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Community-acquired Legionnaires' Disease in Nottingham – too many cases?

W. S. LIM[1]*, R. SLACK[2], A. GOODWIN[2], J. ROBINSON[3], J. V. LEE[4], C. JOSEPH[5] AND K. NEAL[6]

[1] *Respiratory Medicine, Nottingham City Hospital, Hucknall Road, Nottingham NG5 1PB*
[2] *Nottingham Health Protection Unit, Standard Court, Nottingham NG1 6GN*
[3] *Nottingham Health Informatics Service, 1 Standard Court, Nottingham NG1 6GN*
[4] *Water and Environmental Microbiology Reference Unit, Health Protection Agency, 61 Colindale Avenue, London NW9 5EQ*
[5] *Communicable Disease Surveillance Centre, Health Protection Agency, 61 Colindale Avenue, London NW9 5EQ*
[6] *Division of Public Health Sciences, University of Nottingham Medical School, Clifton Boulevard, Nottingham NG7 2UH*

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SUMMARY

The aim of this study was to compare the incidence of community-acquired Legionnaires' Disease in Nottingham with England and Wales and to explore reasons for any difference observed. Based on data from the National Surveillance Scheme for Legionnaires' Disease (1980–1999), the rate of infection in England and Wales was 1·3 per million/year compared with 6·6 per million/year in Nottingham. Domestic water samples were obtained from 41 (95%) of 43 Nottingham cases between 1997 and 2000. In 16 (39%) cases, *Legionella* sp. were cultured in significant quantities. Proximity to a cooling tower was examined using a 1:4 case-controlled analysis. No significant difference in the mean distance between place of residence to the nearest cooling tower was noted (cases 2·7 km *vs.* controls 2·3 km; $P=0·5$). These data suggest that Nottingham does have a higher rate of legionella infection compared to national figures and that home water systems are a source.

INTRODUCTION

Legionnaires' Disease (LD) was first described in England in a patient admitted to the Nottingham City Hospital (CHN) with severe pneumonia in June 1976 [1]. By October 1978, 41 patients with features suggestive of LD were identified, 21 from Nottingham. In 1981, a 13-month prospective study of 127 patients admitted to CHN with community-acquired pneumonia (CAP) identified 19 (15%) cases of LD while a further study of 42 patients with CAP in 1983 identified 2 (5%) cases of LD [2, 3]. Based on records held by the Nottingham PHLS, a total of 79 cases of LD were identified between 1972 and 1984, most occurring between 1977 and 1981 [4]. In contrast, since 1980, the annual number of cases of LD in England and Wales reported to the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC) has ranged from 112 to 279, travel-associated and community-acquired cases each accounting for 46% [5]. Although Nottingham had a relatively large nosocomial outbreak in 1988–1989 with twelve cases associated with domestic hot-water supplies at Queen's Medical Centre there have been no subsequent documented outbreaks [6].

The aim of this study was to determine whether Nottingham has a higher incidence of LD compared to England and Wales and to explore reasons for any difference observed.

* Author for correspondence.

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METHOD

In 1979, the National Surveillance Scheme for Legionnaires' Disease in Residents of England and Wales was set up at the PHLS Communicable Disease Surveillance Centre (CDSC). Cases of LD are reported to the scheme voluntarily by PHLS, NHS or private hospital laboratories; consultants in communicable disease control (CCDC); and other health-care workers. Clinical and epidemiological information is obtained for each case using follow-up questionnaires sent to reporting doctors. Agreed case definitions for LD and other forms of legionellosis including travel-associated cases are used [5]. Briefly, cases are defined by clinical or radiological evidence of pneumonia and a microbiological diagnosis by culture of the organism from respiratory specimens, a fourfold rise in serum antibody levels against *L. pneumophilia* serogroup (sg) 1, or detection of *L. pneumophilia* antigen in urine. Alternatively, presumptive cases require clinical or radiological evidence of pneumonia and a microbiological diagnosis of a single high antibody level against *L. pneumophilia* sg 1 or a seroconversion demonstrated against *Legionella* sp. and serogroups other than *L. pneumophilia* sg 1. Travel-associated cases are defined by one or more overnight stays in holiday accommodation in the United Kingdom or abroad during the 10 days before the onset of illness. Using this national database, rates of infection for Nottingham (based on post code data) were estimated using Office of National Statistics population figures for years 1981, 1986, 1991 and 1996 as appropriate and compared to rates of infection for England and Wales. Cases linked to the same outbreak were considered as single cases when calculating rates of infection.

