Journal of Patient-Centered Research and Reviews

Volume 9 | Issue 2 Article 6

4-18-2022

# Association of Natural Waterways and *Legionella pneumophila* Infection in Eastern Wisconsin: A Case-Control Study

Hannah M. William
Kayla Heslin
Jessica J. F. Kram
Caroline P. Toberna
Dennis J. Baumgardner



## Recommended Citation

William HM, Heslin K, Kram JJ, Toberna CP, Baumgardner DJ. Association of natural waterways and *Legionella pneumophila* infection in eastern Wisconsin: a case-control study. J Patient Cent Res Rev. 2022;9:128-31. doi: 10.17294/2330-0698.1872

# Association of Natural Waterways and *Legionella pneumophila* Infection in Eastern Wisconsin: A Case-Control Study

Hannah M. William, BS,[1,2,3] Kayla Heslin, MPH,[1,2,4] Jessica J. F. Kram, MPH,[2,4,5] Caroline P. Toberna,[1,2,4] Dennis J. Baumgardner, MD[2,4,5]

*[1]Advocate Aurora Research Institute, Advocate Aurora Health, Milwaukee, WI; [2]Center for Urban Population Health, Milwaukee, WI; [3]University of Wisconsin School of Medicine and Public Health, Madison, WI; [4]Aurora UW Medical Group, Advocate Aurora Health, Milwaukee, WI; [5]Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health, Madison, WI*

**Abstract** Preliminary research has suggested possible associations between natural waterways and *Legionella* infection, and we previously explored these associations in eastern Wisconsin using positive *L. pneumophila* serogroup 1 urine antigen tests (LUAT) as diagnostic. This case-control study was a secondary analysis of home address data from patients who underwent LUAT at a single eastern Wisconsin health system from 2013 to 2017. Only zip codes within the health system's catchment area that registered ≥3 positive cases and ≥50 completed tests, as well as geographically adjacent zip codes with ≥2 positive cases and ≥50 tests, were included. A 1:3 ratio of cases to randomly selected controls was used. Home addresses were geocoded and mapped using ArcGIS software (Esri); nearest waterway and distance to home was identified. Distance to nearest waterway according to ArcGIS was verified/corrected using Google Maps incognito. Distances were analyzed using chi-squared and 2-sample *t*-tests. Overall, mean distance to nearest waterway did not differ between cases (2958 ± 2049 ft) and controls (2856 ± 2018 ft; P=0.701). However, in a subset of nonurban zip codes, cases were closer to nearest waterway than controls (1165 ± 905 ft vs 2113 ± 1710 ft; P=0.019). No association was found between cases and type of waterway. Further research is needed to investigate associations and differences between natural and built environmental water sources in relation to legionellosis. (*J Patient Cent Res Rev.* 2022;9:128-131.)

**Keywords** *Legionella*; pneumonia; bacteria; fresh water; waterways; Legionnaire's disease; environment

*Legionella pneumophila* serogroup 1 is the predominant bacterium responsible for Legionnaires' disease, a serious respiratory infection that presents as pneumonia.[1] Acquisition of *L. pneumophila* pneumonia can occur through inhalation of aerosolized particles from various built environmental water sources, including indoor plumbing fixtures, outdoor cooling towers, and even street cleaners.[1-10] Inhalation of aerosolized particles from various natural water sources also may occur.[1,2,6,7,11-15] In both built and natural aqueous environments, *Legionella* can parasitize protozoa, resulting in another effective mode of transmission.[15]

Corresponding author: Dennis J. Baumgardner, Aurora Sinai Medical Center, 1020 N. 12th St., #4180, Milwaukee, WI 53233 (djbaumga@wisc.edu)

