

A Large Community Outbreak of Legionnaires' Disease Associated With a Cooling Tower in New York City, 2015

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Abstract

Objectives: Infections caused by *Legionella* are the leading cause of waterborne disease outbreaks in the United States. We investigated a large outbreak of Legionnaires' disease in New York City in summer 2015 to characterize patients, risk factors for mortality, and environmental exposures.

Methods: We defined cases as patients with pneumonia and laboratory evidence of *Legionella* infection from July 2 through August 3, 2015, and with a history of residing in or visiting 1 of several South Bronx neighborhoods of New York City. We describe the epidemiologic, environmental, and laboratory investigation that identified the source of the outbreak.

Results: We identified 138 patients with outbreak-related Legionnaires' disease, 16 of whom died. The median age of patients was 55. A total of 107 patients had a chronic health condition, including 43 with diabetes, 40 with alcoholism, and 24 with HIV infection. We tested 55 cooling towers for *Legionella*, and 2 had a strain indistinguishable by pulsed-field gel electrophoresis from 26 patient isolates. Whole-genome sequencing and epidemiologic evidence implicated 1 cooling tower as the source of the outbreak.

Conclusions: A large outbreak of Legionnaires' disease caused by a cooling tower occurred in a medically vulnerable community. The outbreak prompted enactment of a new city law on the operation and maintenance of cooling towers. Ongoing surveillance and evaluation of cooling tower process controls will determine if the new law reduces the incidence of Legionnaires' disease in New York City.

Keywords

Legionnaires' disease, outbreak, cooling tower

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Legionnaires' disease is a pneumonia caused by the genus *Legionella* that occurs predominantly in people who are older, have impaired immunity, have a history of tobacco use, or have abnormal pulmonary function.¹ The incubation period is 2 to 10 days, and initial symptoms are nonspecific, including fever, chills, myalgia, and headache. The age-adjusted incidence of Legionnaires' disease increased 286% in the United States (from 0.4 per 100 000 population in 2000 to 1.6 in 2014) and 316% in New York City (from 0.6 per 100 000 population in 2000 to 2.5 in 2014).^{2,3} Many factors likely contributed to the increase. The aging population and people with chronic illness who live longer have created a larger population that is susceptible to the disease. Electronic laboratory reporting was phased in during the 2002-2009 period and may have contributed to increased reporting. Whether the number of environmental *Legionella* sources has increased or conditions favoring transmission have changed is not known.

Legionella are environmental bacteria that live in fresh and brackish water ecosystems but also can inhabit human-made water systems, such as hot water plumbing, showerheads, faucets, hot tubs, and cooling towers. Infection of humans occurs through inhalation of contaminated aerosols and, less frequently, aspiration of contaminated water.⁴ Person-to-person transmission was not suspected or documented until a single case report appeared in 2016.⁵ Legionnaires' disease is most often diagnosed in the United States by urine antigen test; physicians infrequently order culture, which is important for linking human disease to an environmental source.⁶ Connecting people with Legionnaires' disease to environmental sources is further complicated by the number of potential reservoirs and the need for special processing and media for culture. In addition, growth on culture plates may be difficult to detect because of competition from other environmental organisms.

In July 2015, the New York City Department of Health and Mental Hygiene (DOHMH) detected an increase in cases of Legionnaires' disease in the South Bronx. The purpose of our investigation was to describe patient demographic characteristics, comorbidities, and environmental exposures, and implement control measures.

Methods

Investigation

Physicians and clinical laboratories are required to report positive *Legionella* test results to DOHMH. For each investigation, epidemiologists review patient medical records, interview the patient (or the patient's proxy) to determine if the report meets the Council of State and Territorial Epidemiologists/Centers for Disease Control and Prevention national case definition for legionellosis,⁷ and identify risk factors and potential exposures.