Nottingham cases

Beginning in 1996, the residences of all cases of LD in Nottingham were routinely visited by an Environmental Health Officer within 2 weeks of diagnosis and water samples from multiple sites, including hot- and cold-water taps in toilets, baths and kitchens, WC cisterns and cold-water storage cisterns, were collected where possible, for the detection of the presence of legionella. These tests were performed at the Water and Environmental Microbiology Research Unit, PHLS, Nottingham. The detection limit was specified as 100 bacteria per litre of water (although lower numbers are reported if detected). Water supplies that tested positive were considered to be implicated as the source of infection.

In order to determine whether cooling towers might be the source of infection in cases of community-acquired LD in Nottingham where domestic water supplies were not implicated, a case-control study was conducted. Cases comprised community-acquired LD diagnosed between 1997 and 2000 where no known source of infection was identified. Four controls, matched by date of birth and sex, were randomly selected from persons registered with the same General Practitioner as each case. Cooling tower locations in Nottingham were obtained from the register supplied by local city councils. Using post code data, locations of cooling towers and residences of cases and controls were mapped to within an area of 50 m using Map Info Professional 6.6. Distances between place of residence of cases and controls, and the nearest cooling tower were compared.

Statistical analysis

Databases were analysed using Excel spreadsheets and SPSS Version 8.0 for Windows. Categorical variables were compared using χ^2 tests while continuous variables were compared using t tests. A P value of $<0{\cdot}05$ was considered statistically significant.

RESULTS

LD in England and Wales from 1980 to 1999

A total of 3714 cases of LD were reported to the CDSC from 1980 to 1999, giving an estimated rate of infection of 3·6/1 000 000 per year. Mean age of cases was 54·5 years and 2721 (73%) were male (Table 1). There were only nine cases aged 15 years or less. An association with recent travel in the last 10 days was noted in 1739 (47%) cases and infection was deemed to have been acquired nosocomially in a further 315 (8·5%). Estimated rates for non-travel community-acquired, nosocomial, and travel-associated infection were 1·6, 0·3 and 1·7/1 000 000 per year respectively. Overall mortality was 13·2%, the highest mortality seen in patients with nosocomial infection (28%). These patients were also significantly older than patients with community-acquired (travel- and non-travel-associated) infection.

Non-travel community-acquired cases

Of the 1677 community-acquired cases, 373 (22%) were linked to 67 outbreaks. Therefore, the rate of

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Table 1. *LD in England and Wales from 1980 to 1999 (n=3714)*

Type of infection	Total no.	Total deaths (%)	Male (%)	Age range (years)	Age not recorded	Mean (S.D.) age (years)
Non-travel, community	1677	204 (12·2)	1294 (77·2)	1–93	80	52·4 (14·2)*
Nosocomial	315	87 (27·6)	202 (64·1)	1–95	9	57·3 (16·2)†
Travel associated	1739	201 (11·6)	1242 (71·4)	10–93	21	55·7 (12·3)
All	3714	489 (13·2)	2721 (73·3)	1–95	110	54·4 (13·7)

* $P<0·001$ (comparison between non-travel and both nosocomial and travel associated cases).
† $P=0·008$ (comparison between nosocomial and travel associated cases).

Table 2. *Rates of community-acquired LD for Nottingham (Nott) compared to England and Wales (E&W), 1980–1999*

	Population*		No. of cases		Rates of infection (per 1 000 000/year)			
Years	E&W	Nott	E&W	Nott	E&W	95% CI	Nott	95% CI
1980–1984	49 592 900	606 900	372	8	1·5	1·3–1·7	2·6	0·8–4·5
1985–1989	50 075 400	616 400	530	8	2·1	1·9–2·3	2·6	0·8–4·4
1990–1994	51 099 500	625 700	282	16	1·1	1·0–1·2	5·1	2·6–7·6
1995–1999	52 010 160	640 485	475	52	1·8	1·7–2·0	16·2	11·8–20·6
Unknown			18					
Total			1677	84				

* Based on Office of National Statistics data for years 1981, 1986, 1991 and 1996.

infection calculated considering cases linked to the same outbreak as a single case, was 1·3/1 000 000 per year.

