Legionnaires' disease outbreak: Victoria's largest identified outbreak

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Abstract

This paper describes and analyses some aspects of an outbreak of Legionnaires' disease in Victoria, commencing in late October 1998. In all, 18 cases caused by *Legionella pneumophila* serogroup 1 were notified within 10 days making this the largest outbreak in Victoria reported to that date. All cases had epidemiological links to an industrial estate in a northern Melbourne suburb. Extensive environmental sampling revealed *Legionella* bacteria in five cooling towers. Molecular sub-typing techniques were used to compare clinical and environmental isolates. Isolates from one tower had a pulsed-field gel electrophoresis pattern that was indistinguishable from clinical isolates from eight cases. Control of outbreaks caused by *Legionella* bacteria requires rapid, coordinated responses to linked cases of disease. The *Legionella* urinary antigen test facilitated a rapid public health response, and culture and molecular sub-typing of clinical specimens assisted in developing epidemiological links. *Commun Dis Intell* 2000;24:199-202.

Keywords: legionellosis, surveillance, urinary antigen, cooling towers, environmental health

Introduction

Legionnaires' disease is caused by *Legionella* bacteria, which are gram-negative intracellular pathogens. The typical presentation is a severe community-acquired or nosocomial pneumonia.[1] European and North American studies have estimated that *Legionella* species may cause between 2% and 15% of all community-acquired pneumonia requiring hospitalisation.[2] In Australia, from national data on notified cases, the rate is approximately 1 per 100,000 persons (Communicable Diseases Network Australia New Zealand National Notifiable Diseases Surveillance System; personal communication). The case fatality rate has been reported as ranging from 5 to 30% depending on underlying risk factors of patients.[3] The disease is a public health priority, since it is potentially preventable through ongoing identification and treatment of environmental sources, and can be treated effectively with antibiotics if diagnosed promptly.

Legionnaires' disease has been notifiable in Victoria by doctors and laboratories since 1979. The definitive laboratory diagnosis for the disease is culture from respiratory specimens on selective culture media.[1] The other methods routinely in use in Victoria are serological testing and the *Legionella pneumophila* serogroup 1 (LP1) urinary antigen test. Most outbreaks of Legionnaires' disease in Australia have been due to LP1.[4-10] Between 1995 and 1998, LP1 comprised 82% of all notifications of Legionnaires' disease in Victoria (unpublished observations).

In Victoria, the case definition for Legionnaires' disease is: - a clinically compatible illness (pneumonia) and at least one of the following: (1) culture isolation of *Legionella* species; (2) fourfold rise in immunofluorescence (IFA) titre in paired sera to at least 128; (3) stable high titre (>512) IFA in convalescent serum; (4) demonstration of *Legionella* species antigens in urine or other specimens.[11] In late October 1998, over 2 days, the Communicable Diseases Section of the Victorian Department of Human Services (DHS) received three notifications of Legionnaires' disease due to LP1. The cases were men who lived or worked in the vicinity of Thomastown, a northern Melbourne suburb. The close temporal and geographical clustering of cases suggested that the three cases were related. An outbreak investigation was initiated to prevent further transmission, to identify undiagnosed cases, and to determine the source(s) of the outbreak.

Methods

We undertook telephone interviews of cases or of their next of kin, using a standardised case questionnaire. All were asked about possible risk factors for infection with LP1 in the 10-day period prior to onset of illness. Results from the case questionnaires were used to direct environmental investigations. Workplaces of cases in employment were contacted to determine whether there were cooling towers at the workplace or in the immediate vicinity.

Enhanced community and hospital surveillance for LP1 was undertaken concurrently with the investigation. This involved media releases directed at the general public, letter-drops to local residents, health alerts distributed by pathology companies to general practitioners, and hospital alerts to local and major regional hospitals. Further

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measures included alerts to local Divisions of General Practice, and workplace illness surveillance for both any workplace with a confirmed case, and all workplaces in the industrial estate where the outbreak appeared to be centred. When a diagnosis of LP1 was made by the *Legionella* urinary antigen test, the clinician was contacted and urged to pursue culture confirmation if possible.

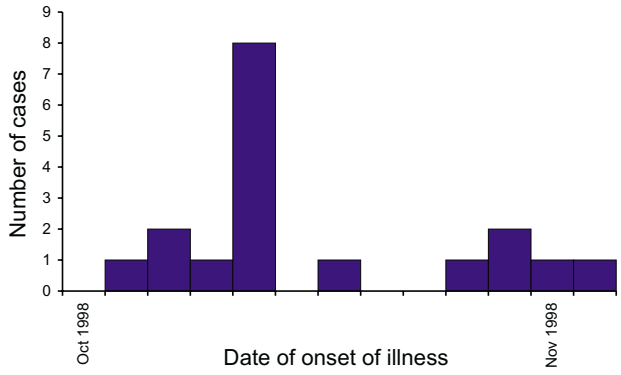
Officers of the Environmental Health Unit of the DHS inspected suspected areas and identified potential exposure sources with the focus on cooling towers. Cooling towers identified in the suspected area were inspected, water samples collected for testing, and owner/managers ordered to organise immediately for the towers to be treated with biocidal agents. Compliance with the Health (Infectious Diseases) Regulations[12] relating to routine tower maintenance was assessed, and water-testing results were reviewed.