Two methods are used to identify clusters that could be community outbreaks of reportable diseases. Each week, the

historical limits method compares case volume in the most recent 4-week period with comparable data from the previous 5 years at the city, borough, and neighborhood levels.⁸ A daily spatiotemporal cluster detection method is based on the space-time permutation scan statistic^{9,10} and computes a "recurrence interval," which is the number of days of surveillance required for the expected number of clusters at least as unusual as the observed cluster to be equal to 1 by chance. Additionally, an automated daily algorithm compares the building identification number (ie, a unique code for every structure in New York City) assigned to the patient's address with a list of health care and congregate living facilities to identify concerning events not already detected by epidemiologists.¹¹ We used a multifocused cluster test with the space-time permutation scan statistic to assess clustering of cases of Legionnaires' disease around cooling towers to guide environmental sampling.¹² After the outbreak was detected, DOHMH monitored emergency department visits for pneumonia using a syndrome derived from *International Classification of Diseases* codes and chief complaint keywords.¹³

We defined an outbreak-associated case of Legionnaires' disease as a patient meeting the national case definition for Legionnaires' disease, modified to include *Legionella pneumophila* serogroup 1 (*Lp1*) DNA detected by real-time polymerase chain reaction (PCR) in postmortem specimens, in either a resident of 1 of 7 South Bronx ZIP codes (ie, the outbreak zone) or in a person who worked in or visited the outbreak zone during the 10 days before his or her onset date (or collection date of the earliest confirmatory test if onset date was unknown) between July 2 and August 3, 2015. We used *Legionella* subtyping, as described hereinafter, to refine the case definition. We defined deaths from Legionnaires' disease as (1) patients meeting the case definition whose death was attributed to Legionnaires' disease within 30 days of the diagnosis date or (2) patients meeting the outbreak definition in which the Office of the Chief Medical Examiner listed *Legionella* pneumonia as the immediate cause of death.

To enhance case finding and encourage prompt medical evaluation, DOHMH issued a press release on July 29, 2015, and conducted media interviews. We sent electronic messages about the outbreak, symptoms of Legionnaires' disease, appropriate antimicrobial treatment, and the importance of culturing respiratory specimens specifically for *Legionella* to physicians and other health care providers in New York City on July 29 and updated information on August 2.^{14,15} DOHMH requested the Office of the Chief Medical Examiner to obtain tissue specimens from deceased patients with known Legionnaires' disease without respiratory cultures and from unattended patients whose deaths were potentially caused by Legionnaires' disease.

We summarized patient demographic and clinical characteristics. We calculated adjusted odds ratios (aORs) and 95% confidence intervals (CIs) using multivariable logistic regression and the mid-*P* exact method to assess the relationship between fatality and comorbidities, smoking status, and

number of days from onset to diagnosis.¹⁶ Odds ratios were adjusted for age and sex. We evaluated 2 possible interaction terms: (1) diabetes and alcoholism and (2) smoking and chronic obstructive pulmonary disease (COPD). We performed statistical analyses using SAS version 9.4.¹⁷ We conducted this investigation as part of public health practice. As such, institutional review board review was waived.

Environmental Source Identification

We prioritized cooling tower sampling in the outbreak zone per the location of patients with Legionnaires' disease and the multifocused cluster test. Although the city had no complete official registry of cooling towers at the time, we identified cooling towers in the area by examining city records of water credit and construction permit applications, in addition to publicly available satellite imagery. When sampling cooling towers, we collected 500-mL aliquots of water in sterile containers treated with sodium thiosulfate (0.5 mL of a 0.1N solution) to neutralize the chlorine in the sample. We sampled from locations in the cooling tower that were thought to be most representative of the water vapor generated. If the cooling tower basin was safe to access, we collected a swab of biofilm. An order to immediately remediate was issued to owners of cooling towers that tested positive for *Legionella* by real-time PCR. An order to decontaminate all cooling towers within 14 days was issued to all New York City building owners on August 6, 2015.

Laboratory

The New York State Department of Health Wadsworth Center and the New York City Public Health Laboratory processed and tested water samples for the presence of *Legionella*. The Wadsworth Center used a previously described real-time PCR that was updated and expanded to include an *Lp1* target.^{18,19} Use of PCR allowed for the rapid screening of samples to prioritize culture and cooling tower remediation. The assay detects and differentiates *Legionella* species, *L pneumophila*, and *Lp1* DNA and uses an internal control to assess for inhibitory substances in the sample. Samples in which *L pneumophila* DNA was detected were processed and cultured at the Public Health Laboratory with standard microbiological methods. Isolates were identified as *Lp1* through direct fluorescent antibody staining (M-Tech, Milton, Georgia) and subsequently subtyped via standard methods of pulsed-field gel electrophoresis (PFGE) based on *Streptomyces fimbriatus* (*Sfi* I) restriction enzyme and whole-genome sequencing single-nucleotide polymorphism analysis.²⁰ Clinical isolates were sent to the Public Health Laboratory and Wadsworth Center by hospital laboratories and were confirmed and serogrouped by direct fluorescent antibody staining or real-time PCR; all *Lp1* isolates were subtyped with PFGE and whole-genome sequencing. PFGE subtyping was performed at the Public Health Laboratory and Wadsworth Center with identical methods.

