



# Outbreaks of Legionnaires' Disease and Pontiac Fever 2006–2017

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## Abstract

**Purpose of Review** The global importance of Legionnaires' disease (LD) and Pontiac fever (PF) has grown in recent years. While sporadic cases of LD and PF do not always provide contextual information for evaluating causes and drivers of *Legionella* risks, analysis of outbreaks provides an opportunity to assess these factors.

**Recent Findings** A review was performed and provides a summary of LD and PF outbreaks between 2006 and 2017. Of the 136 outbreaks, 115 were LD outbreaks, 4 were PF outbreaks, and 17 were mixed outbreaks of LD and PF. Cooling towers were implicated or suspected in the a large portion of LD or PF outbreaks (30% total outbreaks, 50% confirmed outbreak-associated cases, and 60% outbreak-associated deaths) over this period of time, while building water systems and pools/spas were also important contributors.

**Summary** Potable water/building water system outbreaks seldom identify specific building water system or fixture deficiencies. The outbreak data summarized here provides information for prioritizing and targeting risk analysis and mitigation strategies.

**Keywords** Legionnaires' disease · Legionellosis · Pontiac fever · Outbreak · Cooling tower · Water · Buildings

## Introduction

Legionnaires' disease (LD) and the milder form of illness, Pontiac fever (PF), are respiratory illnesses caused by infection with the bacteria *Legionella spp.* Infection results when the bacteria are inhaled or aspirated. *L. pneumophila* is the most common cause of LD and PF [1]. Legionnaires' disease is a reportable illness in Europe, the USA, Canada, New Zealand, Japan, Singapore, and Australia [2]; however, specific source attributions or systematized, cross-regional data collection regarding water system deficiencies resulting in outbreaks is

sparse. Infections are typically of concern for the elderly and those with underlying health conditions [3].

Although there are over 50 species of *Legionella* [1] and a growing list of at least 16 serogroups of *L. pneumophila* [4], the majority of human infections are determined by the predominant urinary antigen testing to be caused by *L. pneumophila* serogroup 1 [2]. However, the dominance of serogroup 1 may be biased due to the fact that the urinary antigen test is designed to identify this serogroup [5••]. Therefore, the importance of infections with other serogroups may be underestimated. *L. pneumophila* serogroup 1 can be further distinguished based on subtypes, determined using monoclonal antibody (MAb) subtyping into monoclonal subgroups such as Allentown/France, Bellingham, Benidorm, Camperdown, Heysham, Knoxville, OLDA, Oxford, and Philadelphia [6, 7]. Additionally, sequence-based typing (SBT) using comparison with seven gene loci proposed by the European Society for Clinical Microbiology Study Group on *Legionella* Infections (ESGLI; formerly the European Working Group on *Legionella* Infections, EWGLI) can be used to determine how closely two isolates are related [5••, 8, 9].

Management of *Legionella* in water systems is complex as it occurs commonly in most aquatic environments and survives readily within biofilms [10]. However, its presence is not necessarily synonymous with risk, resulting in varied

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philosophies regarding monitoring [11, 12]. Some evidence from longitudinal studies has indicated that outbreaks are most likely to occur in health care settings when more than 30% of distal sites in the water system were colonized [13, 14].

Despite the existence of numerous guidance documents for preventing *Legionella* proliferation and mitigating risks in engineered water systems [15], the reported number of legionellosis cases (where legionellosis includes LD and PF and the estimate incorporates sporadic cases) has increased from 0.42 to 1.62 per 100,000 persons in the USA from 2000 to 2014 [16], and recent large outbreaks have drawn attention to the need for analysis of outbreak information for prioritizing resources [17]. Sources of outbreaks have included cooling towers [18], building water systems, decorative water features, and other common water uses [19] and often have resulted from deficiencies in water quality management, including operating conditions and maintenance [20, 21].