Methods for isolation of *Legionella* from sputum, for LP1 urinary antigen analysis, and subtyping by pulsed field gel electrophoresis are described elsewhere.[1]

Results

In all 18 epidemiologically linked cases satisfying the case definition were identified. Figure 1 is the epidemic curve for the outbreak. The first case was confirmed on 29 October on the basis of the urinary antigen test. This case was culture confirmed on 30 October, but the next positive clinical isolate was only obtained on 2 November, although additional cases had been confirmed by the urinary antigen test on 30 October.

Figure 1. Legionnaires' disease cases, Melbourne, Victoria, 21 October to 2 November 1998, by date of onset of illness

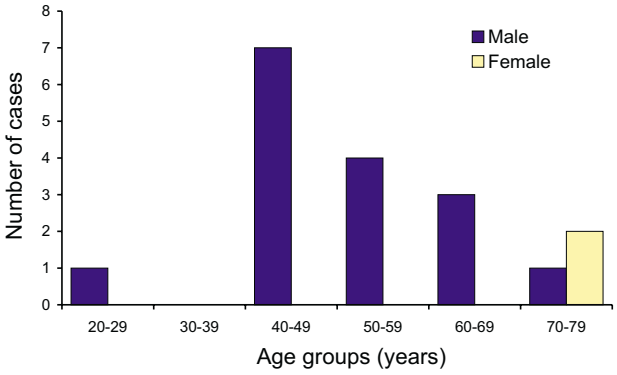


Case demographics

The age and sex distribution of cases is shown in Figure 2. Of the cases, 16/18 (89%) were male (male/female ratio = 8:1), with the median age for males being 50 years. Of the males, 13/16 (81%) were employed full-time, two were retired and one was on sickness benefits. The two females were retirees aged 71 and 74 years (for cases of Legionnaires' disease in Victoria, the median female age between 1995 and 1998 was 61 years).

Of the cases, 15/18 (83%) were hospitalised, with 2/15 (13%) hospitalised cases ventilated in intensive care. There were no fatalities. The major risk factors for illness were being a working male aged 40-70 years who smoked (14/18

Figure 2. Legionnaires' disease cases, Melbourne, Victoria, 21 October to 2 November 1998, by age group and sex



(78%) were regular smokers) and had epidemiological links to the implicated area through either work, residential address or travel on the major arterial road. From the epidemic curve, it can be estimated that the period of likely exposure for most cases was the third week of October 1998.

Of the cases, 16/18 (89%) were initially notified on the basis of a positive *Legionella* urinary antigen result, with 7/16 (44%) of these subsequently being culture-confirmed. For seven of the urinary antigen-positive cases, sputum culture was negative for *Legionellae* or other respiratory pathogens. Sputum was not available for testing from the two other urinary antigen-positive cases. For the seven urinary antigen- and sputum-positive cases (all hospitalised), the median time from hospital admission until sputum collection was 1 day (range 0-1 days). For the six urinary antigen-positive but sputum-negative cases hospitalised, the median time from hospital admission until sputum collection was 2 days (range 1-7 days).

Three suspected cases identified through active case finding in local hospitals had negative urinary antigen tests initially, but these proved positive after the initial urine specimens were concentrated and retested. These three cases were subsequently confirmed by culture.

One non-hospitalised case was initially notified from a positive sputum isolate; this case had a negative urinary antigen result on urine collected 3 days after onset of illness. One hospitalised case did not have sputum collected (and was negative by urinary antigen test on urine collected 6 days after onset of illness) but had a high titre acute serology result. For the 16 urinary antigen positive cases, there was a median time of 5 days from onset of illness until urine was collected (range 1-9 days).

Environmental investigations

Twenty-three premises were inspected and their compliance with the Health (Infectious Diseases) Regulations 1990[12] assessed. Most premises were found to have complied with the Regulations. A minority had only partially complied with the regulations, while some were found to have not complied with any aspect of them. Only one of the premises was found to have had recent routine biocidal treatment of its cooling tower; this had been done the day before DHS testing. Premises with lack of evidence of compliance with the regulations were informed of their

regulatory responsibilities and educated by DHS on the optimisation of their cooling tower maintenance practices. These premises were subsequently attended to ensure that appropriate practices for maintenance had been instituted.

After sampling, towers in the implicated area were treated with biocidal agents. Decontamination was carried out on cooling towers where *Legionella* bacteria were isolated. In total, of the 65 cooling towers sampled, five tested positive for LP1. Some of these LP1-positive cooling towers were compliant with the minimum requirements for maintenance, emphasising there may be a need for higher levels of maintenance for particular sites.