Results

Investigation

DOHMH was initially alerted on July 17, 2015, when the daily spatiotemporal cluster detection analysis identified 8 reports of Legionnaires' disease centered in the South Bronx with a radius of 1.6 miles (recurrence interval = 1.4 years). Of the 8 reports, 2 were from a single South Bronx census tract. The next week, a Bronx hospital called to report an increase in cases of Legionnaires' disease among emergency department visits and admissions. On July 27, the historical limits method signaled for 2 South Bronx neighborhoods comprising 7 ZIP codes. The number of cases in each neighborhood exceeded the historical mean by 7.6 and 24.5 standard deviations.

Patient Characteristics

In total, 138 patients met the outbreak case definition of Legionnaires' disease, and 128 (93%) were hospitalized. Illness onset peaked on July 26, and the last patient linked to the outbreak became ill on August 3, 2015 (Figure 1). Sixteen (12%) patients died, including 5 who died in their homes. Emergency department pneumonia syndrome visits in the outbreak zone peaked in late July and returned to near baseline in early August (Figure 2).

The median age of patients was 55 (range, 29-90), and 86 (62%) patients were men. Seventy-eight (57%) patients were non-Hispanic black, 4 (3%) non-Hispanic white, 54 (39%) Hispanic, and 2 (1%) of unknown race/ethnicity (Table). The most commonly reported symptoms were fever (117 of 132, 89%), cough (97 of 130, 75%), and shortness of breath (70 of 130, 54%). A total of 107 (78%) patients had ≥ 1 chronic health condition—defined as alcoholism, asthma, cancer, COPD, diabetes, human immunodeficiency virus (HIV) infection, immunosuppressive therapy (chemotherapy, radiation, steroids), organ transplants, and renal disease requiring dialysis. Diabetes was present in 43 (31%), alcoholism in 40 (29%), HIV infection in 24 (17%), and COPD in 14 (10%) patients. Of 138 patients, 46 (33%) had >1 chronic health condition, and 20 (14%) had >2 chronic health conditions. Seventy-five percent of patients (98 of 130) reported a history of smoking cigarettes, and 57% (78 of 136) were current smokers. Of the 11 patients without a chronic health condition, 6 were either current smokers or former smokers. Of the 24 HIV-infected patients, 20 (83%) had a CD4 count ≥ 200 cells per mm³, and 15 (63%) had a suppressed viral load (<200 copies per mL).

The multivariable logistic regression model exploring factors associated with death during the outbreak, adjusted for age and sex, included alcoholism (aOR = 3.9; 95% CI, 1.2-13.4), diabetes (aOR = 3.2; 95% CI, 0.9-11.7), and COPD (aOR = 4.0; 95% CI, 0.8-17.9). The associations of current or ever smoking and death were not significant in bivariate analyses. Diabetes was not an effect modifier of the association between alcoholism and death.