Eighty percent of LD cases are sporadic in nature [3], and while the source of sporadic LD and PF cases is seldom explored, outbreaks represent a valuable opportunity to analyze causes of adverse events when outbreak investigations are carried out [22]. As a result, we performed a systematic review of LD and PF outbreaks for studies published from 2006 through 2017. The goals of this review are to (1) summarize quantitative data for LD and PF outbreaks with  $\geq 5$  confirmed cases, (2) determine which sources contribute most significantly to the recent outbreak-associated LD and PF disease burden with the goal of prioritizing prevention resources towards the riskiest sources, (3) and identify information gaps for future study and risk mitigation strategy development.

## Methods

A literature review was conducted for outbreaks of LD and PF. The Web of Science and PubMed were searched using the keywords (legionella OR legionnaires OR legionellosis OR pontiac fever) AND outbreak AND (2006/01/01: 2017/12/31) for peer-reviewed and government documents. References were imported into an Endnote<sup>®</sup> library with duplicate removal. Studies that were multiple publications of a primary study were included where unique aspects of the outbreak were covered, and details from multiple reports were combined in a single table entry for each outbreak where applicable. Inclusion criteria included:

- Peer-reviewed or government documents published between January 1, 2006, and December 31, 2017. The outbreak(s) described by each published study was included if it occurred in the 10 years prior to the publication inclusion dates (between January 1, 1996, and December 31, 2017). This caveat is included as some government reports provide summaries of outbreaks occurring over a large

historical time period for which the original peer-reviewed papers describing the outbreak were published before the inclusion dates.

- For publications that reported multiple outbreaks, each outbreak was included as a separate data point. Data from summary reports were cross-checked with the peer-reviewed reports and combined where identified to represent the same outbreak.
- Outbreaks were defined as five or more diagnosed (confirmed) cases of LD or PF linked epidemiologically to the outbreak [18].
- Study described provides primary information about an outbreak investigation.
- Study is reported in English.

## Results and Discussion

**Literature Review Results** The literature review returned 485 records. One hundred sixteen records met the inclusion criteria and were the focus of the current review. These records covered 136 unique LD and/or PF outbreaks with 3642 total confirmed cases of LD, 725 cases of PF, and 251 total deaths (Table 1; Supplemental Table S1). Information for interpreting US Centers for Disease Control and Prevention (CDC) criteria for strength of evidence and deficiency attributions are described in Supplemental Tables S2 and S3, respectively.

### Legionnaires' Disease Surveillance and Outbreak Detection

Outbreak surveillance and case ascertainment differ by region [2], and variations in measured outbreaks may not necessarily indicate lesser occurrence in some areas. Although outbreaks were not reported from some regions, this is not likely to be due to an absence of *Legionella*, and diagnostic and analytical capabilities may vary globally. Additionally, there is currently no agreed-upon case definition of PF [2, 23–25], making it challenging to interpret PF cases specified as “confirmed” versus “probable”; for the purposes of the current work, these categories were combined. *Legionella* occurrence in water and wastewater is thought to be ubiquitous and is not limited to those countries with surveillance programs [26, 27].

Reporting for *Legionella* began in the USA in 2001. From 2001 to 2006, *Legionella* was identified as the causative agent of 38 of 833 US drinking water outbreaks from all source water types (389 cases), and from 1971 to 2006, it was identified as the cause of all reported drinking water-associated acute respiratory illness (ARI) [28]. In 2005–2006, ARI surpassed acute gastrointestinal illness (AGI) as the leading cause of waterborne illness from drinking water in the USA [29]. Major European LD outbreaks and clusters up to 2004 and 2005 are reported in Bartram et al. 30 and Joseph and Ricketts [31], respectively. From 1995 to 2005, 656 outbreaks

**Table 1** Summary of Legionnaires' disease and Pontiac fever outbreaks 2006–2017. "Potable water systems" refers to building water systems and components connected to building potable water supply unless otherwise noted as defined by US Centers for Disease Control and Prevention (CDC) definitions provided in McClung et al. [82]

