Legionellosis

Caused by the bacterium *Legionella* with 80 to 90 percent of reported cases linked to *Legionella pneumophila* (Lp)

**Legionnaires’ disease (LD):** a pneumonia-like syndrome with 3% to 33% cases leading to death

**Pontiac Fever:** an acute, nonfatal mild upper respiratory infection that resembles acute influenza. Pontiac fever resolves spontaneously and often goes undiagnosed

Risk factors for legionellosis include:
- Age
- Gender
- Smoking
- Immunosuppression
Increasing incidence of legionellosis in the United States from 2000 to 2017

Public health hospitalization costs associated with contaminated U.S. drinking water*

- CDC estimates drinking water disease costs > $970 million/year
- Less so fecal pathogens, largely Legionnaires’ disease, *otitis externa*, and non-tuberculous mycobacterial with >40,000 hospitalizations/year

<table>
<thead>
<tr>
<th>Disease</th>
<th>Annual costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptosporidiosis</td>
<td>$46M</td>
</tr>
<tr>
<td>Giardiasis</td>
<td>$34M</td>
</tr>
<tr>
<td>Legionnaires’ disease</td>
<td>$434M</td>
</tr>
</tbody>
</table>


Legionella transmission is primarily through inhalation of contaminated aerosols into the respiratory system

Some of the common sources of infection include:

- Showers and faucets
- Cooling towers (parts of large air conditioning systems)
- Hot tubs
- Decorative fountains
Outbreaks of Legionnaires’ Disease

• Dutch flower show 1999, over 300 cases, 32 deaths, whirlpool spas and sprinklers
• Melbourne aquarium, 2000, 125 cases, 4 deaths, cooling tower
• Norway 2005, 56 cases, 10 deaths, wastewater treatment plant aeration ponds
• Toronto 2013, 43 cases, unknown source
• Portugal 2014, 377 cases, 14 deaths, cooling tower
• New York City (Bronx) Summer 2015, 128 cases, 12 deaths, cooling tower
• Flint, MI, 2014-2015, more than 80 cases, 12 deaths, water supply changes
• Quincy Illinois State Veterans' Home 2016, 14 deaths, contaminated premise plumbing
40 years since the discovery of *L. pneumophila*

- Much has been learned about the bacteria’s biology and ecology
- Less progress has been made in preventing Legionnaires’ disease
- Methods for monitoring both the disease incidence and water samples have evolved
- Treatment of water systems to reduce colonization is not well understood

In late 2017, the National Academies of Sciences, Engineering, and Medicine convened an expert committee (the Committee on Management of *Legionella* in Water Systems) to review the state of the science with respect to *Legionella* contamination of water systems and issue a report.
Committee’s Statement of Task

• **Ecology and Diagnosis:** Describe the microbial ecology of water supplies as it relates to *Legionella*. How can diagnosis be improved?

• **Transmission via Water Systems:** What are the primary sources of human exposure to *Legionella*? What features/characteristics of water systems make them likely to support growth of *Legionella*?

• **Quantification:** What is known about the concentration of *Legionella* in water systems and the prevalence of Legionnaires’ disease over the last 20 years? Is there a minimum level of contamination required to cause disease?

• **Prevention and Control:** What are the most effective strategies for preventing and controlling *Legionella* amplification in water systems?

• **Policy and Training Issues:** What policies, regulations, codes, or guidelines affect the incidence, control, quantification, and prevention of Legionnaires’ disease? How might they be built upon to better protect the public?
Committee Members