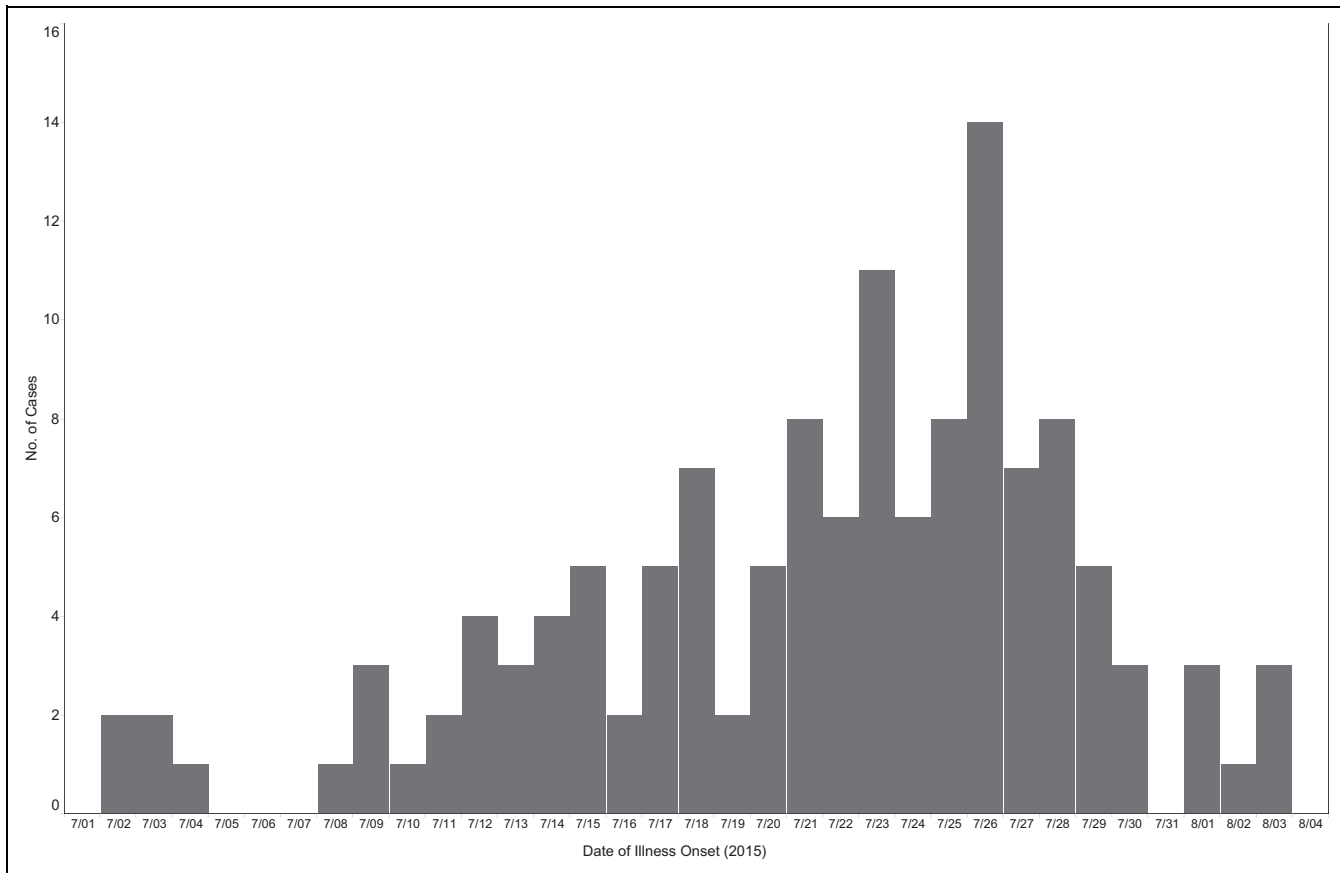


Figure 1. Outbreak of Legionnaires' disease, by date, South Bronx, New York City, July 2 to August 3, 2015 (n = 132). The date of illness onset was obtained from patient interviews and was missing for 6 patients who were unable or refused to be interviewed.

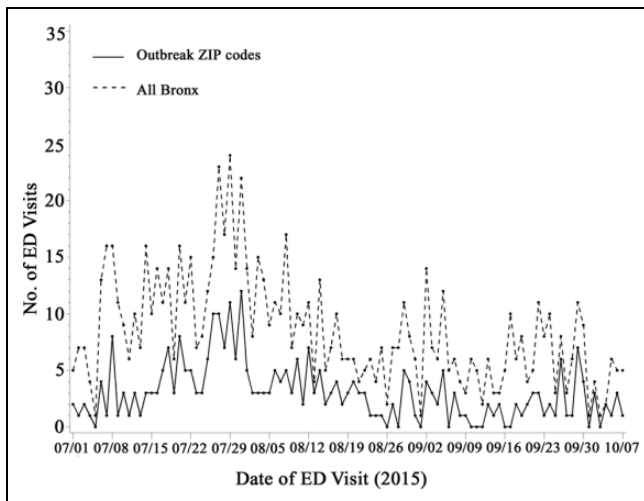


Figure 2. Emergency department (ED) visits for pneumonia syndrome in the Bronx and Legionnaires' disease outbreak zone, New York City, July 1 to October 7, 2015. Keywords included pneumonia, *Legionella*, Legionnaires' disease; *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes 480-486.