Source	Total confirmed LD cases	Total suspected/probable LD cases	Total PF cases*	Deaths	Average case fatality rate (%) (range in outbreaks with $\geq 1$ fatality)
Potable water/building water systems	564	50	7	43	6.2 (7.7, 30)
Non-potable water systems, excluding cooling towers	94	31	139	9	8.1 (5.6, 33.3)
Pools or spas	319	283	433	16	3.6 (8.7, 14.3)
Cooling towers, air conditioning units, or evaporative condensers	2083	236	146	151	8.4 (1, 22)
Unknown sources	219	28	0	12	6.2 (3.5, 33.3)
Multiple sources	363	43	0	20	16.4 (1.4, 40)
Total	3642	671	725	251	7.2 (1, 40)

\*PF cases include cases identified as "confirmed" and "suspected" as there is no standardized case definition criteria for PF [2, 23–25]

(over 32,000 cases) of legionellosis from 35 European countries were reported to The European Working Group for Legionella Infections (EWGLI) [31]. These outbreaks were associated with nosocomial infection (100), community-acquired pneumonia (160), travel (390), and other causes (6), with the most frequently identified major sources reported as building water systems (207), cooling towers (57), and spa pools (33) [31]. From 2005 to 2006, 214 outbreaks were reported (11,980 cases) across 35 countries with a case fatality rate (CFR) of 6.6% [32].

**Outbreak Investigation** Outbreak detection is dependent on the clinical surveillance methods used. The most common methods for defining a clinical case of LD in the reported outbreaks were (1) epidemiologic (temporal, spatial) association with the outbreak source; (2) culture from clinical respiratory isolates; (3) positive urinary antigen; (4) clinical symptoms; (5) radiographically confirmed pneumonia; (6) serological evidence of infection via indirect fluorescent antibody (IFA) assay, enzyme-linked immunosorbent assay (ELISA), and/or a fourfold increase in antibody titer to *Legionella* (seroconversion). Polymerase chain reaction (PCR) was also used to confirm *Legionella* in clinical samples in some cases [33–41]. Matching of patient clinical samples and environmental samples from the source using serotyping and/or molecular subtyping was successfully obtained in 48 (35%) of outbreaks and performed but unsuccessful in 7 (4%) of outbreaks. Matching of clinical and environmental samples is established using sequence-based typing (SBT) and monoclonal antibody (MAb) profiles [5••]. In addition to the bias of the urinary antigen test towards serogroup 1 as a contributing factor to underreporting of LD outbreaks, sensitivity and specificity of other methods used for diagnosis and lack of recognition of the disease in hospitalized patients with other serious

conditions are contributing factors [8]. The sensitivity of the indirect serotype 1–6 immunofluorescence antibody test (IFAT), the rapid microagglutination test (RMAT) IgM serotype 1 antibody assay, and ELISA for IgM and IgG serotype 1–7 antibodies has been reported as 61, 44, and 64%, respectively, for normal titer levels and 86, 48, and 75% for high standing titers that would be representative of an epidemic situation [42]. Additionally, Binax and Biotest kits were found to have sensitivities ranging from 51.4 to 81.8% and from 28.6 to 42.4%, respectively [43].

**Legionella Species and Subtypes Implicated** *Legionella* spp. isolates can be characterized according to their species which are comprised of serogroups, subtypes, and sequence-based types. With regard to species and serogroups observed, the majority of outbreaks in the current literature review were observed to be due to *L. pneumophila* serogroup 1, with the exception of one outbreak where *L. maceachernii* was isolated from patients exposed to a pool/spa [29], two outbreaks due to *L. longbeachae* in pitting soil [35, 44], and one outbreak due to *L. pneumophila* serogroup 1 with unproven linkage to *L. longbeachae* from a cooling tower at a rural dairy processing plant [45]. *L. longbeachae* has been demonstrated to occur in soil and has previously been associated with soil-associated disease clusters [46, 47], but rarely, if ever, with waterborne transmission. However, concerns regarding clinical reliance on the *Legionella* urinary antigen test (which captures only *L. pneumophila* serogroup 1) have created a "blind spot" for non-*Legionella pneumophila* serogroup 1 strains [5••], which as a result may be underreported. Additionally, one outbreak reported *L. pneumophila* serogroup 1 and *L. pneumophila* serogroup 3 attributed to a cold mist ultrasonic humidifier in neonates [48].