Several published reports have suggested that acquisition of *L. pneumophila* pneumonia may be associated with certain natural waterways. A 2018 study found that zip codes surrounding 6 rivers in Connecticut saw statistically significant differences in the incidence of legionellosis.[11] Zip codes within 10 km of the Quinebaug River and the Hockanum Brook were associated with increased legionellosis incidence (4.37 times and 1.71 times, respectively). Additionally, legionellosis risk was significantly increased in areas within a close distance from the Naugatuck and Farmington rivers.[11] The same study found conflicting evidence in that areas near other rivers (Saugatuck and Shetucket) showed a negative relationship between river proximity and legionellosis.[11] There was a potential association between precipitation and increased incidence of *Legionella* infection (48% increased risk 2 weeks after precipitation).[11] Precipitation may disrupt the biofilms in which *Legionella* are naturally present, thus resulting in increased aerosolization of the infectious particles.[3,11] Aerosolized particles have the potential to travel relatively long distances from their source.[4,5] A Norwegian study identified an isolate from a natural river identical to those found in a patient with *L. pneumophila* pneumonia.[5] Case reports have suggested hot springs as a source of *Legionella* infection,[7] and some associated bodies of water are linked to power plants, creating an interface between built and natural water sources.[12] In addition, a study from Toronto has associated *Legionella* case occurrence with local, temporal watershed ecological factors, including river/creek levels.[14] Thus, processes that alter characteristics of natural waterways may provide an environment conducive to the growing and thriving of *L. pneumophila*.[12]

In a prior publication,[16] we described the epidemiologic features of *L. pneumophila* serogroup 1 infection via *Legionella* urine antigen test (LUAT), which has been shown to be diagnostic for that serogroup,[17] in a single eastern Wisconsin-based health system. Given that these previous reports suggest a potential association between *Legionella* infection and natural waterways,[3-5,11,12] we performed additional analyses on our previous LUAT data[16] in order to explore or identify associations between *L. pneumophila* serogroup 1 cases and proximity to natural waterways (lakes, rivers, streams, ponds, etc) in eastern Wisconsin.

## METHODS

Following institutional review board approval for secondary analyses, a retrospective case-control study using home address location data of patients who underwent LUAT testing from 2013 through 2017 within an integrated health system serving eastern Wisconsin was conducted. As done previously,[16] this study included inpatients and outpatients of all ages, genders, and ethnicities whose addresses were obtained from the electronic health record. Only the first positive test result was included for patients who had multiple tests with positive test results. Similarly, for the control group, only the first negative test result for each patient was included.

During the study time period, the health system's catchment area comprised a total of 412 zip codes. To ensure adequate within-region matching, to increase the likelihood that at least one subject from each zip code was actually exposed to *Legionella* (from any type of source) near their home, and to minimize other geographic biases due to outliers, only zip codes in which there were 3 or more positive cases with 50 or more completed tests, as well as adjacent zip codes in which there were 2 or more positive cases and 50 or more completed tests, were investigated. For every positive case within these identified zip codes, 3 randomly selected negative LUAT controls were selected from the same zip code (1:3 ratio).

Addresses were geocoded and mapped using ArcGIS Desktop 10.6 (Esri). Nearest waterway and distance (in feet) to the home address at the time of LUAT was identified. Nearest waterway and distance by ArcGIS were verified/corrected by hand with use of Google Maps (Google LLC) point-to-point distance measurement tool on a secure browser and computer to protect sensitive patient information. The bodies of water were classified per the Wisconsin Department of Natural Resources[18] to differentiate between lakes/ponds (including types [seepage lake, spring lake, drained lake, drainage lake, and impoundments]) and rivers/streams.

Minitab® statistical software (Version 13, Minitab, LLC) was used for basic descriptive and inferential statistics. Verified distances between the home addresses and bodies of water were analyzed using 2-sample *t*-tests (as positive and negative distance distributions approximated normal by Kolmogorov-Smirnov test and both curves were similar) and categorical data with chi-squared goodness-of-fit tests or Fisher's exact test, as appropriate. P-values less than 0.05 were deemed statistically significant.

