Comparison of *Legionella longbeachae* and *Legionella pneumophila* cases in Scotland; implications for diagnosis, treatment and public health response

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The reported incidence of Legionnaires’ disease caused by *Legionella longbeachae* has increased since 2008 in Scotland. While microbiological and epidemiological studies have identified exposure to growing media as a risk factor for infection, little is known about the differences regarding disease risk factors, clinical features and outcomes of infection with *L. longbeachae* when compared with *L. pneumophila*. A nested case–case study was performed comparing 12 *L. longbeachae* cases with 25 confirmed *L. pneumophila* cases. Fewer *L. longbeachae* infected patients reported being smokers [27 % (95 % CI 2–52 %) vs. 68 % (95 % CI 50–86 %), \( P = 0.034 \)] but more *L. longbeachae* patients experienced breathlessness [67 % (95 % CI 40–94 %) vs. 28 % (95 % CI 10–46 %), \( P = 0.036 \)]. Significantly more *L. longbeachae*-infected patients received treatment in intensive care [50 % (95 % CI 22–78 %) vs. 12 % (95 % CI 0–25 %), \( P = 0.036 \)]. However, the differences in diagnostic methods between the two groups may have led to only the most severe cases of *L. longbeachae* being captured by the surveillance system. No differences were observed in any of the other pre-hospital symptoms assessed. Our results highlight the similarity of Legionnaires’ disease caused by *L. pneumophila* and *L. longbeachae*, and reinforce the importance of diagnostic tools other than the urinary antigen assays for the detection of non-*L. pneumophila* species. Unfortunately, cases of community-acquired pneumonia caused by *Legionella* species will continue to be underdiagnosed unless routine testing criteria changes.

**INTRODUCTION**

*Legionella pneumophila* is the most common cause of Legionnaires’ disease in countries worldwide, apart from Australia and New Zealand where *Legionella longbeachae* infection is more common (O’Connor et al., 2007; Graham et al., 2012). Since 2008 in Scotland, Legionnaires, disease cases caused by *L. longbeachae* have been reported every year, with peaks in incidence in 2013 and 2014 (Fig. 1). Previous studies have found that cases are commonly keen gardeners with exposure to plant-growing media (Pravinkumar et al., 2010; Potts et al., 2013). Indeed, in a survey of 24 bagged potting composts in the UK, 16 % of the plant-growing media contained *L. longbeachae* (Currie et al., 2014). The rest of the UK has not observed an increase in the incidence of *L. longbeachae* infection, most likely reflecting underascertainment, and the increase in Scotland is probably due to improved detection (Fig. 1).

Anecdotal reports from local health protection teams have suggested augmented virulence of infection with *L. longbeachae*. Accordingly, the aim of this study was to determine the differences, if any, to those infected with *L. pneumophila* in relation to patient characteristics, outcomes, signs and symptoms. It is important to appreciate these differences to aid in timely, appropriate diagnosis and the detection of potential outbreaks with resultant source elucidation (Pravinkumar et al., 2010; Potts et al., 2013).

**METHODS**

Health Protection Scotland (HPS) undertakes passive, enhanced national *Legionella* surveillance and collects demographic and clinical information on each Legionnaires’ disease case through collection of
Ten confirmed and two probable cases of *L. longbeachae* reported to HPS between 2008 and 2014 were identified according to the European Centre for Disease Prevention and Control (ECDC) case definitions (ECDC, 2012). According to ECDC definitions, all Legionnaires’ disease cases must have a clinical diagnosis of pneumonia (ECDC, 2012). Laboratory diagnosis is required to define Legionnaires’ disease cases must have a clinical diagnosis of pneumonia (ECDC, 2012). Laboratory diagnosis is required to define whether a case is confirmed or probable, with cases being confirmed if (i) *Legionella* is cultured from respiratory secretions or a normally sterile site; (ii) if *L. pneumophila* serogroup 1 antigen is detected in urine; or (iii) a case has a specific antibody response to *L. pneumophila* serogroup 1 (ECDC, 2012). A case is defined as probable if (i) *L. pneumophila* antigen is detected in respiratory secretions or lung tissue; (ii) *Legionella* nucleic acid is detected in a specimen; (iii) the patient has a specific antibody response to non-*L. pneumophila* serogroup 1; or (iv) a single high titre to a *Legionella* species (ECDC, 2012) is found. Additionally, a case can be defined as probable if it meets the clinical and epidemiological criteria of exposure to the same common source or environmental exposure. Epidemiological criteria are commonly utilized in outbreak situations. Cases included in the study were diagnosed through a combination of culture, serology, PCR and, in the situation of most *L. pneumophila* serogroup 1 cases, urinary antigen testing. In Scotland, the majority of clinicians utilize the urinary antigen assay routinely for diagnostic testing of suspected *Legionella* infection, however, clinical protocols in some NHS health boards alert clinicians to perform PCR and culture on samples from patients with severe pneumonia (HPS, 2014). Two *L. longbeachae* cases in this study were culture negative but, through a combination of *Legionella* species nucleic acid detection in respiratory secretions and evidence of an immune response (either a fourfold rise in titre or a single high titre of antibodies to *L. longbeachae*), these cases were identified as probable cases by the Scottish Haemophilus, Legionella, Meningococcus and Pneumococcus Reference Laboratory (SHLMPRL).

