

Outbreak of Legionnaires' disease at University Hospital, Nottingham. Epidemiology, microbiology and control

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SUMMARY

Twelve patients in a large teaching hospital contracted Legionnaires' disease over a period of 11 months. The source was a domestic hot water system in one of the hospital blocks, which was run at a temperature of 43 °C. Five different subtypes of *Legionella pneumophila* serogroup 1 have been isolated from water in different parts of the hospital, over a period of time. Only one subtype, Benidorm RFLP 14, was implicated in disease. Circumstantial evidence suggested that the outbreak may have been due to recent colonization of the hot water system with a virulent strain of *Legionella pneumophila*. The outbreak was controlled by raising the hot water temperature to 60 °C, but careful surveillance uncovered two further cases in the following 30 months. Persistent low numbers of *Legionella pneumophila* were isolated from the domestic hot water of wards where Legionnaires' disease had been contracted, until an electrolytic unit was installed releasing silver and copper ions into this supply.

INTRODUCTION

Water systems in large modern buildings are prone to colonization with *Legionella* species [1–3]. In 1982 the Public Health Laboratory Service conducted a survey of water systems in hospitals and hotels. Fifteen percent of water samples contained one or more *Legionella* species. In most buildings positive for the organism, there was no evidence of legionellosis. Further survey work was conducted in 1984 (Public Health Laboratory Service, unpublished), which included the Queen's Medical Centre in Nottingham, of which the University Hospital (UHN) is a part. Four of 15 samples contained *Legionella pneumophila* serogroup 1. Positive sites included both a cooling tower and shower.

The Public Health Laboratory in Nottingham is experienced in the diagnosis and investigation of Legionnaires' disease (LD). It was among the first centres to confirm the diagnosis of a clinical case in the UK [4], and in 1984 was providing a diagnostic and reference service. In 1981 a study of community-acquired pneumonia in the city showed a rate of 15% for LD [5]. This unusually high rate has never been explained. Nevertheless throughout the period when LD was being

regularly diagnosed as a cause of community-acquired pneumonia, there was no evidence of nosocomial infection from any Nottingham hospital.

In 1988 the first case of hospital-acquired Legionnaires' disease (HALD) was diagnosed in the University Hospital. This heralded an outbreak in which 12 cases were eventually uncovered. In this paper we describe the investigation and control of this outbreak.

MATERIALS AND METHODS

Hospital setting

The Queen's Medical Centre in Nottingham comprises four interconnecting blocks, each with a central courtyard, constructed around a services area (Fig. 1). Three of the blocks form the University Hospital of approximately 1200 beds. The fourth houses the medical school. The medical school was occupied in 1976, West block in 1978, East block 1981 and finally South block in 1984. There are five wet cooling towers on the site. Two are on the roof of each of East and West blocks, and one is on the medical school. South block has no cooling tower. The medical school and West block have 6 floors, East block 5 and South block 4.

Water was supplied by the public utility until November 1988, since when a private deep borehole has been used for parts of the site. Water is distributed to each block from common storage towers. The cold water is chlorinated to 0.4 p.p.m. of free chlorine and the water for the domestic hot water systems is softened in a base exchanger. There are no secondary storage tanks within the blocks.

In the medical school and West blocks water is heated in storage calorifiers and circulated at 60 °C. East and South blocks each have two hot water circulation systems heated by non-storage instantaneous heat generators in which heat stratification cannot occur. Until April 1989 water to domestic areas such as kitchens and sluices was circulated at 60 °C, and patient areas, baths, showers and handbasins were supplied at a circulating temperature of 43 °C. This had been designed to avoid the risk of scalding susceptible patients, in the era before Legionnaires' disease was described.

In each block services are distributed within unheated service voids, 2 m high, between floors. A core adjacent to the lift shafts connects the voids. On each floor, the domestic hot water is distributed from the core by two circuits, one supplying the area to the right, the other the area to the left of the core. The two lowest floors, A and B, are supplied from the void between them. On all the other levels only the floor above the corresponding void is served.

Bacteriological

Clinical specimens

Sputum and post-mortem lung were the only samples submitted for legionella culture. These were examined by the direct fluorescent antibody test (DFAT), using a monoclonal antibody specific for *Legionella pneumophila* serogroups 1-14 (Genetic Systems, Seattle, USA). Specimens were inoculated onto buffered charcoal yeast extract medium (BCYE) with growth supplement and selective antibiotic supplements (CYE agar base, Legionella BCYE growth supplement, BMPA selective supplement; Oxoid, Basingstoke, Hampshire). Serum samples