## RESULTS

No specific bodies of water were identified as being overrepresented among all positive cases in eastern Wisconsin identified as part of the previously published (parent) study (N=135 cases across 71 zip codes; Figure 1).[16] Among the 71 zip codes with at least 1 positive case represented in Figure 1, 49 zip codes were excluded from this secondary analysis based on inclusion criteria. Of those 49, 20 zip codes had less than 50 subjects (range: 2–47) and only 1 positive case; the mean positivity rate for these excluded zip codes was 5.0% (range: 2.1%–50.0% [1 of 2 subjects]), higher than the 1.6% positivity rate (range: 0.4%–6.3%) seen in all those zip codes with 50 or more subjects ($P<0.001$). Also excluded were 29 zip codes with 50 or more subjects but only 1 or 2 positive cases, thereby failing to meet the latter criterion for inclusion. The percentage of positive cases in those 29 zip codes was 1.0%, lower than the 2.1% positivity seen in the 22 zip codes ultimately included for analysis ($P<0.001$).

Following exclusions, secondary case-control analysis involved 22 total zip codes, of which 80 LUAT-positive cases and 240 LUAT-negative controls were included. Of these, 18 zip codes were located in urban Milwaukee County (ie, 532xx, which had overall positivity rate of 2.1% [68 of 3307]). The other 4 zip codes in eastern Wisconsin that met the study's selection criteria were located outside of Milwaukee County and are more suburban/rural in nature; overall positivity rate for these 4 zip codes was also 2.1% (12 of 560).

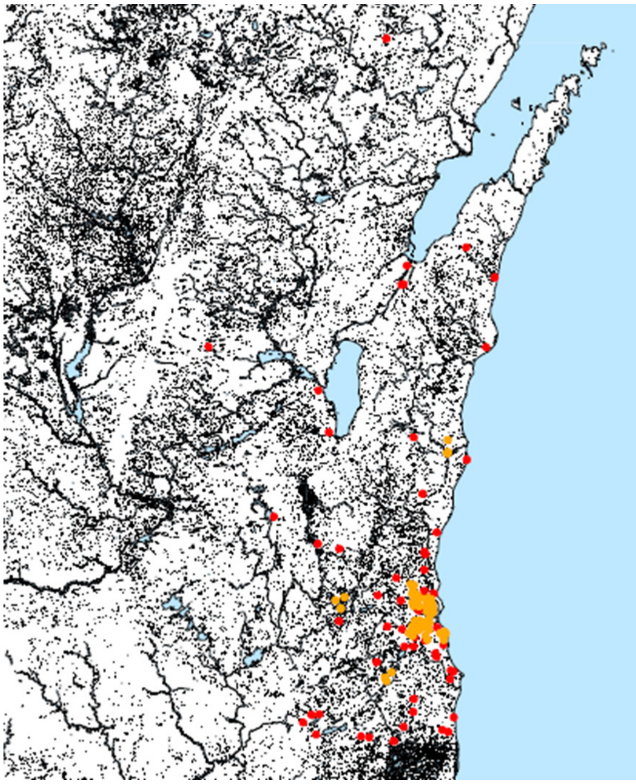

***Figure 1.** Dot map of eastern Wisconsin home address locations of individuals with positive* Legionella pneumophila *serogroup 1 urine antigen tests, as obtained for the parent study.[16] Orange dots represent positive cases included in the follow-up case-control study reported herein. Red dots represent those positive not meeting criteria for inclusion in this follow-up study.*

Types of nearest waterways did not differ between LUAT-positive cases and controls (Table 1). Lake Michigan was the closest waterway for 0 of 80 cases and 4 of 240 controls.

Overall, for the positive cases, mean distance from the home address to the nearest body of natural water was 2958 ± 2049 ft (ie, 0.56 ± 0.39 miles) and ranged between 108 and 7483 ft (ie, 0.02–1.42 miles). For negative controls, mean distance from home address to nearest waterway was 2856 ± 2018 ft (ie, 0.54 ± 0.38 miles) and ranged between 61 and 8340 ft (ie, 0.012–1.58 miles). These mean distances were not significantly different (P=0.701). In addition, cases were no more likely than controls to be within 1320 ft (ie, one-quarter mile) of a waterway (31.3% vs 27.9%; P=0.621).

In contrast to the overall study cohort, among the 4 non-Milwaukee County zip codes only (n=48 total addresses), positive cases (n=12) were significantly closer to nearest waterway than controls (1165 ± 905 ft vs 2113 ± 1710 ft; P=0.019). In addition, cases in the non-Milwaukee County group were disproportionately within 1320 ft of a waterway (8 observed cases vs 3.50 expected cases; P=0.004), a significant difference not seen in the urban/Milwaukee County zip codes group (17 cases vs 19.55 expected cases; P=0.495).