The 12 cases of *L. longbeachae* were compared with 25 confirmed cases of *L. pneumophila* reported to HPS between 2008 and 2014. These cases were also defined according to the ECDC classifications (ECDC, 2012). Cases of both *L. pneumophila* and *L. longbeachae* infection were excluded if pneumonia status and clinical date of onset were unknown or not reported, if symptoms were not recorded in the database or if the cases had travelled to another country two to ten days before onset of symptoms. As the majority of Legionnaires’ disease cases in Scotland are travel related, only a small number of cases were eligible for inclusion in the study. Further, *L. pneumophila* cases were excluded if they were part of an outbreak, as case definitions may have been altered during the incident. Data were entered into SPSS 21 (SPSS, Chicago IL) for analysis. Fisher’s exact test and the independent-samples t-test were undertaken to assess differences between cases, and *P*<0.05 was considered significant.

**RESULTS AND DISCUSSION**

Twenty-five *L. pneumophila* cases and 12 *L. longbeachae* cases were included in the study. The majority of cases were male in each group and the mean age was 58 years and 66 years for *L. pneumophila* and *L. longbeachae* cases, respectively. Excluding the year 2012, when a large outbreak of Legionnaires’ disease occurred in Edinburgh, the average annual incidence of Legionnaires’ disease since...
2005 in Scotland is 6.4 cases per million population. This is smaller than the annual incidence in Europe, which is approximately 11 cases per million population, but is higher than the average incidence reported in England and Wales for the last three years (5.4 cases per million population) (ECDC, 2014; PHE, 2015).

From our analysis, significantly more *L. pneumophila*-infected patients reported being smokers compared with patients infected with *L. longbeachae* (Table 1). This is consistent with an early Australian study (Cameron et al., 1991), but differs from the results of a New Zealand study comparing *L. longbeachae* with *L. pneumophila* cases which found no difference in smoking status between cases (Amodeo et al., 2010). Half of the individuals infected with *L. longbeachae* were treated in intensive care, which was significantly more than the 12 % (95 % CI 0–25 %) of *L. pneumophila* cases. *L. longbeachae* cases were older than *L. pneumophila* cases, but this was not significant. Significantly more *L. pneumophila*-infected patients reported breathlessness, but no differences were observed in any other pre-hospital symptoms. These results are consistent with the findings of the aforementioned New Zealand study that found little difference in clinical features between cases of *L. longbeachae* and *L. pneumophila* (Amodeo et al., 2010). Most cases in both groups had a date of onset in the spring or summer months (March to August), and there was no significant difference in the time of year of onset for cases. The proportion of deaths was comparable between the two groups, and the proportion of patients with underlying conditions was similarly high in both groups.

Smoking is a risk factor for infection with both *L. pneumophila* and *L. longbeachae* (Fields et al., 2002; O’Connor et al., 2007); however, our study suggests that smoking may be less influential in *L. longbeachae* infection. More *L. longbeachae*-infected individuals were treated in intensive care, suggesting that disease may be more severe in this group. However, differences between the two groups are difficult to interpret due to both the small sample size, which is reflected in the wide confidence intervals, and the differences between the diagnostic methods utilized to confirm infection, which are discussed later.

This study has several limitations, of which small sample size is a particular issue. Reporting bias is a concern as this study relied on data collected through surveillance forms in which some signs and symptoms may not have been reported but were experienced by the patient, leading

### Table 1. Characteristics, clinical symptoms and outcome of patients infected with *Legionella pneumophila* and *Legionella longbeachae*

