International Journal of Hygiene and Environmental Health 240 (2022) 113906

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh

A review of legionnaires' disease and public water systems – Scientific considerations, uncertainties and recommendations

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ARTICLE INFO

Keywords:
Legionella
Legionnaires' disease
Public water
Municipal water

ABSTRACT

Legionella is an opportunistic premise plumbing pathogen and causative agent of a severe pneumonia called Legionnaires' Disease (LD). Cases of LD have been on the rise in the U.S. and globally. Although *Legionella* was first identified 45 years ago, it remains an 'emerging pathogen." *Legionella* is part of the normal ecology of a public water system and is frequently detected in regulatory-compliant drinking water. Drinking water utilities, regulators and public health alike are increasingly required to have a productive understanding of the evolving issues and complex discussions of the contribution of the public water utility to *Legionella* exposure and LD risk. This review provides a brief overview of scientific considerations important for understanding this complex topic, a review of findings from investigations of public water and LD, including data gaps, and recommendations for professionals interested in investigating public water utilities. Although the current literature is inconclusive in identifying a public water utility as a sole source of an LD outbreak, the evidence is clear that minimizing growth of *Legionella* in public water utilities through proper maintenance and sustained disinfectant residuals, throughout all sections of the water utility, will lead to a less conducive environment for growth of the bacteria in the system and the buildings they serve.

1. Introduction

Legionella is an opportunistic premise plumbing pathogen and causative agent of legionellosis. Legionellosis is a disease grouping which includes Legionnaires' Disease (LD), a severe pneumonia often requiring treatment in a hospital, Pontiac fever, a generally milder illness, and additionally extrapulmonary infections. An estimated 8–18,000 people are hospitalized annually with LD in the United States, and yet only about 10% of cases are clinically diagnosed (Adams et al., 2013; Cassell et al., 2019). From 2007 to 2018, the incidence of LD has more than tripled (NAS, 2019). *Legionella* has been identified as the leading cause of waterborne outbreaks in the US (Benedict et al., 2017), and, nationally, health insurers paid $434 million dollars annually for LD alone (Collier et al., 2012).

The bacteria are commonly found in the freshwater environment and reproduce in high numbers inside free-living amoeba in warm (25–45 °C) stagnant water (Fliermans et al., 1981). The primary human exposure route to *Legionella* is the inhalation of aerosolized water containing the microorganism, typically from showers, whirlpool spas and outdoor cooling equipment, humidifiers, misters and respiratory therapy devices. LD cannot be transmitted person-to-person or by swallowing contaminated water, however aspiration is also an important mode of disease transmission. Older adults, smokers, individuals with immunocompromised conditions and comorbidities are at higher risk of LD (Silk et al., 2013). Yet, a large majority of cases (as many as 96%) are sporadic with no identified source (Orkis et al., 2018a).

Legionella pneumophila, especially serogroup (SG1), is the most common etiologic agent of LD in the U.S., accounting for approximately 85–90% of reported clinical cases (Fields et al., 2002; Yu et al., 2002) though that differs in other continents. Since a urinary antigen test specific to *L. pneumophila* SG1 is the primary means of diagnosing LD in the U.S., and although infections by other serogroups may be captured by this test, generally infections with other species and serogroups are being missed (Mercante and Winchell, 2015; Muyldermans et al., 2020).

Over 40 years after *Legionella* was first discovered, the Water Research Foundation identified *Legionella* as an 'emerging pathogen' (Jang et al., 2014). Indeed, when outbreak investigations are covered by news and media, it is often suggested that the public water system may be the source of the outbreak and water utilities may continue to become the subject of litigation as building owners more frequently test the

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https://doi.org/10.1016/j.ijheh.2021.113906
Received 8 October 2021; Received in revised form 2 December 2021; Accepted 13 December 2021
Available online 16 December 2021

incoming water during public health outbreak investigations (AWWA, 2017). A recent LD outbreak in Flint, Michigan in 2014–2015, occurring after water utility-wide deficiencies, has brought attention to the role of public water systems in LD outbreaks (Rhoads et al., 2017). There are additional instances when public water systems have been implicated in LD outbreak investigations (Cohn et al., 2015; Rhoads et al., 2020). Public health professionals, drinking water regulators and water utilities alike are increasingly required to have a productive understanding of the evolving issues and complex discussions of the contribution of the public water utility to *Legionella* exposure and LD risk. To this end, this review provides a brief overview of scientific considerations important for understanding this complex topic, a review of findings from investigations of public water and LD, including data gaps, and recommendations for professionals interested in investigating public water utilities and risk of LD.