**Table 1.** Nearest Waterway Type

| Waterway type (P=0.602) | Cases (N=80) | Controls (N=240) |
|---|---|---|
| Seepage lake, n (%) | 18 (22.5) | 59 (24.6) |
| Spring lake, n (%) | 0 (0.0) | 3 (1.3) |
| Drainage lake, n (%) | 16 (20.0) | 34 (14.2) |
| River/stream, n (%) | 46 (57.5) | 144 (60.0) |

## DISCUSSION

This study revealed an association between home addresses of *L. pneumophila* serogroup 1 pneumonia cases and closer proximity to the nearest waterway, as compared to controls, but only in a subset of nonurban zip codes. This relationship was not seen in the urban zip codes within Milwaukee County, despite identical rates of positive tests in both subsets. Our findings add evidence to the few studies suggesting an association of *L. pneumophila* pneumonia with ambient-temperature natural waterway systems.[5,11] This observation is similar to that described with two waterway systems in relatively rural/suburban areas of Connecticut,[11] per that state's classification parameters.[19]

The primary mode of *Legionella* infection and origin of the bacterium may be different in urban vs suburban settings. Acquisition of *L. pneumophila* pneumonia in urban settings may be more strongly correlated with built environmental water sources such as cooling towers.[4,6] As previously suggested,[14] natural bodies of water may be more important to acquisition of *L. pneumophila* pneumonia than previously thought, particularly in nonurban settings, directly or by influencing home water supplies.[14] Because our study focused solely on proximity to natural waterways, consideration of public vs private sources of potable water per residence among this cohort of cases falls beyond its scope.

Our study, which is strengthened by the utilization of street addresses at the time of LUAT (not just zip code centroids like in the Connecticut study),[11] has several limitations. First, while our study was of moderate size, data are from a single health system in a limited geographical region and include only cases of *L. pneumophila* serogroup 1 diagnosed by LUAT. Second, as risk factor interviews and property site inspections were not done in the parent study,[16] we have no assurance that cases were exposed at their respective place of residence and exposure could have been associated with another primary water source (eg, recreational) within or remote from the residence (or even nosocomial).[2-10] Lastly, the study's exclusion criteria and differences in testing practices among health system facilities in different locations may have contributed to bias with respect to case identification (likely mitigated by use of controls from the same area). The small number of positive cases (n=12) in the non-Milwaukee County group may have made that subset analysis particularly sensitive to these potential biases.

Ultimately, additional studies are needed to determine if proximity to natural waterways is consistently associated with *L. pneumophila* pneumonia. Moreover, studies on the relative importance of natural versus built environmental water sources in the acquisition of Legionnaires' disease in different geographic regions is warranted.

### Patient-Friendly Recap

- It has been suggested that close proximity to a natural waterway may promote acquisition of legionellosis, a type of pneumonia more commonly known as Legionaire's disease.
- Authors studied the geography surrounding home residences of confirmed cases of *Legionella* infection throughout eastern Wisconsin.
- There was no association tying distance to natural water and *Legionella* test positivity among patients living in the state's urban zip codes of Milwaukee County. However, a subset of suburban/rural areas did indicate cases lived closer to a waterway.


### Acknowledgments

The authors thank Brian Buggy for prompting this investigation, Julie Prabucki for initial laboratory data acquisition for the parent study, and Alexander Schwank for helpful research suggestions.


### Author Contributions

Study design: Heslin, Kram, Baumgardner. Data acquisition or analysis: all authors. Manuscript drafting: William, Kram, Baumgardner. Critical revision: all authors.

### Conflicts of Interest

None.