1. Joan B. Rose, *chair*, Michigan State University, Lansing
2. Nicholas J. Ashbolt, University of Alberta, Edmonton
3. Ruth L. Berkelman, Emory University, Atlanta, GA
4. Bruce J. Gutelius, New York City Department of Health and Mental Hygiene
5. Charles N. Haas, Drexel University, Philadelphia, PA
6. Mark W. LeChevallier, Dr. Water Consulting LLC, Morrison, CO
7. John T. Letson, Memorial Sloan Kettering, Bronxville, NY
8. Steven A. Pergam, Fred Hutchinson Cancer Research Center and the University of Washington
9. Michèle Prévost, Polytechnique Montréal, Quebec
10. Amy Pruden, Virginia Polytechnic Institute and State University, Blacksburg
11. Michele S. Swanson, University of Michigan, Ann Arbor
12. Paul W. J. J. van der Wielen, KWR Watercycle Research Institute, Nieuwegein, The Netherlands
13. Lan Chi Nguyen Weekes, La Cité, Ottawa, ON
• *Legionella* was first documented as a cause of human disease in 1976, after an outbreak of pneumonia of unknown origin was described among members of the American Legion who had attended a conference at the Bellevue-Stratford Hotel in Philadelphia

• The history and evolution of knowledge on this waterborne disease is recorded to a large extent via outbreaks

• It is clear that the built environment is a major ecological niche for the bacteria and controls focus on biocides for cooling towers and hospitals
• There are 61 known species of *Legionella*

• *L. pneumophila* is the most dominant species isolated from patients

• Other pathogenic species include *L. micdadei, L. bozemanii, L. dumoffi* and *L. longbeachae*

• Genetics and complex ecology of *Legionella* being revealed
Ecology and Transmission

- The bacteria can exist in numerous forms. This includes transmissive, replicative, and mature infectious forms, as well as viable-but-nonculturable (VBNC).

- The primary growth habitat of *L. pneumophila* is within amoebae or other free-living protozoa associated with biofilms.

- There are various forms of packaged *Legionella* that are released.

- Cell forms, and how they are packaged, differ in their infectivity, virulence, resistance to treatment, etc.
Chapter 2 Conclusions and Recommendations

• Protocols should be developed to generate, identify, enumerate, and report distinct *Legionella* cell types

• Whether *L. pneumophila* enters into a VBNC state that is both resilient and reversible remains an urgent question

• Ecological studies should be focused on the growth, survival, and inactivation of other *Legionella* species

• Direct observations and metagenomic studies of microbial diversity are required to identify the protozoa that control pathogenic *Legionella*

• How does *Legionella* cause Pontiac fever? Role of the aspiration pathway to total disease? Survival of *Legionella* in aerosols?
Chapter 3: QUANTIFICATION OF LEGIONELLA AND LEGIONNAIRES’ DISEASE

Topics covered:

• Disease surveillance for Legionnaires’ disease
• Committee’s estimated rate for Legionnaires’ disease
• Environmental monitoring of Legionella
• Compilation of Legionella data from across the world
• Quantitative Microbial Risk Assessment for Legionella pneumophila
Evolving Methods for Quantification of *Legionella*

**Purpose:** Diagnosis, Outbreak investigation, Routine monitoring, Mitigation assessment, and Research

- Urinary antigen test (UAT) which detects only *Lp1*
- Certified standard culture methods vs. New culture methods
- Sequencing
- Associated amoeba

- The diagnosis of LD caused by *Legionella* spp. other than *Lp1* is very difficult with the current routine approaches
- Need evaluation, training, proficiency testing, national approaches for surveillance
- New investment in modified culture and molecular tools is needed
Committee Estimate of Current Rate

- The Committee conservatively estimated that the number of persons with Legionnaires’ disease ranges from **52,000 to 70,000 in the United States each year** or a rate of 20.5 to 27.4/100,000

- Estimate is about 10 times higher than the current reported disease incidence (see graph above)

- This extent of underestimation of national reported data is supported by other studies
A *Legionella* concentration of $5 \times 10^4$ CFU/L should be considered an “action level”, that is, a concentration high enough to warrant serious concern and trigger remediation.