2. *Legionella* growth in public water

Legionella is part of the normal ecology of a public water system and is frequently detected in regulatory-compliant drinking water (Hsu et al., 1984; USEPA, 2016). Currently there are no national drinking water regulations for *Legionella* in the U.S. The United States Environmental Protection Agency (USEPA) considers *Legionella* to be controlled if and when water systems treat their water for the removal/inactivation of Giardia and viruses. The USEPA states that *Legionella* can enter a facility from the source water, and the "environmental conditions and processing of the water once it enters a building can lead to the growth of *Legionella*, which could result in increased risks of infection" (Hsu et al., 1984; USEPA, 2016). This paradigm is also proposed by American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE), an industrial professional society which promulgates standards and guidelines reflecting best practices and current science for the building industry (ASHRAE, 2020).

Legionella is commonly detected as part of the complex water utility pipe biofilms (Waak et al., 2018). *Legionella* contained inside amoebae, in the environmentally hardy cyst, frequently escape the treatment plant unimpaired and enter the distribution system and ultimately indoor plumbing, where *Legionella* and their protozoan hosts are incorporated within biofilms (Nisar et al., 2020). The protozoan hosts facilitate the replication and viability of *L. pneumophila* (Nisar et al., 2020). Numerous reports describe the existence of *L. pneumophila* harbored within protozoans from thermally-, chemically-, and UV radiation-treated potable water supplies and storage reservoirs (Kim et al., 2002).

Additional mechanisms of colonization may involve insufficient cleaning of water mains during construction or repair (Colbourne and Trew, 1986) and leaking mains affected by transient negative pressure spikes that pull in soil/sewage line microorganisms. Other mechanisms of colonization of premise plumbing distinct from public water system "seeding" of building premise plumbing could include improper or insufficient backflow prevention from cross-connections between potable and non-potable water and introduction from elevated building water storage tanks.

Areas of low flow frequently are sites of increased sedimentation and reduced disinfection residual as well as a source of additional nutrients for *Legionella* growth. Corroded mains can provide greatly expanded surface area for biofilm formation (LeChevallier et al., 1993; NAS, 2019). Tuberculation also increases the availability of iron, which is a nutrient for *Legionella*. Extended water age in a distribution network is known to be associated with a loss of chlorine residual due to reaction with the main and any corrosion products, biofilm lining the main, sediments in the main and soluble organic material in the water.

Under conditions conducive for growth, *Legionella* that may be present in low numbers within the biofilm can begin to proliferate, whether in the biofilm of water utility-owned distribution pipes or within building premise plumbing. Although even low levels of *Legionella* may be associated with cases of LD (Demirjian et al., 2015), the active growth and explosion of high numbers of *Legionella* are most anticipated to cause disease despite a lack of known infectious dose (CDC, 2018). Proliferation of the organism remains the largest health concern because it indicates the presence of viable and pathogenic bacteria (Colbourne and Dennis, 1985). Factors known to influence *Legionella* growth within buildings include temperature, disinfection, hydraulic conditions, presence of nutrients, pipe materials and presence of distal devices; factors which may be relevant to public water utilities (NAS, 2019).