All clinical and environmental isolates of LP1 were subtyped by pulsed-field gel electrophoresis (PFGE). A total of eight clinical isolates and five isolates from different cooling towers were analysed. All eight clinical isolates were indistinguishable by PFGE, and generated an electrophoretic pattern not previously reported in Victoria. The same novel pattern was seen in an isolate from one of the cooling towers sampled. This tower had not been maintained in accordance with the Regulations. Isolates from other cooling towers demonstrated electrophoretic patterns different from that of the outbreak strain. One isolate from a cooling tower did not survive to be able to be submitted for subtyping.

Discussion

Availability and use of the *Legionella* urinary antigen test allowed earlier outbreak identification, and earlier confirmation of most suspected cases of Legionnaires' disease, If *Legionella* urinary antigen testing had not been available, the outbreak would not have been identified until 4 days later (on 2 November). The initial case was culture-confirmed on 30 October, but the next positive clinical isolate was not until 2 November. Until that time, DHS would have been investigating the initial case as a sporadic case, rather than an outbreak. This means that the extensive measures specifically undertaken in this outbreak would have been delayed. These included the extensive environmental inspections and sampling undertaken, and the range of alerts to the general public, doctors and hospitals initiated on the 30 October.

Furthermore, the use of the urinary antigen test meant that we were able to have laboratory confirmation on some cases on the day they first presented to doctors. This greatly enhanced the early stages of the investigation, when we were confronted by a number of hospitalised patients with pneumonia which could have been due to any of a range of pathogens. This relative ease of obtaining prompt confirmation of cases contrasts with experiences reported from an outbreak of LP1 in Sydney in 1992, where direct immunofluorescent staining (DFA) was used as a rapid diagnostic tool.[13]

Of urinary antigen-positive cases, 7/16 (44%) were subsequently culture-confirmed. It was noted that, in contrast with those with negative sputum cultures, the hospitalised cases with culture confirmation had sputum collected soon after admission. Once cases were hospitalised and had commenced antimicrobial therapy - and the longer they were on that therapy - the less likely was *Legionella* to be cultured from their sputum. Thus to optimise culture-confirmation of cases, sputum should be collected as soon as possible from suspected cases of Legionnaires' disease

It is important to recognise the limitations of the urinary antigen test. It is valid only for LP1 and moreover, although a positive test is considered to be almost 100% specific, a negative test does not exclude *Legionella* infection.[14] However, concentration of urine specimens by ultrafiltration increases test sensitivity without loss of specificity.[15] This proved helpful in this outbreak since three sputum positive cases, initially testing negative on routine urinary antigen testing, were positive after urinary concentration.

For this outbreak, 9/16 (56%) of the urinary antigen-positive cases had urine collected 5 days or less after the onset of illness, which indicates the urinary antigen test is useful in diagnosis in the very early stages of illness. One study has reported that antigen was detectable in some cases as early as 2 days after onset of illness.[16] Another has reported that urine samples collected within the first 5 days of the disease may be negative.[17] The two cases in this outbreak with negative urinary antigen results had urine collected for testing 3 and 6 days after the onset of illness. Urine may continue to test antigen-positive for many weeks after onset of illness. It has been reported that 10% of culture-confirmed cases of Legionnaires' disease are still urinary antigen test-positive after 60 days.[1] Another study reported that most cases were urinary antigen-positive between 3 and 5 weeks after illness onset.[18]

Our results suggest that, because urine antigen testing was used, most cases were identified earlier and treated appropriately; alternatively less severe cases were identified which may not otherwise have been correctly diagnosed.

Although an alternate source was not excluded, a possible source of the outbreak was the cooling tower where the LP1 isolate with a PFGE pattern indistinguishable from the clinical isolates was found. This tower had not been maintained in accordance with the Regulations. The latter require regular cleaning and disinfection of towers, monthly microbiological monitoring by Total Bacteria Counts, and maintenance of documentation to confirm these activities.[12] The role of the cooling tower with the LP1 isolate which did not survive to permit PFGE analysis is uncertain.

As a result of our experience from this outbreak, we recommend the following practices in the investigation of cases of Legionnaires' disease. Clinicians should be encouraged to use the *Legionella* urinary antigen test. The test should be used in conjunction with culture of respiratory specimens (to allow molecular sub-typing) and collection of serological specimens (in case urine and sputum tests are negative, and to exclude alternate causes of atypical pneumonia). If the initial urinary antigen test is collected in the first week of illness and is negative for a suspected case, it is worth repeating the test in the second week of illness. Opportunities exist for collaboration between clinicians, public health practitioners and diagnostic laboratories to develop algorithms for determining which urinary specimens should be concentrated to improve sensitivity. Used appropriately, the urinary antigen test can be a valuable tool in the investigation of sporadic cases or outbreaks in jurisdictions where there is a high proportion of cases due to LP1.

We recommend that cooling towers in Victoria be maintained in accordance with the Regulations.[12] Appropriate cooling tower design and maintenance has been shown[19] to minimise the risk of proliferation of *Legionella* bacteria in cooling towers: this may reduce the risk of the latter

becoming sources of infection for sporadic cases or even outbreaks of Legionnaires' disease.

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Editorial Statement. The October/November 1998 outbreak reported by the authors was the largest recorded outbreak in Victoria at the time their article was first submitted to *Commun Dis Intell* (29 October 1999).