Investigation of an outbreak of Legionnaires’ disease: Hereford, UK 2003

David Kirrage\textsuperscript{a}, Gary Reynolds\textsuperscript{a}, Gillian E. Smith\textsuperscript{b}, Babatunde Olowokure\textsuperscript{b,*}, for the Hereford Legionnaires Outbreak Control Team\textsuperscript{1}

\textsuperscript{a}Health Protection Agency, Hereford and Worcestershire Health Protection Unit, Issac Maddox House, Shrub Hill Road, Worcester WR4 9RW, UK
\textsuperscript{b}Health Protection Agency, Regional Surveillance Unit (West Midlands), 9th Floor, Ladywood House, 45 Stephenson Street, Birmingham B2 4DY, UK

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Summary
This report describes the investigation and control of a community outbreak of Legionnaires’ disease in Hereford, UK, in November 2003. Outbreak investigation consisted of epidemiological survey, identification and environmental investigation of potential sources, microbiological analysis of clinical and environmental samples and mapping the location of potential sources and the movement and residence of cases. Each identified source was allocated a ‘composite score’ based on different zones of exposure and wind direction. Altogether, 28 cases were identified, with an overall case fatality rate of 7%. All cases had epidemiological links to Hereford city centre. The ‘composite score’ identified a cluster of cooling towers as being the most likely source of the outbreak. Environmental samples from one of the cooling towers in the cluster and clinical samples from two patients were positive for \textit{Legionella pneumophila} serogroup 1 and were indistinguishable by molecular sub-typing. In this outbreak, the use of microbiological, environmental and epidemiological techniques facilitated the rapid identification of a cooling tower as the source of this outbreak. This study illustrates the continuing importance of cooling towers.

\*Corresponding author. Tel.: +44 121 634 8757; fax: +44 121 634 8702.
E-mail address: babatunde.owolokure@hpa.org.uk (B. Olowokure).

\textsuperscript{1}Hereford Legionnaires’ Outbreak Control Team: Health Protection Agency, Hereford and Worcestershire Health Protection Unit: Joan Lewis, Darryl Pemnells, and Alan Tweddell. Herefordshire Council, Environmental Health Department, Hereford: Paul Nicholas and David Stacey. Hereford Hospitals NHS Trust, Microbiology Laboratory, County Hospital, Hereford: Tim Coleman, Gill Hill, Mary McDonald, and Jane Simmons. Herefordshire Primary Care Trust, Hereford: Mike Deakin. West Midlands South Strategic Health Authority, Redditch: Sue Ibbotson. Health Protection Agency, Regional Surveillance Unit (West Midlands): Adam Bodley-Tickell, David Hunt, and Yasmin Rehman. Health Protection Agency, Local and Regional Services: Jeremy Hawker and Brian McCloskey. Health Protection Agency, Centre for Infections: Tim Harrison, Carol Joseph, and John V. Lee.
Introduction

Legionnaires’ disease (LD) is an environmentally acquired bacterial pneumonia caused by Legionella species which are widely distributed in man-made and natural environments.\(^1\)\(^2\) Transmission of the disease may, in susceptible people, follow inhalation of aerosol contaminated with Legionella.\(^3\) Documented sources of contaminated aerosols include cooling towers, fountains, showers, water taps and whirlpool spas.\(^4\)\(^\_\)\(^11\)

This paper describes an outbreak of LD that occurred in October 2003 in Hereford, a city in a mainly rural part of the West Midlands region, UK. At the time of the outbreak the estimated population of Hereford was 177,000 persons.\(^12\)

On 24 October 2003 the Consultant in Communicable Disease Control (CCDC) for Herefordshire was informed of a case of LD in an elderly man from Hereford City who subsequently died. On 27 October the CCDC was informed by the local microbiology laboratory of a further case in an elderly lady from a village 3 miles from the city. The diagnosis in this case was made following a post-mortem. The two cases were investigated for evidence of a common link. Other than a close association in time and place, no common factors were detected.