2.1. *Disinfection level*

There are requirements for free chlorine residual levels in surface water systems (Pressman, 2020). However, these regulations are intended to control gastrointestinal pathogens, and not specifically *Legionella* or their associated biofilm protozoan hosts. These regulations require a detectable residual (0.05 mg/L) at 95% of sampling locations throughout the utility. Evidence of the influence of disinfection level and type on *Legionella* occurrence and LD risk is strong. Localized low chlorine residuals (<0.2 mg/L) could be an indicator of insufficient bacterial control. LeChevallier (2019b) suggests that utilities should maintain a chlorine disinfectant residual of at least 0.1 mg/L in all parts of the distribution system, while much higher levels are recommended for health care building systems. The World Health Organization (WHO) estimated that healthcare facilities need 0.3–0.5 mg/L to keep *Legionella* proliferation under control and as much as 50 mg/L is needed to kill *Legionella* embedded within biofilm (WHO, 2007). Notably, some protozoans are more resistant to chlorine when infected by *Legionella* (Boamah et al., 2017).

2.2. *Disinfection type*

Disinfectants used to create a residual in the distribution system are chlorine, chlorine dioxide and chloramines. A microbiological survey of a water system before and after the disinfection type was switched from chlorine to chloramine found that while *Legionellae* was widely distributed in source water and in the distribution system, and was the dominant biofilm bacteria in some samples, it was not detectable in the distribution system in the months after the switch to chloramine disinfection (Pryor et al., 2004). Chloramine disinfection has been demonstrated to reduce *Legionella* detections in multiple water surveys (Donohue et al., 2014; Flannery et al., 2006; Moore et al., 2006; Pryor et al., 2004) and to reduce hospital-associated LD outbreaks (Heffelfinger et al., 2003; Kool et al., 1999). The greater disinfection efficacy of chloramine is thought to occur because chloramines are selectively reactive, allowing deeper penetration into biofilms (Xue et al., 2014), and because chloramines can kill *Legionella* inside amoebae (Dupuy et al., 2011). However more research is needed to understand the exact mechanism for improved effectiveness (NAS, 2019).

2.3. *Water source*

Some research suggests systems using a surface water supply are more likely to be associated with LD (Wullings and van der Kooij, 2006), which may be expected because surface waters typically have the amoebae that supports *Legionella* growth. However, *Legionella* is known to naturally exist in groundwater, and higher levels of *Legionella* have been found in homes served by private groundwater wells as compared to those served by public water (Mapili et al., 2020). An ecological analysis of census tract LD incidence rates in NJ did not confirm an increased association among census tracts served by public water utilities with a surface water source compared to census tracts served by groundwater (Gleason et al., 2017).

2.4. *Other factors*

A growing body of research suggests that warm, wet, humid weather is associated with increased incidence of LD, which is likely an indicator that these meteorological conditions increase the proliferation of *Legionella* in the water environment (Fisman et al., 2005; Gleason et al., 2016; Passer et al., 2020).

3. *Legionella* occurrence in public water utilities

Despite the acceptance of that fact that *Legionella* is detected in regulatory compliant drinking water, there remains a lack of consensus regarding the prevalence of *Legionella* in distributed water, and, further, whether there would be an acceptable detection concentration. A limited amount of research provides *Legionella* sample results from public water distribution systems and even less real-world evidence of factors which may increase *Legionella* detection in a water utility distribution system (Donohue et al., 2019).

A detailed picture of *L. pneumophila* in a municipal water system was obtained by States et al. (1987). Raw water, water at different stages in the treatment plant, and finished water in several reservoirs were tested by a culture method. There was no detection in raw water, sporadic detection at different points in the treatment process, but persistent detection in the three reservoirs (one covered, two open). Chlorine residuals were always >0.2 mg/L. Other culture-based studies have found *Legionella* throughout water utility distribution systems (Stout et al., 1992; Tison and Seidler, 1983). *Legionella* concentrations, as measured by the quantitative polymerase chain reaction method (qPCR), were found to decline with each step of the treatment process (Lin et al., 2014). *L. pneumophila* was detected by qPCR in 25% of the source water samples collected from 25 drinking water treatment plants in the U.S. but in only 4% of treated water samples (King et al., 2016).