A lower level may be necessary for at-risk individuals.
Chapter 3  Conclusions and Recommendations

• Urgent need to **develop better clinical tools** that will capture more cases of Legionnaires’ disease and identify pathogenic *Legionella* beyond *Lp1*

• Determining the most common sources of **sporadic disease** will require well-funded, population-based studies in multiple jurisdictions

• **Regional Centers of Excellence** could serve as a backbone to strengthen the capacity of state health departments to detect and investigate cases of LD

• **Systematic comparison** of culture methods for *Lp* (and other pathogenic legionellae) ddPCR, qPCR, viability-qPCR, and reverse transcriptase qPCR needed

• **Quantitative microbial risk assessment** is ready to determine concentrations that could be used to set standards/targets for routine monitoring, for determining the effectiveness cleanup, and for regulations
Topics covered:

• Main control strategies for *Legionella*
• Their application to different building and device types
• Confounding influence of green buildings and water and energy conservation
• *Future of prebiotic and probiotic controls*
• *Other opportunistic pathogens in buildings*
## Strategies for *Legionella* in Various Water Systems

<table>
<thead>
<tr>
<th>Control Strategy</th>
<th>Building Water Systems</th>
<th>Large Engineered Systems</th>
<th>Other Devices</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Large Institutional Buildings</td>
<td>Green Buildings</td>
<td>Households</td>
</tr>
<tr>
<td>Temperature Control</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Disinfection</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Manage Hydraulics</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Nutrient Limitation</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Plumbing Materials</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Distal Portion of Plumbing</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Aerosol Control</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

✓—Evidence of control working, ?—Potential for control working but some limitations, X—building type works against a control
Chapter 4 Conclusions and Recommendations

• For all types of buildings, hot-water heater temperature should be maintained above 60°C (140°F), and the hot-water temperature to the distal points should exceed 55°C (131°F)

• Compared to free chlorine, a monochloramine residual better controls Legionella risk from distribution systems AND building water systems, although the reasons are not yet clear

• Research is needed to better understand the persistence of distribution system disinfectant residuals within building plumbing

• Guidance about Legionella is needed for homeowners, especially consumers from at-risk segments of the population
Chapter 4 Conclusions and Recommendations con’t

• **Low-flow fixtures should not be allowed** in hospitals and long-term care facilities because of these buildings’ high-risk occupant populations

• **New designs** are needed to help advance control of *Legionella* in **cooling towers and humidifiers**, particularly use of temperature control in cooling towers

• **Green buildings and water and energy conservation** have worsened many of the problems with *Legionella*
The Safe Drinking Water Act does not provide protection from Legionella

- The role of water utilities today
  - Responsive to SDWA
  - Providing DS disinfectant residual
  - Responsibility ends at the service connection

- Differences between premise plumbing and main distribution system (length, surface/volume ratio, water age)

- No evidence that residuals persist within buildings
1. *Legionella regulations* in the United States that require water management plans and/or monitoring of water systems for *Legionella* currently cover:
   - Healthcare facilities in New York State
   - Cooling towers in NYC and New York State
   - Healthcare facilities within the VA system
   - Hospitals/healthcare facilities receiving Medicare/Medicaid funds

2. **Voluntary** creation of water management plans using such guidance as ASHRAE 188. Success in reducing building risk has been shown to be related to presence of a *Water Management Plan*

3. All other buildings and private residences are potentially protected from *Legionella* only through the application of building and plumbing codes which are inadequate!
Water management plans capture what controls will be used in a building or for a device type to prevent growth of *Legionella*. Basic elements:

- Establish a program team
- Describe each water system
- Analyze where potential hazards may exist, develop, or propagate.
- Identification of control measures and where they should be applied.
- Monitor certain parameters (perhaps including *Legionella*) to determine if control measures are working.
- Confirm that the program is being implemented as designed (verification) and that the program effectively controls the hazard (validation).
- Document plan and analyses
Current Status of *Legionella* Management in the U.S. today

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### Selected International *Legionella* Regulations