Of 128 hospitalized patients, the median length of stay was 5 days (range, 1-48). Of the 132 patients with complete data, the median time from symptom onset to diagnosis was

5 days (range, 0-21). For the 117 patients with illness onset before the public notification on July 29, the median time from onset to diagnosis was 5 days; for the 15 patients with illness onset on or after the public notification, the median time was 1 day. Twenty-six patients (19%) were confirmed by culture as *Lp1*. All outbreak-associated culture-positive patients had an indistinguishable PFGE pattern (designated O-1). Twenty-six patient isolates were indistinguishable by whole-genome sequencing. One patient, initially considered as part of the outbreak, had a whole-genome sequence with 3 single-nucleotide polymorphisms and was excluded. One patient who had onset during the outbreak, PFGE pattern O-1, and an indistinguishable whole-genome sequence initially denied being in the outbreak zone. Upon reinterview, the patient was determined to have been exposed and was included as outbreak associated.

Patient Exposures

A total of 108 patients (78%) resided in the outbreak zone. Of the remaining 30 patients, 16 resided in other Bronx ZIP codes, 9 in other New York City counties, 2 in other New York State counties, and 3 in other states. Patient interviews did not reveal an association with a single building or other common source of *Legionella* exposure; however, 37 of 121 patients recalled

Table. Characteristics of patients with outbreak-related *Legionella pneumophila* serogroup 1, Bronx, New York City, 2015

Characteristic	No. (%) or No. (Range)
Median age, y	55 (29-90)
Age group, y	
25-44	25 (18)
45-64	85 (61)
65-74	21 (15)
≥75	8 (6)
Male	86 (62)
Race/ethnicity	
Non-Hispanic black	78 (57)
Non-Hispanic white	4 (3)
Hispanic (all races)	54 (39)
Unknown race/ethnicity	2 (1)
Presenting symptoms	
Fever	117 of 132 (89)
Cough	97 of 130 (75)
Shortness of breath	70 of 130 (54)
Chills	62 of 129 (48)
Diarrhea	52 of 132 (39)
Myalgia	44 of 123 (36)
Headache	43 of 128 (34)
Change in mental status	20 of 126 (16)
Residence	
County of the Bronx, outbreak zone	108 (78)
County of the Bronx, non-outbreak zone	16 (12)
Other New York City counties	9 (7)
Other New York State counties	2 (1)
Non-New York State residents	3 (2)
Hospitalized	128 of 138 (93)
Median length of hospital stay, New York City residents, d	5 (1-48)
Median time from onset to diagnosis, d	
All patients with known onset (n = 132)	5 (0-21)
Before public announcement on July 29, 2015 (n = 118)	5 (0-21)
On or after public announcement on July 29, 2015 (n = 14)	1 (0-7)
Comorbidity	
Any chronic health condition (excludes other category)	107 (78)
Alcoholism	40 (29)
Asthma	29 (21)
Cancer	12 (9)
COPD (includes chronic bronchitis and emphysema)	14 (10)
Diabetes mellitus (type I and II)	43 (31)
HIV infection	24 (17)
Immunosuppressive therapy (chemotherapy, radiation, steroids)	15 (11)
Organ transplant	2 (1)
Renal disease requiring dialysis	4 (3)
Other chronic health conditions reported (excluding listed categories) ^a	20 (14)
Smoking, current	78 of 136 (57)
Smoking, current or past	98 of 130 (75)
Died	16 (12)

Abbreviations: COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.

^aCardiovascular disease (n = 11), complement deficiency (n = 1), epilepsy (n = 1), hepatitis C (n = 3), psychiatric disorder (n = 2), obesity (n = 3), and substance abuse (n = 8). Note that some patients had multiple conditions.

visiting a 3-block area of the main thoroughfare that included building A in the 10 days before illness onset. The next-most frequent location, recalled by 19 patients, was a subway hub 0.6 miles west of building A.

