tube (NGT) was significant (p = 0.0004), however only 5/9 case-patients and 1/27 controls had an NGT for any time.

Table 5: Risk Factors, Tests of Significance

Risk Factor	Case (Any Exposure)	Control (Any Exposure)	OR	CI	P value
Alcoholism	0/9	0/24	Undefined	n/a	0.41
Ever Smoke	6/9	6/23	3.5	0.69–4.4	0.07

Table 6: Risk Factors, Mean Days Exposed

Risk Factor	Case Any Exposure	Mean	Control Any Exposure	Mean	P value
Pre-op Shower	3/9	0.7	3/25	0.2	0.13
NPO	7/9	2.2	17/25	0.7	0.06
O2	6/9	5.6	14/27	1.9	1.07
Nebs	3/9	2.6	6/27	1.4	0.42
NGT	5/9	3.7	1/27	0.3	<0.05

Use of chemotherapy in the month prior to admission did not prove to be a risk factor, nor did corticosteroid use in the month prior to admission. However, a large intravenous corticosteroid dose during CABG and cardiac catheterization is standard procedure and six case-patients received corticosteroids in this manner; the OR for corticosteroid use after admission was 7 (CI = 1.3–37, p = 0.02). The mean number of days between steroid dose and disease onset for case-patients was 6 days (range 2–9 days).

Long Term Decontamination Solutions: In conjunction with the hospital's environmental hygienist, efforts continued to maintain the levels of *Legionella* in the hospital's water supply at "not detected". Environmental surveillance will continue per the CDC protocol. Currently, supplemental chlorine is being added to the plumbing system to maintain the free chlorine levels at the distal sites at 0.3–0.5 mg/L. The equipment to supplement the system was purchased and put into place in order to conduct the hyper-chlorination effort. A regulator which keeps the chlorine levels from rising too high, which can be detrimental to the plumbing system, was installed. Additional efforts (e.g., another hyper-chlorination flush) will be conducted as needed. DWP will complete plans to add monochloramine to the water supplying the hospital area. At that time the hospital will reconsider their plans.

Once *Legionella* was no longer detected in the water samples, potable water restrictions were removed. Clinical surveillance remained in place at a high level of intensity until the hospital Infection Control Committee determined it was appropriate to be less aggressive.

Communication Efforts: In addition to many informal meetings, formal presentations by ACDC staff were an important part of maintaining good communication with the hospital. On June 7 and June 27, hospital grand rounds were given by ACDC staff. Meetings with hospital public relations staff occurred with ACDC staff and with the LAC media offices. Additionally, ACDC staff met with the hospital Infection Control Committee, the Medical Executive Committee, and the Hospital Board of Directors.

On July 2, news of this outbreak was picked up by the local media. Subsequently, the hospital began providing a letter about Legionnaires' disease to all patients and guests entering the hospital. The hospital

was then directed by ACDC to inform both current and past patients of the potential risk for contracting Legionnaires' disease at the hospital. Once potable water levels of *Legionella* were negative, these letters were determined to no longer be necessary.

DISCUSSION

In summary, we determined that 9 patients who spent time at the same hospital prior to respiratory illness became ill with pneumonia-like symptoms and had positive urinary antigen tests for *Legionella. Legionella* species were detected throughout the hospital water supply. Decontamination of the hospital water supply was undertaken with the assistance of a privately contracted environmental hygienist. No patient isolates existed to confirm the link between water cultures and clinical cases. No specific exposure was identified and no clear risk-factors were identified secondary to small numbers compromising statistical analysis.

The delay in identification of *Legionella* in the hospital water supply allowed for a false sense of security after the initial cases were identified. The determination of nosocomial legionellosis is complicated and many factors were considered when deciding to initiate the outbreak investigation. However, the strength of this outbreak investigation was that once *Legionella* was identified in the water system, despite the inability to link the species to patient disease, the public health message was clear: decontaminate the water system and reduce risk to patients while this was being done. Once this was determined, the hospital moved quickly to respond with patient prevention and decontamination efforts.

Active clinical surveillance of nosocomial pneumonias for legionellosis was conducted in a thorough manner by the hospital laboratory, who took the initiative to train staff and obtain materials to perform on-site urine antigen testing for *Legionella* in order to improve turn-around time for test results.

No patients admitted after potable water restrictions were in place became ill with nosocomial legionellosis.

The difficulty in eliminating *Legionella* from a plumbing system was evident in the positive results found after super-heating. However, because the PHL only reports "detected/not detected" we were unable to determine if the follow-up testing perhaps represented a decline in *Legionella* levels found in the water supply. The goal of the second private environmental laboratory contracted by the hospital was to detect any *Legionella* in the environmental samples, rather than in the clinical samples at a later date (i.e., prevent disease); therefore, its laboratory is considered one of the most sensitive in the country. The usefulness of tracking levels of CFU in a water system is for determining if levels have decreased and perhaps identify areas which need more stringent decontamination.

The hot water temperature within the hospital was found to be lower than recommended and this problem was corrected. The pH levels detected in the hospital were with in the appropriate range. City chlorine levels appeared to be normal, but once water entered into the hospital, there were varying levels of free chlorine. DWP could not explain this and the hospital water is now being supplemented within the hospital system and levels are more than adequate to treat the water supply.

The identification of *Legionella bozemanii* in numerous water samples indicates that contamination persisted, however since all of the case-patients were diagnosed by urinary antigen testing, which does not detect *L. bozemanii*, it was unlikely to have been a source of disease.

The practice of keeping patients closer to the nursing station (i.e., out of distal rooms) may create "dead leg" space in the plumbing system, allowing *Legionella* to propagate. However, there is no evidence that the risk or quantity of bacteria was any greater on the 4th floor than anywhere else in the hospital. The hospital developed a protocol for flushing the pipes in end rooms when not used for a period of time.

The case-control study showed that case-patients were more ill than controls, based on having poorheart function, co-morbid conditions, and the length of stay. However, with so little data, more sophisticated analyses could not be performed.

Cardiac disease is not a common risk factor for contracting Legionnaires' disease. However, individuals with cardiac disease often have known risk factors such as a history of tobacco use, COPD, and DM. In this outbreak, it appears that the cardiac patients were actually the sickest (and thereby the most immunocompromised) patients at the hospital. The hospital reported high turnover for cardiac patients and is a referral hospital, seeing the sickest patients who could not be managed at a smaller hospital.

Limitations: The primary limitation of this study is the unavailability of patient isolates to compare to environmental cultures. Also, chart abstraction about important potential risk factors such as showering, tap water consumption, and use of ice, was difficult because such factors are not routinely documented in the chart. Case-patients were queried when possible.

Without laboratory isolates of Legionella species cultured from patients, it is impossible to definitively implicate the hospital water supply in case-patient illness. This issue was further complicated by the difficulty in clinical diagnosis of legionellosis. Because the urinary antigen test for *Legionella* can be positive for a long time following exposure, patients may have been exposed prior to entering the hospital. For example, the attending physicians of one case-patient determined by bronchoscopy that the patient did not have pneumonia; however this case-patient was included in the case-control study because the case-definition was met.

Finally, the small number of cases limits our ability to conduct advanced statistical analysis.