As a result of active case-finding, on 6 November two inpatients at the local hospital tested positive for Legionella urinary antigen. A multidisciplinary Outbreak Control Team (OCT) was convened that day involving members of the newly formed Health Protection Agency (HPA) as well as the Primary Care Trust, Hereford County hospital, and Local Authority. The purpose of the OCT was to formally declare an outbreak, define the magnitude of the outbreak, prevent further transmission and investigate the source of infection. Over the next 3 weeks a further 24 cases of LD were reported to the OCT as a result of active case finding including retrospective testing of patients admitted to the local acute district hospital with pneumonia. The outbreak received extensive television and print media coverage.\(^13\)\(^\_\)\(^15\) This paper describes the results of the investigation.

Methods

Epidemiologic investigation

The OCT agreed that the case definitions for LD of the HPA should be used for the investigation of this outbreak (Table 1).\(^16\)

LD is not statutorily notifiable in England and Wales therefore cases were identified prospectively and retrospectively by reviewing laboratory reports and medical records to identify all persons with pneumonia since 1 August 2003. The case notes of suspected patients were abstracted and reviewed to identify those who had a community-acquired pneumonia or a diagnosis of LD. Those persons deemed retrospectively to be suspect cases were contacted via their general practitioner and serum and urine samples collected for testing. Additionally, local general practitioners, clinicians in neighbouring hospitals, and public health colleagues throughout England and Wales were alerted to the outbreak and asked to forward details of cases that met the case definitions to the OCT.

To try and identify the source of the outbreak, investigators interviewed all cases (or a proxy) using a questionnaire based upon the Legionella questionnaire of the HPA. Information was collected on aspects such as predisposing risk factors, demographic factors, recent movements within and outside Hereford and specific visits or proximity to an aerosol-generating system (such as domestic potable water system, cooling towers, decorative fountains or car washes) during a 14-day period up to and including the day of onset of symptoms. The information obtained from each case was then used to generate hypotheses about potential sources of exposure. For all cases interviews were conducted as soon as possible after the case had been identified. Time to interview after identification varied for those identified retrospectively (after the outbreak investigation had started) but was within a few days of diagnosis for those identified prospectively.

Patient data were collected and validated by the outbreak team, entered and stored on a Microsoft Access database and analysed using Epilinfo version 6. The locations of cooling towers in and around Hereford city centre were obtained from a register supplied by the Local Authority. Postcode data for cooling towers and residences of cases were mapped using a Geographical Information System (GIS), MapInfo. Distances between place of residence of cases and the nearest cooling tower were documented.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Confirmed case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>Clinical diagnosis of pneumonia</td>
</tr>
<tr>
<td>Date of onset</td>
<td>After 1st October 2003</td>
</tr>
<tr>
<td>Epidemiologic</td>
<td>Lived in, worked in or had visited Hereford within 2 weeks of the date of onset of their disease</td>
</tr>
<tr>
<td>Laboratory</td>
<td>Isolation of Legionella species from clinical specimens; or a four-fold or greater increase in the titre of serum antibodies against L. pneumophila serogroup by indirect immunofluorescent antibody test (IFAT); or the detection of Legionella antigens in urine</td>
</tr>
</tbody>
</table>

Table 1 Criteria used for case definitions in the Hereford 2003 Legionnaires’ outbreak.\(^16\)
Microbiological investigation

The Department of Microbiology and Immunology, County Hospital, Hereford analysed all clinical specimens. Urine samples were tested for _L. pneumophila_ antigen using a commercial enzyme immunoassay kit (Bartels ELA kit, Intracel, USA). According to standard HPA procedures for the identification of _Legionella_, sputum samples were plated directly onto selective media. Specific antibody levels were assessed using indirect fluorescent antibody test (IFAT) at the reference laboratory for _Legionella_ in the UK, the HPA Respiratory and Systemic Infection Laboratory (RSIL), Specialist and Reference Microbiology Division (SRMD).