| Characteristics          | *L. pneumophila* n=25 | *L. longbeachae* n=12 | \(P\)  
|--------------------------|-----------------------|-----------------------|--------  
| Mean age (years)         | 58 (SD 11.4)          | 66 (SD 10.9)          | 0.058‡  
| Diagnosis by culture     | 7 (28 % [95 % CI 10–46 %]) | 10 (83 % [95 % CI 62–100 %]) | –      
| Pneumonia                | 25 (100 %)            | 12 (100 %)            | 1      
| Patient characteristics  |                       |                       |         
| Male                     | 16 (64 % [95 % CI 45–83 %]) | 9 (75 % [95 % CI 51–100 %]) | 0.711  
| Smoker                   | 17 (68 % [95 % CI 30–86 %]) | 3 (27 % [95 % CI 2–52 %])* | 0.034  
| Chronic condition§       | 18 (72 % [95 % CI 54–90 %]) | 10 (83 % [95 % CI 62–100 %]) | 0.687  
| Immunocompromised        | 6 (26 % [95 % CI 9–43 %]) | 3 (27 % [95 % CI 2–52 %])† | 1      
| Onset in summer          | 16 (64 % [95 % CI 45–83 %]) | 8 (67 % [95 % CI 40–94 %]) | 1      
| Treatment in intensive care | 3 (12 % [95 % CI 0–25 %]) | 6 (50 % [95 % CI 22–78 %]) | 0.036  
| Signs and symptoms       |                       |                       |         
| Fever                   | 10 (40 % [95 % CI 21–59 %]) | 3 (25 % [95 % CI 1–50 %]) | 0.476  
| Chest pain              | 6 (24 % [95 % CI 7–41 %]) | 2 (17 % [95 % CI 0–38 %]) | 1      
| Cough                   | 13 (52 % [95 % CI 32–72 %]) | 7 (58 % [95 % CI 30–86 %]) | 1      
| Confusion               | 8 (32 % [95 % CI 14–50 %]) | 2 (17 % [95 % CI 0–38 %]) | 0.445  
| Gastrointestinal        | 11 (44 % [95 % CI 25–63 %]) | 2 (17 % [95 % CI 0–38 %]) | 0.149  
| Headache                | 4 (16 % [95 % CI 2–30 %]) | 0 (0) | 0.282  
| Lethargy                | 8 (32 % [95 % CI 0–19 %]) | 3 (25 % [95 % CI 1–50 %]) | 1      
| Breathlessness           | 7 (28 % [95 % CI 10–46 %]) | 8 (67 % [95 % CI 40–94 %]) | 0.036  
| Muscle pain             | 7 (28 % [95 % CI 10–46 %]) | 1 (8 % [95 % CI 0–23 %]) | 0.232  
| Collapse                | 2 (8 % [95 % CI 0–19 %]) | 1 (8 % [95 % CI 0–23 %]) | 1      
| Outcome                 | 4 (16 % [95 % CI 2–30 %]) | 3 (25 % [95 % CI 1–50 %]) | 0.659  

*Missing for one case.
‡Missing for three cases.
§Independent-samples *t*-test.
§Defined as a case with a chronic condition that may have increased their risk of Legionnaires’ disease before admission to hospital.
to inflation of the differences between cases. This is particularly true for signs and symptoms or characteristics requiring self-reporting from patients. Furthermore, smoking history of cases was self-reported. Differences in the sensitivity of different methods of diagnosis may also have led to misclassification of some cases, especially as the proportion of cases confirmed with \( L. \) pneumophila using culture is not comparable to \( L. \) longbeachae-infected cases (Table 1). \( L. \) pneumophila serogroup 1 can be diagnosed with relative ease using the urinary antigen assay, which does not detect \( L. \) longbeachae, and the diagnosis of infection with \( L. \) longbeachae (and other Legionella species) requires a sputum sample. A sputum sample is most readily obtained in intensive care, and therefore the observation that more \( L. \) longbeachae patients were treated in intensive care may be subject to bias.

The similarity of clinical symptoms between cases infected with \( L. \) longbeachae and \( L. \) pneumophila highlights the need for the widespread use of diagnostic tests other than, or in conjunction with, the urinary antigen assay, which cannot detect \( L. \) longbeachae or other non-\( L. \) pneumophila species, particularly since our findings suggest that patients infected with \( L. \) longbeachae present with disease severity comparable to \( L. \) pneumophila infection. Serum and respiratory secretions from patients with moderate to severe community-acquired pneumonia and no discernible cause should be sent for PCR and culture, particularly if the case has a connection to gardening (Pravinkumar et al., 2010). Earlier detection would reduce delays in targeted, optimal treatment, for while current empirical therapy for severe community-acquired pneumonia (a combination of a macrolide and a \( \beta \)-lactam) is active against Legionella species, animal studies and a recent systematic review and meta-analysis suggest that fluoroquinolones may have higher activity against Legionella species (Burdet et al., 2014; Pedro-Botet and Yu, 2006). Indeed, while more research is required to fully elucidate the clinical significance, fluoroquinolones are the recommended choice of antimicrobial for treatment of Legionnaires’ disease in the British Thoracic Society’s guidelines for the management of pneumonia (Lim et al., 2009). The use of diagnostic methods other than the urinary antigen test will also aid in the timely detection of non-\( L. \) pneumophila serogroup 1 strains and other Legionella species in outbreak and environmental investigations. The various systemic symptoms experienced by patients with Legionnaires’ disease also highlights that supportive therapies, including rehydration therapy and pain relief, are important for successful clinical management.

Legionnaires’ disease caused by non-\( L. \) pneumophila species in Scotland is most likely under-ascertained, especially in regions where respiratory samples are not routinely taken for culture and PCR. A recent study performed in New Zealand reported a fourfold increase in the number of cases of Legionnaires’ disease following the implementation of the routine use of PCR on samples from patients hospitalized with pneumonia, and highlights the level of under-ascertainment (Murdoch et al., 2013). Under-ascertainment of disease caused by Legionella species may also have implications for public health action and understanding the epidemiology of Legionnaires’ disease, and could lead to patients receiving suboptimal antimicrobial therapy regardless of the causative species. It is clear that additional research is needed to fully understand Legionnaires’ disease caused by non-\( L. \) pneumophila species. The widespread utilization of diagnostic methods other than the urinary antigen assay should facilitate this.

**REFERENCES**


Results from a *Legionella longbeachae* case-control study in South Australia. *Epidemiol Infect* 135, 34–39.