Multiple subtypes were found in patient clinical samples including Philadelphia [49–51], Benidorm [22, 37, 49, 52,

53], Knoxville [51, 53–58], Allentown/France [59–62], and Bellingham [52, 55], or a mixture of strains [49]. More than 20 different sequence types were identified across outbreaks. The most common sequence types were ST23 (4 outbreaks) and ST222 (3 outbreaks). Sequence types are known to demonstrate considerable spatial and temporal variability [63].

**Sources of Outbreaks** One hundred nineteen outbreaks (98 LD outbreaks, 4 PF outbreaks, and 17 mixed LD and PF outbreaks) reported an attributed source or suspected source, and in some cases, multiple sources were suspected. It is noted that the CDC defines drinking water or potable water as water for human consumption (e.g., drinking, bathing, showering, hand washing, teeth brushing, food preparation, dishwashing, maintaining oral hygiene) and includes water collected, treated, stored, or distributed in public and individual water systems, as well as bottled water” [64]. For waterborne outbreaks reported in the Morbidity and Mortality Weekly Report (MMWR), some outbreaks are classified as attributable to a “potable water” or “drinking water” source [16]. Although outbreaks associated with *Legionella* spp. are generally categorized using codes for “contamination of water at points not under the jurisdiction of a water utility or at the point of use” [65], the term “potable water system” is used in accordance with reported terminology in summary tables when a specific deficiency or setting was not reported. The term “potable/building water systems” is used to refer to the combined category. Attributed or suspected attributed sources for combined LD and PF outbreaks were as follows: 42 outbreaks (30%) potable water/building water systems; 10 (7%) non-potable water sources excluding cooling towers; 41 (30%) cooling towers, air conditioners, or evaporative condensers; 19 (14%) pools or spas; 7 (5%) multiple sources; and 17 (13%) had an unknown source.

Case fatality rates were up to 30% for potable/building water system outbreaks, up to 33.3% for non-potable system outbreaks, 14.3% for pools and spas, 22% for cooling towers, 33.3% for unknown sources, and 40% for outbreaks with multiple sources. Attack rates varied substantially and were up to 6% for potable/building water systems, 90% for non-potable systems, 33.7% for pools or spas, and up to 76.7% for cooling towers. The greatest number of confirmed LD cases was associated with cooling towers (2083 confirmed cases, 151 deaths), potable water/building systems (564 confirmed cases), outbreaks with multiple sources (363 confirmed cases), pools or spas (319 confirmed cases), and unknown sources (219 cases). The greatest number of PF cases were associated with pools or spas (433 cases); cooling towers, air conditioning units, or evaporative condensers (146 cases); and non-potable water systems (139 cases). Cooling tower outbreaks were therefore associated with the largest disease burden, identified as a direct contributor or associated factor in 50% of confirmed LD and PF outbreak-associated cases and 60% of outbreak-associated deaths.

Of the outbreaks that were potentially attributed to elements of indoor building water systems, showers were implicated in two outbreaks [16, 65], bathroom taps in one outbreak [65], and hot water systems in three outbreaks [65–70]. In a 2010 outbreak of LD in a nursing home in Slovenia with a chlorinated, “circular” system and unidentified outbreak source, “water flow disturbances” and “closed pipes that were walled up and had no water flow” were suggested as probable risk factors for *Legionella* growth due to renovation on some of the bathrooms in the facility [71, 72]. An epidemiological link was made by genotyping a patient isolate and matching it to cold and hot water samples from sink faucets, shower heads, air conditioners, and other locations throughout the nursing home. Water stagnation and elevated water temperatures are known to exacerbate *Legionella* growth [73]; furthermore, proper management of hot water systems is important for mitigating *Legionella* concentrations observed at the point of use [74].