Analysis of sediment samples from municipal drinking water storage tanks in 18 community water systems across ten U.S. states using qPCR found potential opportunistic pathogens dominated with the highest detection of occurrence being *Mycobacterium* spp., followed by *Legionella* spp. with a 66.7% detection frequency (Lu et al., 2015). Diverse *Legionella* spp. including *L. pneumophila*, *L. pneumophila* SG1 and *L. anisa* were identified, each of which might cause legionellosis. All sampled tanks had detectable residual chlorine, 39% were from surface water-based systems, and temperatures ranged from 2 to 29 °C. However, unfortunately, there was no reported analysis of occurrence by these factors. A small-scale field study of 35 residential water meter biofilms found *L. pneumophila*, through molecular techniques, in 14% of samples, and occurrence was in only one area, indicating that environmental differences in the water distribution system may impact *Legionella* occurrence (Schwake et al., 2015).

A national occurrence study (Donohue et al., 2019) of cold-water samples (n = 108) taken during 2009–2014 at building and residential cold-water taps, using two sensitive primer/prober qPCR sets, found that a quarter of the taps showed presence of low levels of *L. pneumophila* SG1 in at least one of the sampling events. Large buildings and residences exhibited a similar number of detections of *L. pneumophila* SG1 (21–24%), and there was no difference between newer and older residences. Considerable lack of persistence (sites testing positive more than once) was observed. Buildings showed more persistence of *L. pneumophila* SG1 than residences and persistent detection at a building location tended to correlate with the detected concentration of *L. pneumophila*. A one-year sampling campaign throughout the Paris drinking water system found that the presence of *L. pneumophila* as quantified by qPCR fluctuated over space and time (Perrin et al., 2019). Lechevallier (2019a; 2019b) found *L. pneumophila* in a small number of tap samples from ten community water systems tested with Legiolert (a culture-based method with detection based on a *Legionella*-specific enzyme) during warm weather months (July–October 2018). Of the 573 tap samples, only 14 were positive, and were associated with low residual chlorine and higher water temperature. Almost all source water and treatment plant effluent samples had no detectable *Legionella*, which may be due in part to the high concentration of disinfectant leaving the plant.

Despite a lack of known infectious dose, alert and action levels for *L. pneumophila* have been established in a few European countries, based on WHO guidance (Hamilton et al., 2019; Van Kenhove et al., 2019). The levels range from 100 to 100,000 colony-forming units in culture per liter (CFU/L), based in part on different intended purposes, such as protecting at-risk populations and triggering different responses.

4. LD outbreak and public water system investigations

4.1. Flint, MI investigation

The largest investigation of the role of public water as a cause of an LD outbreak occurred after the City of Flint (in Genesee County, Michigan) switched the source of their drinking water from water purchased from the Detroit Water and Sewerage Department to the Flint River in 2014. The new source water was treated to bring the finished water to a free chlorine level that was more than double the level that it had been with the original source water but lacked sufficient corrosion control (Rhoads et al., 2017). The lack of corrosion control led to widespread iron corrosion in the mains and leaching of lead from leaded plumbing. There were areas of the distribution system that barely maintained a chlorine residual, water had a higher temperature in the summer months than with the old water source, and there were increased main breaks which may have increased microbial contamination (Rhoads et al., 2017). Flint switched its source water back to purchased drinking water in October 2015 and implemented enhanced corrosion control. During the same time frame, outbreaks of LD occurred during the summers of 2014 and 2015, receding in 2016. Given the timing of the community outbreaks of LD, it was hypothesized that they were related to the water utility failures. The National Academy of Sciences (2020) report on management of *Legionella* presents a timeline of events. It is instructive to examine the available epidemiologic investigation findings, environmental sampling results and genomic comparisons, and the often-disparate conclusions of investigators regarding the role of the utility - which are reviewed in the sections that follow.

4.2. Flint, MI – epidemiologic investigation data

The final case numbers provided by the Michigan Department of Health and Human Services (MDHHS) are 90 cases and 12 deaths (MDHHS, 2018a, b). During 2014–2015, 61 of the LD cases (68%) lived in a residence not serviced by the City of Flint water system during their incubation period, while 56% of cases, or as many as 65% when restricted to cases with complete exposure history, were patients at McLaren Hospital, making the hospital the most frequently visited location among all of the case patients. The MDHHS report concluded that McLaren Hospital was a common source that explains the majority of cases and that the 2015 outbreak ended before the switch back to Detroit water.