Several events helped focus the investigation on 1 potential cooling tower source. On July 28, DOHMH received a

physician inquiry about a cluster of respiratory illnesses among residents of a supportive housing residence for people with medical needs, including HIV infection, and the building identification number analysis identified 2 reports of Legionnaires' disease from this building. On July 29, the Centers for Disease Control and Prevention notified

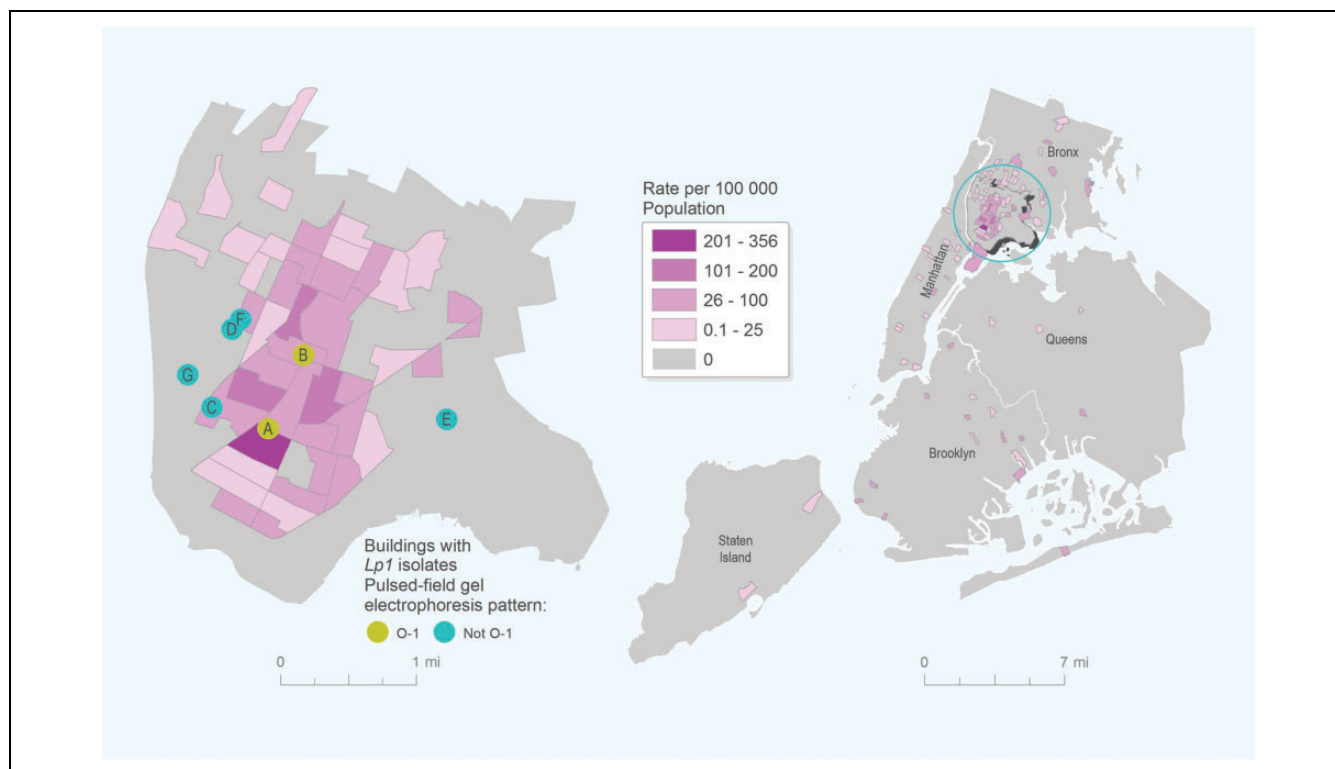


Figure 3. Crude attack rates of Legionnaires' disease by census tract and cooling towers testing positive for *Legionella pneumophila* serogroup 1 (*Lp1*), Bronx, New York City, July 2 to August 3, 2015. Circles indicate buildings with cooling towers in which *Lp1* was isolated. All buildings have 1 cooling tower except for building F, which has 2 cooling towers. DNA subtyping performed through pulsed-field gel electrophoresis: olive circles indicate buildings with cooling towers having the O-1 strain, which was indistinguishable from 26 patient isolates; white circles indicate buildings with cooling towers that had non-O-1 strains (ie, not related to patient isolates). Abbreviation: PFGE, pulsed-field gel electrophoresis.

