Improving the Detection and Investigation of Legionellosis

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Key Messages

• Legionnaires’ disease is not an atypical pneumonia
• Legionnaires’ disease is more than just about outbreaks and plumbing
• There are smarter ways of testing for Legionnaires’ disease
• Know your local epidemiology
Legionnaires’ disease is not an atypical pneumonia

Legionnaires’ Disease

- Pneumonia caused by *Legionella* bacteria
  - *L. pneumophila* is the predominant cause of most reported human disease
- Often severe and life-threatening
- No human-to-human transmission*
- Requires specific antibiotic treatment

Clinical Presentation of Legionnaires’ Disease

• Clinical and radiographic features are indistinguishable from other community-acquired pneumonias (i.e. the features are not atypical)
• Clinical scoring systems are unreliable
• There are no distinguishing biomarkers
  – although C-reactive protein is useful

Legionnaires’ disease caused by Legionella longbeachae: Clinical features and outcomes of 107 cases from an endemic area

Characteristics of L. longbeachae pneumonia are similar to those reported for community-acquired pneumonia in general except for the spring/summer seasonality

Respirology 2016; 21: 1292-9
Prevalence of Legionnaires’ Disease Among Patients with Pneumonia

• Adults with community-acquired pneumonia, worldwide:
  – Typically 1-10%, with mean of ~5%\(^1\)
• Adults with community-acquired pneumonia, Christchurch, New Zealand during spring/summer:
  – 19\(^2\)
  – ~25% during November\(^2\)
• Children with community-acquired pneumonia:
  – Very uncommon

2 *Eur Resp J* 2014;43:644-6

Worldwide Epidemiology of Legionnaires’ Disease

<table>
<thead>
<tr>
<th>Country</th>
<th>Rate per 1 million people</th>
<th>Age distribution (% ≥50 years)</th>
<th>Male:female ratio</th>
<th>Case fatality rate (%)</th>
<th>Peak incidence months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe(^1)</td>
<td>9.2 (0.0-21.4)(^†)</td>
<td>77.0%</td>
<td>2.8:1</td>
<td>10.3%</td>
<td>July-Sept</td>
</tr>
<tr>
<td>USA(^4)</td>
<td>10.8</td>
<td>74.0%</td>
<td>1.8:1</td>
<td>8.0%</td>
<td>June-Oct</td>
</tr>
<tr>
<td>Canada(^4)</td>
<td>4.9</td>
<td>75.0%</td>
<td>1.5:1</td>
<td>NR</td>
<td>July-Oct</td>
</tr>
<tr>
<td>New Zealand(^4)</td>
<td>14.0 (2.5-0.2)(^†)</td>
<td>Highest rate in 50-59 year age group</td>
<td>1.7:1</td>
<td>5.1%</td>
<td>Sept-Nov and March-May</td>
</tr>
<tr>
<td>Japan(^7)</td>
<td>2.0-7.0(^†)</td>
<td>90.8%</td>
<td>4.3:1</td>
<td>NR</td>
<td>June-Nov</td>
</tr>
<tr>
<td>Singapore(^8)</td>
<td>6.5</td>
<td>76.1% (≥55 years)</td>
<td>1.4:1</td>
<td>2.2%</td>
<td>NR</td>
</tr>
<tr>
<td>Australia(^9) (NNDSS 2012)</td>
<td>13.0</td>
<td>87.0-89.0% (≤45 years)</td>
<td>1.9:1</td>
<td>NR</td>
<td>Sept-Nov and March-May</td>
</tr>
</tbody>
</table>

New Zealand has the highest reported incidence of Legionnaires’ Disease in the world

*Lancet Infect Dis* 2014;14: 1011-21
Legionnaires’ disease is more than just about outbreaks and plumbing
## Legionnaires’ Disease Epidemiology

### Global view

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>Uncommon</td>
</tr>
<tr>
<td><strong>Main species</strong></td>
<td><em>L. pneumophila</em></td>
</tr>
<tr>
<td><strong>Transmission</strong></td>
<td>Outbreaks</td>
</tr>
<tr>
<td><strong>Sources</strong></td>
<td>Water</td>
</tr>
<tr>
<td><strong>Seasonality</strong></td>
<td>None</td>
</tr>
</tbody>
</table>