Alternatively, other investigators provide analysis indicating the Flint Water was associated with the LD outbreaks. An analysis of LD incidence as a function of free chlorine residual and estimated water age in the Flint Water system mains found a 7.2-fold increase of census tract incidence of LD after the water was switched to the Flint River, and the risk subsided after the switch back (Zahran et al., 2018). When average weekly chlorine levels were <0.5 mg/L, the likelihood of a census tract presenting with LD increased 2.9 times (95% CI 1.4, 6.3) and increased 3.9 times (95% CI 1.7, 8.7) when the chlorine levels were <0.2 mg/L. Notably, McLaren Hospital was located in the high water-age, low-chlorine part of the distribution system. However, other possible sources of exposure including poor building water management at McLaren Hospital were not adequately addressed by the authors. Additional criticisms included the inclusion of only 25 out of 42 cases exposed at McLaren Hospital, inadequate resolution of case residence issues (MDHHS, 2018b), poor exposure assessment for City of Flint water, how cases were classified as commuters, certain model assumptions, misclassification of case illness onset, and that some LD cases classified as receiving City of Flint water only did so two months after the switch back of water source (Smith et al., 2019).

An independent retrospective investigation of the outbreak (based on 86 cases) including epidemiologic, environmental sampling and genomic data found evidence for three sources of the outbreak: 1) McLaren Hospital, 2) residences receiving City of Flint water, and 3) cooling towers and other outdoor aerosol exposures (Smith et al., 2019). Smith et al. (2019), concluded that there was strong evidence for a hospital-associated outbreak in 2014 and 2015, as well as some evidence that in 2014 a proportion of cases were associated with residences served by City of Flint water and select cooling towers in Flint. Importantly, Smith et al. noted the lack of timely sampling of all potential sources. The most frequently reported exposure was to McLaren Hospital (49%). Investigators also found that individuals receiving City of Flint water were at increased risk of developing LD than other Genesee County residents in 2014 but not 2015. Notably, after excluding cases with exposure to McLaren Hospital, the relative incidence rate of LD in Genesee County was still higher than expected. Unfortunately, only a minority of the hospital-associated cases had whole genome molecular subtyping, and, among the eight cases in 2015 that were tested, only three were of a *Legionella* type that matched the *Legionella* typing in the hospital plumbing, sampled a year later in 2016 (Garner et al., 2019; Smith et al., 2019).

4.3. Flint, MI – environmental sampling data

Both hot- and cold-water culture detections of *L. pneumophila* SG1 in McLaren Hospital were found in 75% of the sampled patients' rooms, and, though the hospital hyperchlorinated their water system on three separate occasions, *L. pneumophila* SG1 was found in more than 95% of patients' areas that were sampled (Smith et al., 2019). McLaren Hospital had higher *Legionella* proliferation than any other building sampled (Schwake et al., 2016). A review of McLaren Hospital records of *Legionella* occurrence in their plumbing system and remedial actions shows that high concentrations of *L. pneumophila* SG1 (>10,000 CFU/L) had been detected in the hospital plumbing system in 2014 and 2015 at several different locations (Smith et al., 2019). McLaren conducted a final remedial event, which included a two-phase water system remediation and water use restrictions. Hospital-associated cases decreased within days, though within a couple of months the Flint system had also switched back to its original water source.

Legionella spp. but not *L. pneumophila* were detected in cold-water taps in single-story buildings in an August 2015 sampling (Schwake et al., 2016). Smaller sampling studies at the same time found DNA markers (qPCR) of *Legionella* spp., but no *L. pneumophila* (Flint Water Study, 2019a, b, c). Additional sampling in March 2016 of homes and small business in Flint were all culture negative. Alternatively, Garner et al. (2019) found a more widespread pattern of *L. pneumophila* detection in sampling during June and August 2016, including in cold-water taps in residences. Garner et al. (2019) suggested that detection of *L. pneumophila* in cold-water taps indicates that its presence was not due to a faulty temperature setting on a hot water heater, but rather represents the community water system as a reservoir for the organism.