It was noted for the two outbreaks in Flint, Michigan, increased water main breaks, instability of chlorine residual in the distribution system, elevated water temperatures during summer months, and elevated iron concentrations consistent with a corrosive water chemistry were contributing factors [17, 75]. Although the report did not meet inclusion criteria for this review, a study by Cohn et al. [76] suggested low disinfectant residuals as a potentially contributing factor in a LD cluster. Centrally located (not individual-building) community water system storage tanks in a water supplier system with low chlorine residual and stagnant water served a geriatric center and nearby high-rise housing complex for seniors [76]; however, limited information was provided regarding the water system.

Several outbreaks were attributed to elements of water systems not designed for potable use. Of the non-potable outbreaks, decorative water features were the most common cause, with ten outbreaks attributed to, or suspected partially to be attributed to, features such as ornamental fountains [16, 22, 29, 39, 64, 77–83]. Within medical settings, one outbreak in neonates was due to a cold mist ultrasonic humidifier [48, 84]. While not included in the review, a similar study reported a contaminated ice bath in a bronchoscopy suite where uncapped syringes were immersed in the ice bath during procedures and was considered a “pseudo-outbreak” [85]. Two outbreaks were due to potting soil [35, 44]. Outbreaks were also reported to be associated with supermarket mist machines [86], an asphalt paving machine [36], dust-controlling spray at a construction site [57], a sprinkler [83], and sullage tanks in a dockyard [87].

Outbreaks associated with long-range dispersal from cooling towers, air scrubbers, air conditioning units, or evaporative condensers were reported with cases up to large distances from the suspected source, with a maximum of 12 km reported for a cooling tower-associated outbreak in Christchurch, New



Zealand [88]. In some scenarios, due to the nature of the outbreak and environmental investigation findings, it was difficult to attribute the outbreak to a single source. For recurring outbreaks in 2001, 2005, and 2008 in areas surrounding a wood-based chemical factory in Fredrikstad/Sarpsborg, Norway, air scrubbers were originally implicated, with additional investigations suggesting that biological wastewater treatment plant aeration ponds from the same plant played a role in both direct dissemination of aerosols and introduction of contaminated effluent to the Glomma river which may have also played a role in dissemination [89–93]. Another investigation of an outbreak in Warstein, Germany, identified the epidemic strain isolate (serogroup 1 Knoxville, ST345) in environmental samples from cooling towers, a sewage treatment plant, and river water [58, 94–96].

Previously identified risk factors for cooling tower outbreaks include population age, smoking status, male sex, and underlying diseases as well as poor cooling tower maintenance and meteorological factors [18]. In addition, cooling towers can be poorly co-located with population dense areas or the presence of immune-compromised individuals. For example, in an outbreak attributed to cooling towers in Barrow-in-Furness, UK [97], the cooling tower mist dispersed into a narrow walkway through which most of the town's population passed to reach a shopping area [8]. Poor maintenance practices were also mentioned in some studies [49, 50, 93, 97–99] as well as cooling tower start-up [100]. Additionally, unusual weather conditions during the outbreak period were indicated as influential by multiple studies [50–52, 58, 101–103]. Meteorological conditions identified included thermal inversions [51, 101], unusually warm temperatures and favorable wind conditions [52, 58], and high humidity [50, 102, 103].