### New Zealand

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>Common</td>
</tr>
<tr>
<td><strong>Main species</strong></td>
<td><em>L. longbeachae</em></td>
</tr>
<tr>
<td><strong>Transmission</strong></td>
<td>Sporadic</td>
</tr>
<tr>
<td><strong>Sources</strong></td>
<td>Soil</td>
</tr>
<tr>
<td><strong>Seasonality</strong></td>
<td>Spring/summer</td>
</tr>
</tbody>
</table>
Legionnaires' Disease in Christchurch, New Zealand

- Is the most commonly identified cause of pneumonia for about half the year
- Has a seasonal peak in activity in spring/summer more predictable than influenza
- About one third of cases require Intensive Care Unit admission and ~10% die
- ~85% of cases are due to *Legionella longbeachae*

Global Distribution of Published Human Cases of *Legionella longbeachae* Infection
Risk Factors for *L. longbeachae* Pneumonia in New Zealand

- **Design:**
  - Case-control study
- **Canterbury region over two summers:**
  - October-March 2013/14
  - October-March 2014/15
- **31 cases, 172 controls**

*Emerg Infect Dis* 2017; 23: 1148-54
## Comorbidities and Smoking

<table>
<thead>
<tr>
<th></th>
<th>Case n(%)</th>
<th>Control n(%)</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>5 (16)</td>
<td>9 (5)</td>
<td>4.2</td>
<td>(1.2, 14.7)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 (16)</td>
<td>12 (7)</td>
<td>2.8</td>
<td>(0.88, 9.0)</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>6 (19)</td>
<td>16 (9)</td>
<td>2.7</td>
<td>(0.91, 7.9)</td>
</tr>
</tbody>
</table>

### Smoking

- **Current smoker**
  - Case: 4 (13)
  - Control: 9 (5)
  - OR: 2.4 (0.66, 8.5)

- **Ever smoked**
  - Case: 19 (61)
  - Control: 63 (37)
  - OR: 2.6 (1.2, 5.7)

- **Smoked less than 20 years**
  - Case: 5 (16)
  - Control: 26 (16)
  - OR: 1.6 (0.5, 5.1)

- **Smoked 20 to <40 years**
  - Case: 4 (13)
  - Control: 17 (10)
  - OR: 2.3 (0.6, 8.0)

- **Smoked 40+years**
  - Case: 10 (32)
  - Control: 15 (9)
  - OR: 5.6 (2.0, 16.0)

*Emerg Infect Dis 2017; 23: 1148-54*

## Gardening Activities

<table>
<thead>
<tr>
<th>Activity</th>
<th>Case n(%)</th>
<th>Control n(%)</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Used compost</td>
<td>26 (84)</td>
<td>84 (49)</td>
<td>6.2</td>
<td>(2.2, 17.3)</td>
</tr>
<tr>
<td>Opened compost</td>
<td>21 (68)</td>
<td>55 (32)</td>
<td>5.2</td>
<td>(2.2, 12.1)</td>
</tr>
<tr>
<td>Used compost indoors</td>
<td>7 (23)</td>
<td>9 (5)</td>
<td>6.6</td>
<td>(2.1, 20.7)</td>
</tr>
<tr>
<td>Moved compost around (with hands or by</td>
<td>26 (84)</td>
<td>70 (41)</td>
<td>9.9</td>
<td>(3.4, 28.3)</td>
</tr>
<tr>
<td>tipping/trowelling)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any opportunity for getting hands near face</td>
<td>16 (52)</td>
<td>36 (21)</td>
<td>4.8</td>
<td>(2.1, 11.1)</td>
</tr>
<tr>
<td>(smoking, eating or drinking, or touching</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>face) before washing hands</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wore a mask while using compost</td>
<td>5 (19)</td>
<td>12 (14)</td>
<td>1.5</td>
<td>(0.46, 4.8)</td>
</tr>
<tr>
<td>Wore gloves while handling compost</td>
<td>17 (65)</td>
<td>50 (60)</td>
<td>1.2</td>
<td>(0.49, 3.1)</td>
</tr>
<tr>
<td>Wet compost down before use</td>
<td>4 (13)</td>
<td>18 (11)</td>
<td>1.6</td>
<td>(0.48, 5.4)</td>
</tr>
</tbody>
</table>

*Emerg Infect Dis 2017; 23: 1148-54*
SHORT REPORT

Legionella longbeachae detected in an industrial cooling tower linked to a legionellosis outbreak, New Zealand, 2015; possible waterborne transmission?