Environmental samples obtained were water and swabs taken from devices that could have supported the growth of _Legionella_ species. The water samples were processed in the Food, Water and Environmental Laboratory (FWE), Department of Microbiology and Immunology, County Hospital, Hereford and referred to the reference laboratory, the HPA FWE Unit, Colindale. The swabs were referred to RSIL, Colindale for PCR and direct immunofluorescence.

Environmental investigation

Environmental investigations focused on cooling towers as the potential source of exposure and registers held by the local environmental health department were examined to identify buildings with aerosol-producing devices. Identified premises or cooling towers located within 1000 m of the city centre were targeted first followed by others located beyond 1000 m. Investigators attempted to identify unregistered premises through a variety of methods including inspection from suitable vantage points.

Several sites with potential aerosol-generating systems, such as domestic potable water systems, cooling towers, car washes, decorative fountains, supermarket food display units with a humidifier and whirlpool spas on display were identified based on the environmental investigation and the information obtained from case questionnaires. These sites were visited, the maintenance procedures and logs were examined, the cooling towers inspected and samples taken. Advice was given to those responsible for the towers to have them decontaminated immediately with biocidal agents. Investigators identified whether or not the cooling towers had been running continuously. Enquiries were also made about the respiratory health status of employees at these sites. Most of the activities associated with the environmental investigation occurred between 5 and 12 November. Further environmental investigations were carried out as more information became available.

Environmental risk assessment

The GIS database was used to produce maps showing the location of potential sources, cases' residential location and movements, and meteorological data. Information on case movements obtained from the questionnaires were transcribed into the GIS system then mapped to provide a pictorial representation of each case’s daily movements for 14 days prior to and including the date of onset of illness. On the basis of the results obtained, seven sites of interest (called A–G) were identified. Site B had two main congregations of cooling towers and these were designated B1 and B2.

To define the area of potential exposure, circles equivalent to 250, 500 and 1000 m were drawn centred on each of the hypothetical sources. A ‘composite score’ was then calculated for each source by allocating one point to each source for each of the cases who had been either: (i) within 500 m of the source; or, (ii) downwind within 1 km from the source at any time during their incubation period. Therefore, the maximum ‘score’ for each hypothetical source was 56 points (28 cases).

Data on the potential sources were input to a Microsoft Excel spreadsheet prior to analysis in EpilInfo version 6. Data are presented as frequencies and proportions with 95% confidence intervals (CIs). When cooling towers were compared, if the 95% CIs for the composite score did not overlap, then the differences between the cooling towers were considered to be statistically significant.

Environmental health officers obtained meteorological data from a local school’s weather station. Wind direction and velocity data for half hour periods from the end of September until mid-November were incorporated into the GIS database. Comparison with data produced by a weather station at another site situated approximately 1 km from the city centre showed sufficient correlation between the two data sets to assume that the data obtained from the school was valid. Further data and advice was obtained from the National Meteorological Office.

We explored the relationship between daily movements and wind direction and mapped all cases for the relevant days they entered the area around the hypothetical sources. We assessed whether they would have been downwind within 1 km from the hypothetical source.

Results

Case finding and descriptive epidemiology

Altogether, 28 epidemiologically linked cases met the confirmed case definition. The dates of onset of disease ranged from 8 October to 20 November 2003. The median age of the 28 cases was 59.5 years (range, 36–91 years) and 21 (75%) were male. All cases had a positive _Legionella_ urinary antigen (LP1) test. In addition, four cases had a single high titre for _Legionella_ antibody and two cases were culture positive. Twenty-three cases (82%) were admitted to hospital and five cases were treated at home. Two hospitalised cases died, therefore the case fatality rate was 8.7% for hospitalised confirmed cases and 7.1% for all confirmed cases. Eight cases (28.6%) had underlying conditions including: two diabetics, three asthmatics, and one with chronic obstructive airways disease, two other cases were reported as being immunosuppressed. Eighteen cases (64%) smoked, six cases were ex-smokers and four cases were recorded as having never smoked. None of the cases had travelled abroad in the 2 weeks before onset.
Environmental inspection and microbiological results