Post codes of places of residence were available in 329 (36%) of 902 cases diagnosed between 1980 and 1989 and in 598 (79%) of 757 cases diagnosed between 1990 and 1999). Based on documented post codes and using 1991 population figures (mid-point), the estimated rate of community-acquired LD in Nottingham over the time period 1980–1999, taking into account cases linked to outbreaks, was 6·6/1 000 000 per year. Rates of infection for nosocomial and travel-associated LD for the same period were 0·7 and 3·0/1 000 000 per year respectively. The higher rate of infection in Nottingham compared with England and Wales was evident throughout the 20-year period, with rates in Nottingham highest over the last 5 years (Table 2).

All primary diagnostic tests for LD are performed in Nottingham by a single public health laboratory situated at the Queen's Medical Centre, Nottingham. The variation in the number of serological tests for LD performed during 1990–1999 in Nottingham was relatively small. The larger number of tests performed in 1998 probably relates to a 1-year prospective study of the microbial aetiology of CAP that was conducted at CHN, one of the two large hospitals covering Nottingham. During the study, all patients admitted to CHN with suspected CAP had acute and convalescent serology for LD performed. Patients from the study alone would have accounted for approximately 500 tests.

Based on adult admissions to Nottingham with pneumonia, the ratio of LD tests performed to pneumonia admissions was about two each year from 1990 to 1998, with little variation observed (minumum 1·6 in 1994 and maximum 2·7 in 1992). This suggests that the use of tests for LD was consistent. In contrast, the ratio of LD tests to LD cases varied from 69 to 498. The observed increase in cases of LD in the late 1990s was not therefore matched by a corresponding increase in diagnostic testing (Fig. 1).

Case-control analysis: distance to nearest cooling tower (see Fig. 2)

Between January 1997 and April 2000, 43 cases of non-travel-associated community-acquired LD were reported to the CCDC, Nottingham. Domestic water supplies were analysed in 41 (95%) cases. Of the

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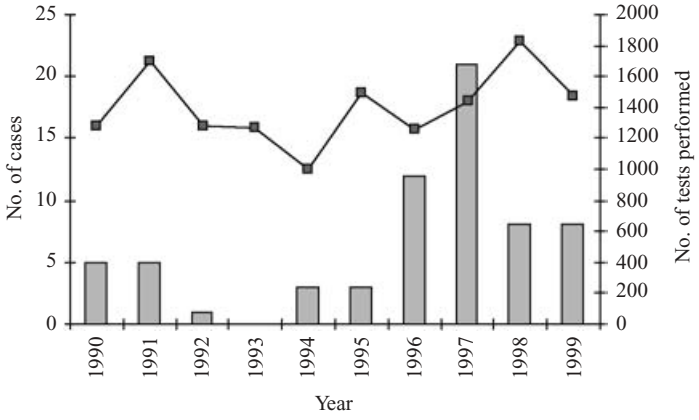

Fig. 1. Yearly variation in the number of cases of LD and number of tests performed in Nottingham (1990–1999) (bars = number of cases).