4.4. Flint, MI – genomic linkage data

Whole-genome sequencing of clinical *Legionella pneumophila* isolates collected during the second of the two outbreaks in Flint was compared with water isolates collected the following year from Flint tap water, after the switch back to Detroit water (Garner et al., 2019). A genetically diverse range of *L. pneumophila* was found across clinical and water isolates, and investigators hypothesize that the LD outbreak could have originated from a variety of different exposure sources. A second genomic comparison of clinical samples and environmental isolates from McLaren's plumbing system and from one cooling tower found environmental isolates from McLaren Hospital in 2016 and 2017 were ST1 and together with three ST1 clinical isolates, formed a genetic cluster. Unfortunately, it is hard to make a strong conclusion based on such a small genetic cluster in environmental samples taken 1–2 years later.

4.5. Flint, MI - summary of findings

The lines of epidemiologic data into sources of the 2014 and 2015 LD outbreaks in Flint, MI are disparate. Despite compelling associations with chlorine residuals and water main breaks with LD case rates, study limitations suggest these findings should be interpreted carefully. Environmental sampling in the community was mixed, may not have included buildings in the high water-age, low chlorine area, and in some cases took place a year after the second outbreak. Although genomic evidence is rarely available in any given investigation of LD, the availability of genomic data in this investigation remained limited and inconclusive. Together, the epidemiologic evidence of shared exposure to McLaren Hospital among most cases and environmental sampling data in McLaren Hospital indicating *Legionella* proliferation, suggest the hospital as the source of the outbreak. However, because the hospital was located in a high water-age zone of the system, it is further possible these issues were compounded by deficiencies in the public water utility.

4.6. Other LD outbreak investigations

Although limited, some additional LD outbreak investigations have explored distributed public water as a source of exposure with varying findings. Following an LD outbreaks (22 cases in 2000 and eight cases in 2006) in the city of Rennes, France (population approximately 200,000), *Legionella* isolates were collected from across the city's entire water distribution system and cooling towers from 2000 to 2009 (Sobral et al., 2011). A few clones were found to colonize the entire water supply system in the city but were not related to the two outbreaks.

An investigation into a multi-year outbreak in Italy that included sampling of 48 points of the unchlorinated municipal water system gave only one positive result in a public drinking water fountain (Scaturro et al., 2015). Investigators also performed residential home sampling including from case-patient homes and a selection of control homes. In patient homes (n = 22), 52% had culture detection of *Legionella,* while 14 out of 16 control homes were negative (12.5% positivity). Along with cooling tower maintenance and disinfection measures, a 0.2 mg/L chlorine disinfection was applied to the municipal water system. Although cases reduced slightly, numbers remained elevated in this area for five years when case numbers returned to background occurrence levels, which coincided with cooling towers going offline due to the shutdown of several factories. The investigators concluded that this investigation remains a reminder of how difficult it can be to identify a source of exposure and the need for clinical isolates for comparison.

In New Jersey, a multiyear sporadic series of LD cases led to an environmental investigation into a section of a community water system (Cohn et al., 2015). The community outbreak included up to eleven SG1 urine antigen-confirmed cases over the course of five years. The case investigation determined that the five-year rate of LD in an area of the community water system near a water storage tank was eight times greater than in the rest of the service area and almost 20 times higher than in the rest of the state. More cases continued to occur in the area after the five-year period. An environmental investigation identified conditions conducive for *Legionella* growth in that area, particularly low chlorine residuals (<0.1 mg/L) during warm weather months over several years, stagnant water in the storage tank, and no flushing program for the distribution system. Two regulatory samples had no chlorine residual. As part of the investigation, *Legionella pneumophila* SG1 was detected by culture at 50% of the sample sites during maintenance flushing of the water mains in the area. The findings from the investigation were not sufficient to conclude there was a direct association with the outbreak and the community water system due to the lack of combined clinical and environmental sequence-based typing and the fact that the sampling of flushed water from the mains occurred several years afterward.