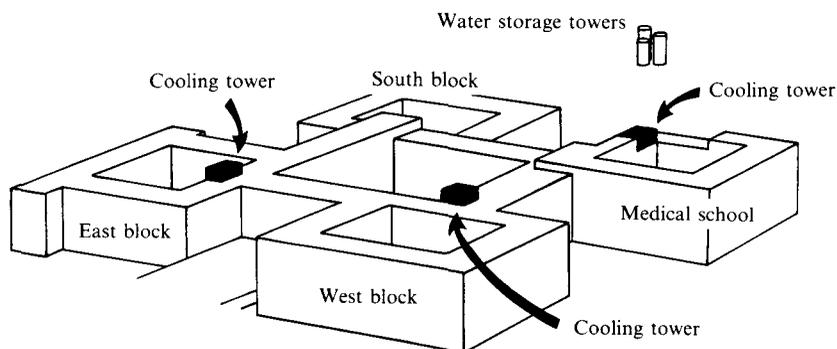


Fig. 1. Queen's Medical Centre, Nottingham.

were examined by the indirect fluorescent antibody test (IFAT) using formalized *Legionella pneumophila* serogroup 1 antigen (NCTC 11192, Division of Microbiological Reagents, PHLS, Colindale). A fourfold rise in titre or a single titre greater than 64 was considered positive.

Environmental samples

One litre water samples were collected without flushing, and filtered, using a Gelman manifold and vacuum pump, through 47 mm diameter, 0.2 μm Sartolon polyamide membranes (Sartorius, Epsom, Surrey). After filtration each membrane was agitated in 10 ml of sterile deionized water which was then centrifuged at 2200 g for 20 min. The deposit was resuspended in 1 ml. The first 35 samples, only, were examined by DFAT. Aliquots of 0.1 ml were inoculated onto BCYE (with growth and selective supplements) directly, and after pretreatment at 50 °C for 30 min. The plates were examined over 14 days at 2- or 3-day intervals under a stereoscopic microscope with incident light. Possible legionellae were subcultured to BCYE and blood agar. Colonies growing on BCYE only were considered putative *L. pneumophila*. Identification was confirmed by direct immunofluorescence with a monoclonal antibody to *L. pneumophila* serogroup 1 (Division of Microbiological Reagents and Quality Control, PHLS, Colindale). The first isolates were confirmed by the Legionella Reference Laboratory, Colindale, where selected strains were also subtyped by monoclonal antibody panel (Mab) [6], and restriction fragment length polymorphism (RFLP) [7].

Epidemiological

Case definitions

Legionnaires' disease was defined as a case with clinical and radiological evidence of pneumonia and demonstration of *Legionella pneumophila* by isolation, or by DFAT, or with serological evidence of infection. A case was considered definitely HALD if in hospital throughout the whole of the incubation period, which was taken as 2–10 days, before the onset of symptoms. Probable HALD cases had been in the hospital at some point during the incubation period.

Case finding

Possible cases of HALD were sought throughout the Nottingham hospitals. Four approaches were used to identify cases of HALD: (1) clinicians were asked to recall likely cases; (2) nursing staff were questioned on ward visits; (3) hospital admission records were searched for readmissions with pneumonia; (4) laboratory records were searched for 'atypical pneumonia' requests without adequate convalescent sera. Any case clinically consistent with HALD was followed up and sera obtained where possible. Cases without laboratory confirmation were not included in the analysis.

Monitoring control measures

To gauge the effectiveness of the outbreak control measures three complementary monitoring programmes were introduced. (1) Physical parameters: hot and cold water temperatures, and cold water residual chlorine, were recorded at randomly selected outlets on a regular basis. (2) Bacteriological: on each floor in South block, hot water outlets furthest from the water heaters were sampled monthly, without flushing, for *Legionella* sp. (3) Active surveillance: a system of reporting possible cases of nosocomial pneumonia by ward sisters and medical staff was coordinated by the infection control sister. This last measure was used in conjunction with laboratory requests, and all suspicious cases investigated by a member of the infection control team. Legionnaires' disease prevention was given a high profile in regular newsletters and publicized at other opportunities.

RESULTS

Cases

In the outbreak period, July 1988 to April 1989, 12 cases of HALD were diagnosed (Table 1). In the following 30 months two further cases were identified. One case was a visitor and another, a member of staff. The remaining cases were in-patients. There were two deaths, both in men with severe ischaemic heart disease. These two patients had had multiple admissions for the treatment of severe heart failure. In one, case 9, the additional diagnosis of pneumonia was only made at post mortem.

Eight patients had significant ischaemic heart disease requiring drug therapy. Two were elderly women having routine cataract surgery, one of whom was taking systemic steroids. None of the other patients was taking any immunosuppressive drugs or had malignant conditions. The mean age was 71, range 34–88; only 3 were under 60. The youngest patient and the member of staff, both males, were heavy smokers.