### References


1. Valavane A, Chaudhry R. The summer of seventy-six – *Legionella pneumophila* monologue. *Emerg Infect Dis.* 2017;23:1202-3. CrossRef
2. Edelstein PH, Roy CR. Legionnaires' disease and Pontiac fever. In: Bennett JE, Dolin R, Blaser MJ (eds). *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Eighth Edition.* Elsevier Saunders; 2015, pp. 2633-44.e6.
3. Prussin AJ 2nd, Schwake DO, Marr LC. Ten questions concerning the aerosolization and transmission of *Legionella* in the built environment. *Build Environ.* 2017;123:684-95. CrossRef
4. Addiss DG, Davis JP, LaVenture M, Wand PJ, Hutchinson MA, McKinney RM. Community-acquired Legionnaires' disease associated with a cooling tower: evidence for longer-distance transport of *Legionella pneumophila*. *Am J Epidemiol.* 1989;130:557-68. CrossRef
5. Nygård K, Werner-Johansen Ø, Rønsen S, et al. An outbreak of legionnaires disease caused by long-distance spread from an industrial air scrubber in Sarpsborg, Norway. *Clin Infect Dis.* 2008;46:61-9. CrossRef
6. Phin N, Parry-Ford F, Harrison T, et al. Epidemiology and clinical management of Legionnaires' disease. *Lancet Infect Dis.* 2014;14:1011-21. CrossRef
7. Orkis LT, Harrison LH, Mertz KJ, Brooks MM, Bibby KJ, Stout JE. Environmental sources of community-acquired legionnaires' disease: a review. *Int J Hyg Environ Health.* 2018;221:764-74. CrossRef
8. Bartley PB, Ben Zakour NL, Stanton-Cook M, et al. Hospital-wide eradication of a nosocomial *Legionella pneumophila* serogroup 1 outbreak. *Clin Infect Dis.* 2016;62:273-9. CrossRef
9. Zahran S, McElmurry SP, Kilgore PE, et al. Assessment of the Legionnaires' disease outbreak in Flint, Michigan. *Proc Natl Acad Sci U S A.* 2018;115:E1730-9. CrossRef
10. Valero N, de Simón M, Gallés P, et al. Street cleaning trucks as potential sources of *Legionella pneumophila*. *Emerg Infect Dis.* 2017;23:1880-2. CrossRef
11. Cassell K, Gacek P, Warren JL, Raymond PA, Cartter M, Weinberger DM. Association between sporadic legionellosis and river systems in Connecticut. *J Infect Dis.* 2018;217:179-87. CrossRef
12. Żbikowska E, Kletkiewicz H, Walczak M, Burkowska A. Coexistence of *Legionella pneumophila* bacteria and free-living amoebae in lakes serving as a cooling system of a power plant. *Water Air Soil Pollut.* 2014;225(8):2066. CrossRef
13. Fields BS, Benson RF, Besser RE. *Legionella* and Legionnaires' disease: 25 years of investigation. *Clin Microbiol Rev.* 2002;15:506-26. CrossRef
14. Ng V, Tang P, Jamieson F, et al. Going with the flow: legionellosis risk in Toronto, Canada is strongly associated with local watershed hydrology. *Ecohealth.* 2008;5:482-90. CrossRef
15. Steinert M, Hentschel U, Hacker J. *Legionella pneumophila*: an aquatic microbe goes astray. *FEMS Microbiol Rev.* 2002;26:149-62. CrossRef
16. Toberna CP, William HM, Kram JJ, Heslin K, Baumgardner DJ. Epidemiologic survey of *Legionella* urine antigen testing within a large Wisconsin-based health care system. *J Patient Cent Res Rev.* 2020;7:165-75. CrossRef
17. Centers for Disease Control and Prevention. *Legionella* (Legionnaires' disease and Pontiac fever). Diagnosis, treatment, and prevention. Last reviewed January 15, 2020; accessed March 20, 2020. https://www.cdc.gov/legionella/clinicians/diagnostic-testing.html
18. Wisconsin Department of Natural Resources. Wisconsin lakes. Booklet (PUB-FH-800) published in 2009; accessed February 10, 2021. https://dnr.wi.gov/lakes/lakebook/wilakes2009bma.pdf
19. U.S. Department of Agriculture Economic Research Service. Connecticut – rural definitions: state-level maps. Accessed February 10, 2021. www.ers.usda.gov/webdocs/DataFiles/53180/25561_CT.pdf?v=0