In Quincy, Illinois, 58 cases of LD occurred during a 2015 outbreak (Rhoads et al., 2020). Although deficiencies in the Veterans' Home were associated with many of the cases, an additional four community-acquired cases were not associated with the Veterans' Home, and investigators expanded their investigation to evaluate possible deficiencies with the water utility. About three to six months before the outbreak, the water utility switched their primary disinfectant and corrosion control, which resulted in a decrease in the chlorine residual throughout the system, though no regulatory violations occurred. Although no conclusions are drawn on whether the community water system was responsible for the outbreak, the authors recommend additional water quality monitoring, distribution system management and clinical monitoring whenever major changes in water treatment or changes in distribution system operation occur.

5. Data gaps and limitations

The lack of clinical and timely environmental *Legionella* isolates remains a major limitation in establishing links between the disease clusters and the drinking water utility (Rhoads et al., 2020; Scaturro et al., 2015). This seems to mirror the state of the science in general and explain why so many outbreaks do not have a clear exposure pathway. Since the introduction of a urinary antigen test (UAT) which provides rapid results for the *L. pneumophila* serogroup 1 antigen, respiratory specimens often are not collected because ordering the UAT is faster and easier. Typically, the request for collecting clinical isolates requires the recognition of a defined outbreak, which would also trigger the collection of environmental isolates. The timeframe for realizing there is a problem, and the subsequent investigation of a water utility is typically lengthy, and this affects all aspects of the investigation. Proliferation in the water mains may occur weeks or more prior to the mobilization/-sloughing of the biofilm. This lag time may also be accompanied by the lack of persistence of specific *Legionella* colonies. As noted above, Donohue et al. (2019) observed that only a small proportion of specific subtypes of *Legionella* persisted between one sample event and the next. Rhoads et al. (2017) noted that in the Flint, MI investigation, appropriate sampling was not done during the most relevant time frame.

Importantly, there is no established guideline for investigating a public water utility during an LD outbreak or cluster. Furthermore, in the U.S., investigators can use a variety of culture and non-culture methods for laboratory detection of *Legionella* which can lead to differing results and conclusions and impact comparably of investigation findings. Internationally, culture-based methods are standard and have the added benefit of identifying *non-pneumophila Legionella* that may cause infection; however, these methods may miss more than 90 percent of active infectious cells present (i.e., active but not able to be grown in culture, though possibly able to seed growth in the body) (USEPA, 2017), and reliance on culture-based methods may exaggerate treatment efficacy (Ashbolt, 2015). Molecular methods provide an alternative to these limitations. For instance, qPCR is a culture-independent approach for pathogen enumeration, the advantages of which include a low detection limit, high specificity, and high throughput which provides rapid results (as much as 10–12 days faster than culture) however, this method cannot differentiate between living and dead organisms (Wang et al., 2012). Although growing in utility and availability, the use of non-culture based molecular methods for detection of *Legionella* in potable water samples are not standardized and vary meaningfully across and within commercial, academic and environmental laboratories (Mercante and Winchell, 2015).

The burden of evidence to conclusively confirm the water utility was the source of an LD outbreak may not be achievable. Even when utility deficiencies that create conditions conducive for the growth of *Legionella* are identified, individuals must be exposed to aerosols. Since aerosol generating devices such as showers and cooling towers are privately owned and operated, finding a link between a potable water isolate and clinical isolate would not conclusively confirm that the water utility was the source of the exposure. Instead, such a conclusion may require cumulative evidence of linkages between potable water isolates from independent buildings and residences serviced by the water utility. The lack of clinical and timely environmental isolates for comparisons, no established guidance for investigating a public water utility, and the delayed timing of investigations further compound the burden of proof.