As most cases were diagnosed serologically in retrospect as part of routine serological testing of pneumonia, specific culture for *Legionella pneumophila* was not usually requested. The only isolation was made from post-mortem lung, which was also positive by DFAT. In case 13 urine was positive for antigen by ELISA (Legionella Reference Laboratory, PHLS, Colindale), in addition to a fourfold rise by IFAT.

Erythromycin either alone or in combination with a beta lactam antibiotic was

Table 1. *Patients with hospital acquired Legionnaires' disease*

Case no	Age	Sex	Date of onset	Date diagnosis confirmed	Ward*	Reason for admission	Additional risk factors
1†	59	F	19.vii.88	26.vii.88†	C54	Ischaemic heart disease	Smoker
2	74	M	12.ix.88	10.x.88	A45	Senile dementia	
3	76	F	12.ix.88	7.xi.88	—	Visitor	Ischaemic heart disease
4	34	M	2.ii.89	10.ii.89	C51	Traumatic ulcer	Smoker
5†	72	M	25.ii.89	25.iv.89	C53	Ischaemic heart disease	Past smoker
6†	78	F	26.ii.89	3.vi.89	B47	Cataract surgery	
7	72	F	20.iii.89	28.iii.89	B50	Anaemia	Ischaemic heart disease
8§	79	M	28.iii.89	14.iv.89	D56	Ischaemic heart disease	Malnutrition
9§	73	M	1.iv.89	14.iv.89	D56	Ischaemic heart disease	Past smoker
10†	62	M	1.iv.89	12.v.89	D58	Ischaemic heart disease	Hypothyroid
11	88	F	6.iv.89	14.iv.89	B49	Ischaemic heart disease	Hypothyroid
12†	88	F	7.iv.89	15.vi.89	B48	Cataract surgery	Systemic steroids
13	58	M	28.viii.89	12.ix.89	—	Staff	Smoker
14	78	M	1.ix.90	20.ix.90	B49	Ischaemic heart disease	Past smoker

*, Letter indicates floor, A lowest, D highest.

†, Discovered in case finding exercise.

‡, Diagnosed in another hospital. Outbreak team not informed until May 1989.

§, Died.

Table 2. *Legionella pneumophila* serogroup 1 typing results

Block	Ward	Source	Monoclonal type	RFLP type
South	A43	Handbasin hot tap	Benidorm	14
South	B49	Assisted bath	Benidorm	14
South	B50	Shower	Benidorm	14
South	C54	Shower	Benidorm	14
South	D56	Patient 8	Benidorm	14
South	D56	Shower	Benidorm	14
Workshops	—	Shower	Benidorm	ND*
Workshops	—	Handbasin hot tap	Benidorm	ND*
East	A25	Assisted bath	Philadelphia	1
East	A23	Assisted bath	Bellingham	46
East	E37	Kitchen hot tap	Bellingham	46
East †	—	Cooling tower	Bellingham	46
West †	Not recorded	Ward shower	Bellingham	10
West †	Not recorded	Ward hot tap	OLDA	1

*. Not done. †, Isolated in 1984 survey.

given to nine patients, as this is the hospital policy for the initial treatment of moderate or severe pneumonia. Case 9 received no antibiotic therapy, cases 5 and 6 received only amoxicillin. One patient was treated in intensive care, received ventilator support and survived. Most of the cases were recognized when convalescent sera were tested as part of routine practice. There were no clinical features which alerted the physicians to the presence of nosocomial LD.

Bacteriology

The sole clinical isolate was identified as *Legionella pneumophila* serogroup 1, monoclonal subgroup Benidorm, RFLP type 14. This was designated the outbreak strain. During the outbreak investigation 89 water samples were examined from the hospital environment; *Legionella pneumophila* serogroup 1 was isolated from ten of these. At the start of the laboratory investigation 35 centrifuged deposits were examined by direct immunofluorescence in addition to culture. Four samples were positive by both techniques and two were positive by culture only. Because direct immunofluorescence was possibly less sensitive than culture, and extremely time consuming, later water samples were examined by culture alone. No *Legionella* spp. were isolated from cooling towers, untreated borehole water, water storage towers, or the sediment from storage towers. During the outbreak investigation and subsequent monitoring programmes, the outbreak strain was only found in South block.

Typing showed that the six isolates from South block were of the outbreak strain (Table 2). No other strains of *Legionella* sp. were isolated from South block. Two strains of *Legionella pneumophila* serogroup 1 were identified in East block, and a further two strains in West block.

Legionellae were found in water samples collected from baths, showers and assisted bath units. The latter are baths that can tilt, and therefore have long flexible hoses. Three of the four assisted bath units in the hospital yielded *Legionella pneumophila* serogroup 1. All the positive outlets were supplied by the 43 °C system.