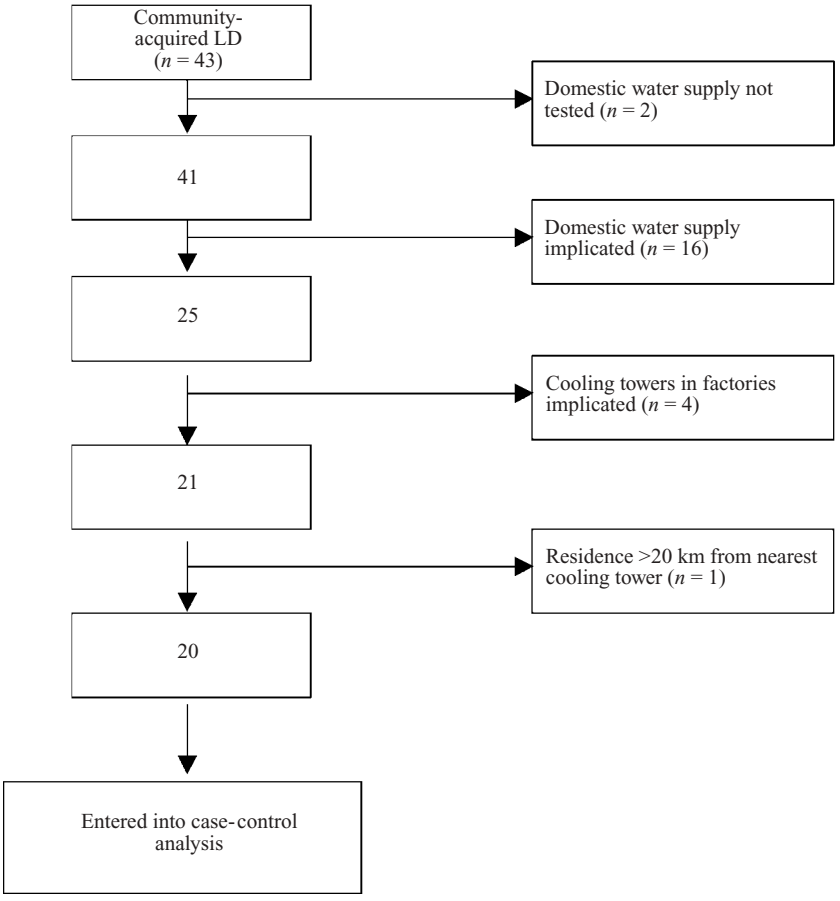

Fig. 2. Patient sample for case-control analysis.

41 households tested, *Legionella* sp. were cultured in significant quantities in 16 (39%). Of the remaining 25 cases, 15 occurred in 1997, 9 of these between June and September. Four of 25 patients worked in factories where cooling towers were identified as the source of infection. In the remaining 21 cases, no evidence of temporal or spatial (residential) clustering was evident. One of these cases lived more than 20 km away from the nearest cooling tower and was therefore omitted from the subsequent case-control analysis. The mean distance between place of residence of the 20 cases where no source of infection was identified to the nearest cooling tower was 2·7 km compared to 2·3 km for controls ($P = 0{\cdot}5$). Eleven controls

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lived within 600 m of a cooling tower compared with none of the cases.

DISCUSSION

The study data suggest that Nottingham has higher rates of LD than the rest of England and Wales. Some, but not all, of this may be explained by better case-ascertainment. The rate of infection of community-acquired LD in Nottingham from 1980 to 1999 was found to be 5 times higher compared with the national average rate for England and Wales while the rate of travel-associated LD was approximately 2 times higher. The incidence of many infectious diseases fluctuate over short periods of time. Short-term studies may therefore incorrectly ascribe temporal variations in incidence to geographical variation [7]. This study included a 20-year series with a consistent case definition for LD. A higher incidence in Nottingham compared to the rest of England and Wales was demonstrated throughout this period. Therefore, it is unlikely that the geographical variation observed was simply due to undetected temporal variation.

Possible biases

Ascertainment bias would be expected to impact on the numbers of community-acquired and travel-associated cases equally. Instead, the ratio of community-acquired compared to travel-associated LD in Nottingham is greater than 2 whereas nationally, this ratio has consistently been approximately 1, each year for over 20 years.

In addition, we note a temporal variation in the incidence of LD within Nottingham that does not vary in accordance with the number of LD tests performed. This finding reflects the experience reported elsewhere and argues against ascertainment bias as being the sole reason for the number of cases detected [8–10].