The epidemiological interviews identified a possible link with Hereford city centre. Twenty-three (82%) of the 28 confirmed cases lived within the boundaries of Hereford City, another two lived in Herefordshire county and had visited or been in the vicinity of the city centre. Of the three remaining cases: two were visitors from Wales and both had visited Hereford on one occasion during their incubation period, one on 23 October (date of onset 3 November) and one on 26 October (date of onset 3 November); the third non-Herefordshire resident visited Hereford on two occasions, 25 October and 1 November (date of onset 7 November). The OCT therefore decided to focus the investigation on potential sources of transmission in and around the city centre.

Altogether, thirty premises were inspected of which six were domestic potable water systems. The environmental investigation also identified 24 business premises with aerosol-producing devices such as cooling towers, decorative fountains, whirlpool spas on display and supermarket food display units with a humidifier. These were assessed to determine their compliance with operating regulations. Following inspection, including examination of maintenance records, sampling was carried out and, immediate decontamination undertaken for all cooling towers. A total of 142 samples were taken from all premises visited. Of these 111 were taken from 50 cooling towers on 11 premises. LP1 was found at three installations within two sites, two cooling towers and a domestic spa pool. Both cooling towers were at site B1. Although the cooling towers at this site had previously been ‘decontaminated’ on 6 November, it was discovered that the biocidal dosing had been sub-optimal. Additionally, the cooling towers were only used seasonally and had been started-up in late autumn. This is consistent with the commencement of the outbreak. The cooling towers were closed down on 12 November and an extensive examination of the towers was undertaken as well as further samples taken. Two samples taken from one of the towers confirmed the presence of *L. pneumophila* in numbers of colony forming units greater than $10^6$ per litre.

Molecular typing was undertaken on the LP1 isolates from the towers and compared with the clinical isolates from two cases. The DNA profiles of the clinical isolates were indistinguishable and matched those obtained from the cooling towers at B1. The isolate from the domestic spa pool tested positive for LP1 but no further testing was conducted given that the epidemiological investigation pointed towards Hereford City Centre as the most probable source of infection.

Environmental risk assessment

Based on the descriptive epidemiology, almost all cases lived or had travelled within 500 m of site A and site B. Site B has two main congregations of cooling towers (B1 and B2). The composite score, defined by distance and being downwind of the suspected source (Table 2), showed that sites A, B1 and B2 had significantly more cases living or travelling within 500 m and who had been downwind of them than all other suspect sources. This is reflected in the composite score for B1 shown in Table 2, which is 53 (94.6%, 95% CIs 85.1%–98.9%). For source B2 the composite score of 52 (92.9%, 82.7%–98.0%) may reflect its close geographic proximity to B1. Despite a concerted effort early in the investigation, site A revealed no suspicious wet systems.

Discussion

LD was confirmed in 28 people who lived, visited or passed within 500 m of Hereford city centre between 8 October and 20 November 2003. Linking together the results from the epidemiological, environmental and microbiological investigations of this outbreak suggested that contaminated aerosols from cooling towers at site B1 were responsible.

*L. pneumophila* are biological contaminants present in cooling towers, however, despite strict regulations concerning the operation and maintenance of cooling towers, they are a recognised source of transmission of LD and outbreaks have been associated with towers that are inadequately maintained or restarted after a period of being shut-down. The results of this investigation support these previous reports and indicate that the onset of disease in the first case coincided with the restarting of a cooling tower that had been inoperative for a while. There were no further cases following closure and cleaning of the cooling tower.