DOHMH about a traveler who had been diagnosed with Legionnaires' disease and had spent part of the incubation period at a hotel in the South Bronx (building A). Building A was located less than a block away from the supportive housing residence, and the cooling tower, which was not previously known to city agencies, was detected through satellite imagery. The multifocused cluster test identified 3 cooling towers in South Bronx, including the one at building A, as having unusual case clustering of Legionnaires' disease around them with recurrence intervals >1 million years, including 1.36 million years for building A. By the end of the outbreak, Legionnaires' disease had been diagnosed in 2 guests of building A, 3 residents of the nearby supportive housing building, and 1 worker from a building across the street from building A. The attack rate of Legionnaires' disease for the census tract that included building A was 356 per 100 000 population, more than double the rate of the next-highest census tract (Figure 3).

Environmental Source Identification

The environmental investigation began on July 28, 2015. During the next 3 weeks, 55 cooling towers from 46 buildings in the outbreak zone were identified, inspected, and sampled. PCR results were available within 24 to 36 hours.

Lp1 DNA was detected by real-time PCR in water samples from 21 cooling towers and successfully cultured from 14 (Figure 3). Molecular subtyping of the 14 *Lp1* isolates revealed that water collected from the cooling tower at building A had PFGE pattern O-1, which was indistinguishable from the 26 clinical isolates (Figure 4). One other sample—from a cooling tower on the roof of building B, a homeless shelter—also had PFGE pattern O-1. This cooling tower was the eighth-most likely source identified by the multifocused cluster test, with a recurrence interval of 71 127 years. Compared with building A, the cluster signal around building B included fewer cases (33 vs 56) and fewer days of the outbreak (14 vs 26). The attack rate of Legionnaires' disease in the census tract containing building B was 58 per 100 000 population. The remaining 12 *Lp1* culture-positive cooling towers had non-O-1 PFGE patterns (Figure 4).

Whole-genome sequencing of the 14 *Lp1* cooling tower isolates revealed the Building A strain to be indistinguishable from the 26 outbreak-associated clinical isolates. Six additional cases of Legionnaires' disease diagnosed in 2015 had PFGE pattern O-1 and underwent whole-genome sequencing. All differed from the outbreak strain by 1 to 3 single-nucleotide polymorphisms. No *Lp1* culture obtained from any patient during the investigation matched to the strain from building B per whole-genome sequencing. Three

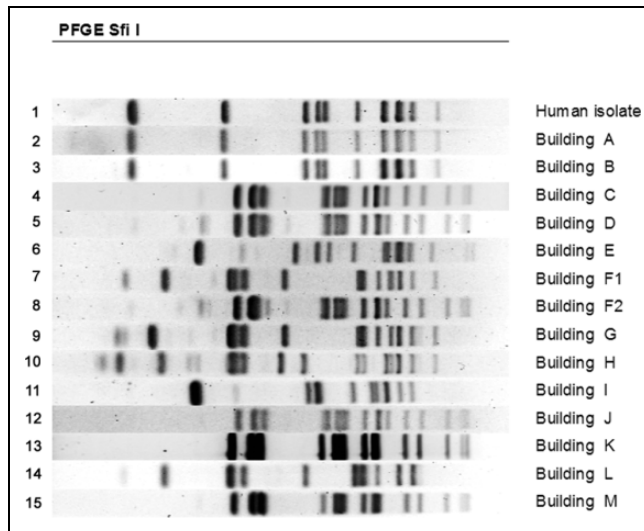


Figure 4. Molecular subtyping of outbreak-associated *Legionella pneumophila* serogroup 1 patients and environmental isolates, Bronx, New York City, 2015. Pulsed-field gel electrophoresis (PFGE) with restriction enzyme *Streptomyces fimbriatus* (Sfi I). Lane 1 is a representative human isolate, and lanes 2 to 15 are the 14 cooling tower isolates from the South Bronx outbreak zone.

isolates from separate environmental samples obtained from the cooling tower on building B had the same single-nucleotide polymorphism difference, thereby making a sequence misread error statistically unlikely.