**Importance of Meteorological Factors and Relationship to Sporadic Cases** The linkage between meteorological variables and sporadic LD and PF cases has been previously demonstrated. These factors are described here as they may also play a role in outbreaks. Several studies have identified thermal inversions as an important factor in the spread of the bacteria over distances as far as 8 km [104–106]. A case-crossover analysis of LD cases in the greater Philadelphia metropolitan area showed an increase in cases with increased precipitation and humidity (but not temperature), with most cases occurring during the summer months [107]. In a similar analysis on national surveillance data from 2003 to 2007 in the Netherlands, multivariate models showed that mean weekly precipitation intensity, mean weekly temperature, and mean relative humidity (RH) accounted for 43.3% of variability in the incidence of LD [108]. Linear models demonstrated that low sunshine, high cloud cover, mean temperatures close to 17.5 °C, high RH, and intense precipitation were associated with higher incidence of LD, but that the warmest days did not overlap with the highest LD incidence throughout the year. Ng et al. [109]

reported that changes in local hydrology such as low watershed levels (OR = 3.6, 95% CI 2.4–5.3) contributed more strongly to LD risk in Toronto, Canada, compared to decreased lake temperature (33% increase, 95% CI 8–64%) or weather factors like humidity (34% increase, 95% CI 14–57%) using a case-crossover design. A study of five US Mid-Atlantic states revealed a 1-cm increase in rainfall was associated with a 2.6% increase in LD incidence; when rainfall increased 5.3 cm from the 1990–2002 summer period to the 2003 summer period, this was associated with a 14.6% increase in LD risk [110]. Ricketts et al. [111] reported an association between RH and LD cases in England and Wales from July to September (2003–2006) but not during winter, with stronger association when maximum temperature was  $\geq 20$  °C. No association was found for wind speed. A summer and autumn seasonal peak of LD is reported in several studies [3, 111, 112]. In a Scotland study, the summer/autumn peak was observed for travel-related cases, but an autumn and early winter peak was noted for non-travel cases from 1978 to 1982 and 1983 to 1986, respectively [113]. Nosocomial cases were clustered during the winter months. Decreases in weather events have been offered as an explanation for a decrease in LD in the Netherlands [114].

**Research Gaps** Outbreaks occurred frequently in susceptible populations such as the elderly in long-term care senior living, retirement, or nursing home facilities (22 outbreaks, 16%), with one outbreak among immune-suppressed patients [78] and another among neonates [115]. Thirty-one (23%) outbreaks occurred in hospital or health care settings. With regard to building types, 20 (15%) outbreaks occurred at hotels and one outbreak occurred in a green building [116]. When evaluating factors associated with legionellosis outbreaks, increased attention to local and building-specific factors can be useful for informing mitigation strategies such as flushing of particular types of fixtures in health care facilities, for example.

To inform *Legionella* spp. risk mitigation strategies, it would be beneficial to prioritize exposure scenarios and populations at risk based on the findings of the current outbreak review with a focus on cooling towers and susceptible populations. Quantitative microbial risk assessment (QMRA) is one approach that can be used to model risks associated with *Legionella* spp. exposures [117], and models have been developed for a variety of indoor and outdoor exposures, including cooling towers [118, 119]. However, current dose-response models used to determine *Legionella* spp. risks have only considered the use of dose-response models for “clinical severity” and “subclinical” infection risks rather than explicitly considering variations across multiple types of susceptible populations [120, 121]. Quantitative relationships between different susceptible population categories and likelihood of infection have not yet been developed for this purpose. The use of outbreak information can help to inform the derivation of such values, as well as provide attack rates (No. ill/No.

exposed) useful for evaluating the plausibility of risk models. As a result, the analysis of attack rates summarized in this review and augmentation of this information with a summary of corresponding environmental concentrations of *Legionella* spp. is recommended for further study.

## Conclusions

- A review of 136 Legionnaires' Disease and Pontiac Fever outbreaks between 2006 and 2017 provides useful information for prioritizing and targeting mitigation strategies.
- Cooling towers, air conditions, and evaporative condensers were implicated in a large portion (60%) of outbreak-associated deaths due to Legionnaires' disease or Pontiac fever between 2006 and 2017.
- Building water systems were also major contributors to outbreak-related cases (13%) and deaths (17%).
- Potable/building water system-associated outbreaks typically are not attributed to a specific failure; however, such information would be useful for risk-ranking purposes.

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## Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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