<table>
<thead>
<tr>
<th>Country/Province</th>
<th>Buildings/Devices Covered</th>
<th>Preferred Treatment</th>
<th>Monitoring Thresholds (All Converted To CFU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Netherlands</strong></td>
<td>Priority premises (large buildings), swimming and bathing facilities, cooling towers</td>
<td>Temperature control, flushing, UV, filtration</td>
<td>&gt;1,000 CFU/L, take response actions</td>
</tr>
<tr>
<td><strong>Germany</strong></td>
<td>Large buildings, cooling towers, swimming pools, bathing water, WWTPs</td>
<td>None, though temperature control and avoiding stagnation evident in codes</td>
<td>&gt;1,000 CFU/L, take response actions</td>
</tr>
<tr>
<td><strong>England</strong></td>
<td>Evaporative cooling systems, cooling towers, hot and cold water systems, spa/pool systems, healthcare facilities</td>
<td>Temperature control, biocides</td>
<td>100-1000 CFU/L, take response actions</td>
</tr>
<tr>
<td><strong>France</strong></td>
<td>Buildings except private residences, cooling towers</td>
<td>None apparent</td>
<td>&lt;1,000 CFU/L target for public facilities, &lt;50 or 100 CFU/L target for prevention of nosocomial infections</td>
</tr>
<tr>
<td><strong>Australia</strong></td>
<td>Premise plumbing in healthcare and aged care facilities, cooling towers</td>
<td>Temperature control, biocides</td>
<td>&gt; 10^6 CFU/L, take response actions</td>
</tr>
<tr>
<td><strong>Canada</strong></td>
<td>Cooling towers, open water systems, HVAC components, and hot- and cold-water systems in 360 government buildings</td>
<td>None</td>
<td>&gt;10^6 CFU/L, take response actions</td>
</tr>
<tr>
<td><strong>Quebec</strong></td>
<td>Cooling towers only</td>
<td>Biocides</td>
<td>≥10^4 to &lt;10^6 CFU/L, take response actions</td>
</tr>
</tbody>
</table>

*Countries/Provinces that have evidence of lower environmental concentrations since regulations went into effect!*
Chapter 5 Recommendations

1. Expand the Centers for Medicare & Medicaid Services memo to require monitoring for *Legionella* in environmental water samples for all hospitals

2. Register and monitor cooling towers

3. Require water management plans in all public buildings including hotels, businesses, schools, apartments, government buildings

4. Require a temperature of 60°C (140°F) at hot-water heaters and 55°C (131°F) to the distal points (the point of connection to fixtures including thermal mixing values)

5. Require a minimum disinfectant residual throughout public water systems
To support the 5 recommendations, the following is needed:

- Guidance on interpretation of monitoring results, e.g., including setting targets (QMRA in Chapter 3)
- Training and education
- Analysis of the cost of implementation; report speaks to timing

<table>
<thead>
<tr>
<th>Devices/Fixtures</th>
<th>Critical Average $L_p$ Concentration (CFU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target Risk Value: $10^{-4}$ infections per person per year</strong></td>
<td></td>
</tr>
<tr>
<td>Conventional faucet</td>
<td>104,000</td>
</tr>
<tr>
<td>Conventional toilet</td>
<td>857,000</td>
</tr>
<tr>
<td>Conventional shower</td>
<td>1,410</td>
</tr>
<tr>
<td><strong>Target Risk Value: $10^{-6}$ DALY per person per year</strong></td>
<td></td>
</tr>
<tr>
<td>Conventional faucet</td>
<td>1,060</td>
</tr>
<tr>
<td>Conventional toilet</td>
<td>8,830</td>
</tr>
<tr>
<td>Conventional shower</td>
<td>14.4</td>
</tr>
</tbody>
</table>

$L. pneumophila$ concentrations in various plumbing fixtures that correspond to target risk levels. NOTE: Median estimates from a Monte Carlo simulation. SOURCE: Hamilton et al. (2019).
Many players will have to be involved to implement these recommendations.
Access and download the report for free: https://www.nap.edu/catalog/25474

How to Submit Questions

Type your question in the Q&A Box
• Hover your mouse at the bottom of your screen and click this symbol.
• Type your question.
• Press send.
We will answer questions as time permits.

Thank you for joining us!