Discussion

A large outbreak of Legionnaires' disease resulted in severe illness and death in a New York City neighborhood. Epidemiologic, environmental, and laboratory investigations implicated a hotel cooling tower as the likely source of the outbreak. We relied on innovative statistical methods that analyzed electronically reported clinical laboratory data to detect this outbreak. Although the outbreak was detected promptly by public health standards, the rapid decline in cases suggests that the implicated cooling tower may have stopped dispersing *Lp1*-containing aerosols before the order to decontaminate was issued. This phenomenon was observed in other outbreaks^{21,22} and likely due to the complex dynamics of *Legionella* ecology in human-made aquatic systems. Although delays in Legionnaires' disease outbreak recognition can be minimized through automated statistical algorithms applied to surveillance data, some delays will persist because of the long incubation period, lack of physician suspicion, unavailability of rapid tests for non-*Lp1*, and patients postponing seeking health care. Although patients sought health care more rapidly after our public notification, maintaining such awareness year-round among the general population would be difficult and unlikely to produce much benefit given the low incidence of Legionnaires' disease. The outbreak response was expedited with a real-time PCR-based assay to screen water samples collected from

cooling towers for the presence of *Lp1* DNA. Previous outbreak investigations relied on culture, which, if successful, can take several weeks to identify and subtype. Using real-time PCR allowed us to rapidly screen, prioritize, and focus control efforts on potential outbreak sources.

The prevalence of diabetes, HIV infection, and alcoholism among patients in the outbreak was higher than in other large community outbreaks of Legionnaires' disease.²³⁻²⁷ Per the American Community Survey, 41% of the estimated 360 000 residents in the outbreak zone had incomes below the federal poverty level.²⁸ Compared with residents in the rest of New York City, residents in the outbreak zone had a higher prevalence of self-reported diabetes (17% vs 11%) and asthma (20% vs 12%),²⁹ and the proportion living with HIV/AIDS was nearly double that of New York City (2.6% vs 1.4%).^{30,31} The population's medical vulnerability likely contributed to the magnitude of the outbreak. This outbreak highlights the need for broad health policies and targeted health services to alleviate conditions (eg, diabetes, tobacco use, substance use, HIV infection) that disproportionately burden impoverished neighborhoods.

Limitations

A major limitation of many outbreak investigations of Legionnaires' disease is the large proportion of patients diagnosed by culture-independent methods. Although the percentage of patients with positive *Legionella* cultures during the outbreak was high when compared with previous Legionnaires' disease investigations, we were unable to confirm that every epidemiologically associated case was caused by the outbreak strain and linked to the cooling tower on building A. One patient who met the outbreak case definition was later excluded, and one who was not initially considered part of the outbreak was reinterviewed and included according to whole-genome sequencing results. PFGE pattern O-1 was initially detected in a Bronx resident in 2007, and 11 clinical isolates from 2007 to 2013 with this PFGE pattern underwent whole-genome sequencing. However, none were an identical match to the current outbreak strain, differing by 2 to 4 single-nucleotide polymorphisms. The limited number of Bronx *Legionella* isolates that we examined during this investigation appeared to be highly conserved, and whole-genome sequencing proved to be a powerful and useful tool to discriminate among isolates where PFGE could not.

Based on historical surveillance data in New York City, we expected to see slightly more than 1 Legionnaires' disease case per day citywide during July; thus, some cases without culture could represent background incidence from other *Legionella* sources. It is also possible that additional outbreak-associated cases in nearby neighborhoods were not recognized as part of this outbreak, because we do not know how far contaminated aerosols may have drifted. Evidence supporting the cooling tower of building A, rather than that of building B, as the source of the outbreak included (1) the presence of disease in guests of building A and residents of

the neighboring housing facility, (2) the absence of people with Legionnaires' disease residing in building B, (3) no human isolate matched by whole-genome sequencing to the isolate from building B's cooling tower, (4) the results of the multifocused cluster test, and (5) the elevated rate of Legionnaires' disease in the census tract containing building A.

Conclusion

After the outbreak, New York City enacted legislation to require the registration, inspection, maintenance, and annual certification of cooling towers and other aerosol-producing engineering devices.³² The effectiveness of the new law will be evaluated through routine inspections of cooling towers to gauge if process controls reduce microbial growth and *Legionella* colonization and by monitoring for a decrease in incidence of Legionnaires' disease.

Authors' Note

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