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2 Regional Public Health, Hutt Valley District Health Board, Lower Hutt, New Zealand
3 Institute of Environmental Science and Research Ltd, Porirua, New Zealand

Presence and Persistence of Viable, Clinically Relevant Legionella pneumophila Bacteria in Garden Soil in the Netherlands

E. van Heijnsbergen, A. van Deursen, M. Bouwknecht, J. P. Bruin, A. M. de Roda Husman, J. A. C. Schalk

National Institute for Public Health and the Environment, Bilthoven, the Netherlands; Regional Public Health Laboratory Kennemerland, Haarlem, the Netherlands; Institute for Risk Assessment Sciences, Utrecht University, Utrecht, the Netherlands

Appl Environ Microbiol 2016; 82:5125-31
There are smarter ways of testing for Legionnaires’ disease

Testing strategies for Legionnaires’ disease in many countries are biased towards detection of *L. pneumophila*
Nucleic Acid Detection (e.g. PCR)

- Diagnostic test of choice for Legionnaires’ disease
- High sensitivity and specificity
- Fast turnaround time
- Detects all species and serogroups
- Lower respiratory tract samples are the preferred specimen type

Australian National Notifiable Diseases Surveillance System surveillance case definitions

**Legionellosis**

**Reporting**
Both confirmed cases and probable cases should be notified.

**Confirmed case**
A confirmed case requires laboratory definitive evidence AND clinical evidence.

**Laboratory definitive evidence**
Isolation of *Legionella*
OR
Presence of *Legionella* urinary antigen
OR
Seroconversion or a significant increase in antibody level or a fourfold or greater rise in titre to *Legionella*.
Australian National Notifiable Diseases Surveillance System surveillance case definitions

Legionellosis

Probable case
A probable case requires laboratory suggestive evidence AND clinical evidence.

Laboratory suggestive evidence
Single high antibody titre to Legionella
OR
Detection of Legionella by nucleic acid testing
OR
Detection of Legionella by direct fluorescence assay.

Which Patients with Pneumonia Should be Tested for Legionnaires’ Disease?

1. Only those with severe disease?
2. Only those with specific risk factors?
3. All hospitalised patients with community-acquired pneumonia?
4. Don’t perform any tests and rely on empiric antibiotic treatment?
5. Only in an outbreak setting?
• Investigations for legionella pneumonia are recommended for:
  – all patients with high severity CAP
  – other patients with specific risk factors
  – all patients with CAP during outbreaks
• Recommended tests:
  – Legionella urinary antigen
  – Legionella culture

• Microbiological tests in community-acquired pneumonia:
  – For patients with moderate- or high-severity community-acquired pneumonia:
    • consider legionella urinary antigen test
• Microbiological tests in community-acquired pneumonia:
  – Patients with severe CAP should at have the urinary antigen test for *Legionella pneumophila*

• Clinical indications for use of *L. pneumophila* urinary antigen test:
  – ICU admission, failure of outpatient antibiotic treatment, active alcohol abuse, travel within past 2 weeks, pleural effusion

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**The Christchurch Approach to Diagnostic Testing**

• Sputum samples will be tested for *Legionella* by PCR if there is any indication that the patient has pneumonia
  – clinical information on the requisition form containing the words “pneumonia” or “consolidation”
  – The patient is immunocompromised
  – *Legionella* or pneumococcal urine antigen testing has been requested from the same patient
  – *Legionella* PCR has been specifically requested
Legionnaires’ Disease Cases
Christchurch 2008-12

Diagnostic Strategy for Legionnaires’ Disease

- Should be informed by local epidemiology
- PCR is the diagnostic of choice
- Urinary antigen test used as the sole diagnostic only in regions where almost all cases are due to *L. pneumophila* serogroup 1
Know your local Legionnaires’ disease epidemiology

Legionellosis Notification Rates in New Zealand

- One third to one half of reported cases come from Canterbury
- Incidence rate in Canterbury is >3 times the national rate

New Zealand Legionnaires’ Disease Case Finding Study

Taking Canterbury’s Approach Nationwide

- 17 of 20 District Health Boards (20 hospitals)
- 96% of New Zealand population
- One year study period - ended 20 May 2016

Aims:
- To better characterise the national epidemiology of Legionnaires’ disease
- To inform regional testing and treatment protocols
- To assess cost-effectiveness of the testing strategy
Findings

- Notifications to Public Health Units have increased 2-3 fold
- Bay of Plenty region has the highest incidence of Legionnaires’ disease with ~9.8 cases per 100,000 population

Key Messages

- Legionnaires’ disease is not an atypical pneumonia
- Legionnaires’ disease is more than just about outbreaks and plumbing
- There are smarter ways of testing for Legionnaires’ disease
- Know your local epidemiology
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