### Table 2 Cooling towers that were identified as potential sources of the Hereford 2003 Legionnaires’ outbreak.

<table>
<thead>
<tr>
<th>Potential site/source of outbreak</th>
<th>No. (% 95% CI) cases within 500 m of source (n = 28)</th>
<th>No. (% 95% CI) cases downwind of source (n = 28)</th>
<th>Composite score (n = 56)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>26 (92.9, 76.5–99.1)</td>
<td>24 (85.7, 67.3–96.0)</td>
<td>50 (89.3, 78.1–96.0)</td>
</tr>
<tr>
<td>B1**</td>
<td>26 (92.9, 76.5–99.1)</td>
<td>27 (96.4, 81.7–99.9)</td>
<td>53 (94.6, 85.1–98.9)</td>
</tr>
<tr>
<td>B2**</td>
<td>25 (89.2, 71.8–97.7)</td>
<td>27 (96.4, 81.7–99.9)</td>
<td>52 (92.9, 82.7–98.0)</td>
</tr>
<tr>
<td>C</td>
<td>10 (35.7, 18.6–55.9)</td>
<td>26 (92.9, 76.5–99.1)</td>
<td>36 (64.3, 50.4–76.6)</td>
</tr>
<tr>
<td>D</td>
<td>4 (14.3, 4.0–32.7)</td>
<td>26 (92.9, 76.5–99.1)</td>
<td>30 (53.6, 39.7–67.0)</td>
</tr>
<tr>
<td>E</td>
<td>4 (14.3, 4.0–32.7)</td>
<td>28 (100.0, 87.7–100.0)</td>
<td>32 (57.1, 43.2–70.3)</td>
</tr>
<tr>
<td>F</td>
<td>10 (35.7, 18.6–55.9)</td>
<td>25 (89.2, 71.8–97.7)</td>
<td>35 (62.5, 48.5–75.1)</td>
</tr>
<tr>
<td>G</td>
<td>5 (17.9, 6.1–36.9)</td>
<td>28 (100.0, 87.7–100.0)</td>
<td>33 (58.9, 45.0–71.9)</td>
</tr>
</tbody>
</table>

*Composite score: obtained by adding score from previous two columns.
**B1 and B2: two clusters of cooling towers on a single site.
The initial investigation of this outbreak was challenging due to the large number of potential sources of environmental contamination located in and around the city centre and the wide-ranging movement of cases. The use of a ‘composite score’ in this outbreak was an innovative attempt by the OCT to identify the source of the outbreak by quantifying the risk of exposure from each potential source using proximity and meteorological data. The composite score was significantly higher for three of the suspect sources and the use of microbiological data enabled the investigation to focus on one particular source. A number of studies have also examined proximity to the source as a measure of risk, including some that have attempted to incorporate the duration of time spent within certain zones in order to determine a dose–response effect. In this study a formal evaluation of the association between disease and time spent at various suspected locations was not conducted. However, the results obtained suggest that even transient exposure downwind of the source was enough to result in infection in some susceptible people. The results obtained using the composite score as a proxy for identifying potential sources of Legionella transmission require corroboration from additional studies.

The diagnosis of LD requires laboratory confirmation and in this outbreak urinary antigen testing was used to confirm the diagnosis in all 28 cases with subsequent culture confirmation in only two cases. It is important to recognise the limitations of the urinary antigen test. Although providing rapid diagnostic identification that aids clinical management and the possibility of timely public health action, it is valid only for LP1 and a small number of other Legionella species. Additionally, although highly specific, a negative result does not exclude Legionella infection particularly if the specimen is collected in the first week after onset of illness. Clinicians should therefore be encouraged to obtain respiratory specimens for culture in addition to using the urine antigen test. Sole reliance on the results of urinary antigen testing leads to underdiagnosis of other forms of Legionella and may hamper public health investigation and control of an outbreak. In this outbreak, as in previous instances, the availability of cultures from both clinical and environmental isolates and their comparison using molecular typing permitted definite identification of the source of this outbreak and the rapid institution of public health action.

In summary, this multidisciplinary investigation combined epidemiological, environmental and microbiological approaches and demonstrated that the source of this outbreak was a cooling tower. The results of this investigation suggest that obtaining, typing and comparing environmental and clinical specimens is of critical importance in the public health investigation of Legionnaires’ outbreaks and greatly improves the outcome of outbreak investigations.

Acknowledgement

We gratefully acknowledge the contribution of all those who participated in bringing this outbreak under control.