Reporting to the National Surveillance Scheme is voluntary and hence under-reporting may be expected. This may have led to an underestimate of the national figure in comparison to figures for Nottingham where strong local interest in LD has had a long history. Such reporting bias may be expected to have been most evident in the early years of the scheme when the benefits of active surveillance were less well appreciated and LD was a less widely recognized cause of respiratory illness. In contrast, we found that the difference in incidence of infection was greatest in the last decade compared to the 1980s. Of note, we found that in 1981, only 2 cases of LD in Nottingham were found on the national database whereas 19 cases were diagnosed as a result of a 13-month prospective study conducted in Nottingham at the time [2]. One explanation for this discrepancy may be the paucity of post-code data recorded in the national database in the early years, resulting in an underestimate of the number of cases identifiable as arising in Nottingham. The main tendency of such loss of data would be towards *lower* estimates of the rate of infection in Nottingham compared to national figures.

The ratio of LD tests performed to LD cases diagnosed was based on the absolute number of serological tests performed. Testing for legionella urinary antigen, which nationally was the single means of diagnosis in 52 (26%) of 201 cases in 1996 [5], only started to any substantial degree in Nottingham in 1998 when 676 tests were performed. This increased to 787 tests in 1999 when small numbers were performed for patients seen outside Nottingham. The impression is that in all instances where urine antigen testing was requested, as when respiratory specimens were submitted for direct fluorescent antibody test (DFAT) and culture, a sample for serological testing was also submitted. We were unable to confirm this practice using the current data. Nevertheless, it remains likely that the number of serological tests performed does indeed capture and reflect the number of patients suspected of LD and in whom microbiological investigations would have been requested.

Potential sources of legionella infection in Nottingham

Of 43 cases diagnosed between 1997 and 2000, no source of infection was identified in 53% despite rigorous efforts. Proximity of residence to a cooling tower was not identified in this study as a risk factor for acquiring LD and no clustering of cases to suggest an unidentified common source was observed. Detailed information regarding place of work was not available, hence an unrecognized source of infection at a workplace clearly cannot be excluded. However, associations involving factories were not evident at the time of diagnosis and reporting to the CCDC. Nevertheless, possible involvement of cooling towers cannot definitely be ruled out. In Nottingham, there is

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a prevailing wind from the south-westerly direction which might influence the dispersal of aerosols. Although no obvious trend was apparent, we were unable to study this formally in our geographical analysis. Interestingly, it was observed that 11 controls and 0 cases lived within 600 m of a cooling tower. While not a statistically significant finding, this could represent a situation where exposure to cooling towers leads to exposure to LD and subsequent immunity.

In a high proportion of community-acquired cases [16 (39%) of 41 households tested], the domestic water supply was identified as the most likely source of infection. This is over twice the proportion of patients' homes found to have at least one positive *Legionella* sp. sample (14·8%) in a national case-control study of legionella in home water systems involving 81 patients with confirmed LD [11]. With respect to disinfection and legionella, the water supply in Nottingham is not known to be any different compared to the rest of the United Kingdom. Water sources include a typical lowland river, impoundment reservoir supply and typical deep borehole supplies. Chlorination is used almost entirely and the process is no different from other parts of the United Kingdom.

Environmental surveys in Canada and the United States have found that up to 32% of hospital and residential water supplies may be contaminated by *Legionella* sp. without evidence of overt clinical disease in persons exposed [12, 13]. Large water distribution systems are most vulnerable to colonization with *Legionella* sp. [14, 15]. Similar surveys in the United Kingdom indicate a lower incidence of *Legionella* sp. in domestic water systems of approximately 5% [11, 15].

Acquisition of LD as a result of contaminated home water supplies has been reported [16, 17]. Consequently, it may be difficult in circumstances where numerous water sources have been found to be contaminated by *Legionella* sp. to ascribe a single supply as the main source of infection. In this study, no other source of infection was identified in all cases where the home water supply was implicated. Ideally, strains isolated from the home water supplies would be matched to the infecting strain. However, as most cases were not diagnosed by cultural techniques and molecular typing methods were not employed, such confirmation was not possible. Nevertheless, our data suggest that home water systems are a likely common sporadic source of *Legionella* sp. infection in patients living in Nottingham and may account for the higher rates of infection in Nottingham compared to England and Wales.

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