6. Recommendations

Public health investigators need to quickly recognize an outbreak of LD and rapidly respond with both clinical and environmental inquiries. The Centers for Disease Control and Prevention (CDC) recommend that disease investigators consider contacting the local water authority to determine issues or changes that could have contributed to *Legionella* growth (e.g., modifications to potable water disinfection, water main breaks, major construction activity, water service interruptions) (CDC, 2020). Outbreak investigations need to access and consider detailed disinfectant residual data, because the system will only have been cited if disinfectant was non-detectable. In addition, chlorine residual test sites in the distribution system are often not sufficiently close to the case residences to reliably estimate the chlorine residual in smaller, usually slower flowing, mains with older water close to those residences. Regulatory sample sites are typically buildings with easy access, such as schools, police and fire stations and commercial buildings which are usually close to larger mains and larger roadways. Water regulators may be able to request additional water quality monitoring in identified high-risk areas of public water utility distribution systems.

Along with considering disinfection residual data, regular flushing of mains, especially in low-flow areas, a need that is frequently ignored because of insufficient water system staffing, funding, or lack of realization of the value, should be examined. As suggested by CDC, information about utility maintenance events, water main breaks or fire suppression events should be collected when investigating clusters of disease (CDC, 2020). If the data from a public water system suggest the presence of conditions conducive to *Legionella* growth, cold-water tap sampling in the area should be performed for *Legionella* monitoring. Widespread building vacancies, as occurred in many business areas following COVID-19 shutdowns or following natural disasters as occurred following Hurricane Sandy, may also impact water use and increase *Legionella* growth in buildings.

Only a small fraction of reported LD cases is observed as part of an outbreak event. In the absence of a reported common source such as the common plumbing in a building or a sudden unexplained increase in reported cases, disease clusters may go undetected due to unusual geographic cluster patterns or high baseline of disease (Edens et al., 2019; Orkis et al., 2018b). To enhance surveillance detection of clusters, some jurisdictions are implementing prospective legionellosis cluster detection systems (Greene et al., 2016). Surveillance methods that can more effectively and efficiently identify geographic clusters in time would help investigators search out broader common exposures such as local or system-wide public water utility deficiencies more rapidly. A clinical response should also be planned. Without clinical isolates to compare to environmental samples by whole genome sequencing, there is no gold standard available for exposure assessment. Healthcare professionals should be encouraged to collect lower respiratory specimens from patients being evaluated for suspected LD.

Active monitoring for *Legionella* in all public water systems, in the absence of disease, may not be warranted due to potential for false negatives leading to a false sense of security, false positives which could lead to financial burdens (Whiley, 2016), and uncertainty in regard to the interpretation of positive findings. For example, LeChevallier

(2019a) noted that a public water utility was advised that a "do not drink" order would be issued if *L. pneumophila* was detected and subsequently decided to not participate in a *Legionella* monitoring project. However, others highlight scenarios whereby water control measures meet recommendations, but widespread *Legionella* colonization exists, which would only be detected through monitoring (Collins and Walker, 2017). *Legionella* monitoring as part of a public health investigation would be informative for establishing effective reduction of *Legionella* growth in buildings following water utility interventions such as increasing chlorine residuals, through enhanced flushing programs, engineering improvements (e.g., cleaning and lining projects), water storage tank cleaning, and storage tank draw down protocols to refresh the water.

In summary, public health investigators need to continue to develop and refine tools for detecting clusters in space and time and subsequently explore possible underlying sources of exposure such as undiagnosed public water utility deficiencies; to continue to promote the collection of clinical specimens, and to conduct investigations within a faster timeframe. Proactive examination of water quality data and close cooperation between public health authorities, environmental protection authorities and water utilities can be invaluable for protecting the public from *Legionella*, as well as preventing future problems. Although current literature is not conclusive in identifying a public water utility as a sole source of an LD outbreak, the evidence is clear that minimizing growth of *Legionella* in public water utilities through proper maintenance and sustained disinfectant residuals throughout all sections of the water utility will lead to a less conducive environment for growth in the system and the buildings the system serves.

Declaration of competing interest

None.

Acknowledgements

We would like to thank our public health and environmental colleagues for their valuable review and suggestions to guide this review forward.

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