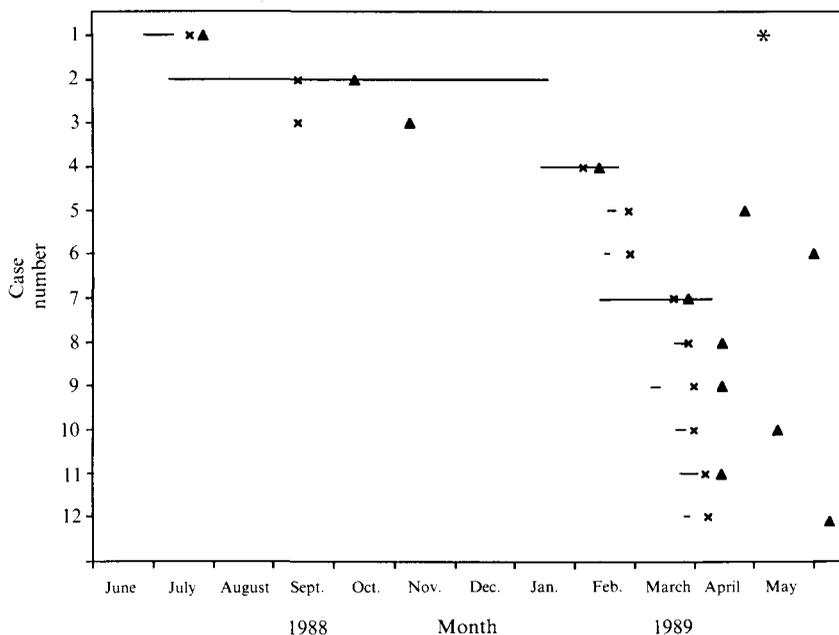


Fig. 2. Hospital admission: onset and diagnosis of Legionnaires' disease. —, Admission during which infected. ×, Onset of symptoms. ▲, Diagnosis. *, Case 1 came to notice of outbreak team. Note. Case 3 was a visitor.

Epidemiology

It was clear from the beginning of the investigation that all the outbreak cases were in the South block of the hospital. This block houses medicine, dermatology, haematology, acute geriatric and psychiatric units. There is a coronary care and high dependency ward. Cases were found on each floor, in wards facing three sides of the block, there being no patient areas on the fourth side. This pattern strongly suggested that the most likely source of the outbreak was the domestic water system. The absence of a wet cooling tower in South block, and a circulating hot water supply to patient areas running at 43 °C, were additional factors that strongly implicated the hot water system. This was confirmed early in the investigation when *Legionella pneumophila* serogroup 1 was isolated from hot water from several wards.

Five of the 12 outbreak cases were identified retrospectively in the case finding exercise. Eleven were in-patients and one a visitor (case 3) who was the wife of the index case (case 2). The in-patients had only been treated in South block during the incubation period, except for brief visits to areas, such as X-ray, used by patients from the whole hospital. The visitor, who developed symptoms of pneumonia on the same day as her husband, only visited the South block of the hospital, using the South block entrance. Three patients had been in hospital throughout the incubation period, cases number 2, 4 and 7 (Fig. 2) and only these were classified as definitely hospital acquired.

Outbreak cases had onset dates between July 1988 and April 1989 (Fig. 2), when control measures were introduced. The first cases to be recognized, in October and

November 1988, were diagnosed on convalescent sera taken up to 2 months after the onset of symptoms. The earliest case, which was diagnosed and treated in another hospital in south-west England, only came to the attention of the outbreak investigators some 8 months after it was diagnosed. The later cases were diagnosed more promptly as staff were made aware of the problem.

Two cases of HALD were diagnosed in the 30-month period of monitoring after control measures were taken. One, case 13, a member of staff, was probably infected in the workshops, which were not in the main hospital building. *Legionella pneumophila* of the outbreak strain was isolated in the workshops, from a handbasin and a shower. The other, case 14, was a patient on a ward which had been affected in the outbreak.

There was no simple connection between infection and the use of showers, baths or wash handbasins, nor in the position of a case's bed in relation to these facilities. At least four patients only washed at the bedside, because they were too ill, from their presenting condition, to use other facilities. *Legionella pneumophila* of the outbreak strain was isolated from all the wards in which cases occurred. The last case in September 1990, was probably infected on a ward in which persistent low numbers of legionellae were isolated over a period of months in spite of efforts to eradicate them.

East block also contains acute geriatric wards, sharing an emergency admission rota with the wards in South block. *Legionella pneumophila*, though not the outbreak strain, was isolated on these wards. Cases 6 and 7 had been in-patients on East block wards, but investigations showed that they had been nursed on South block wards during the incubation period. No cases of HALD were found to have been infected in East block.

Staff

Staff were invited to undergo serological examination for evidence of exposure to *Legionella pneumophila* during investigation of the outbreak in April/May 1989, and on a second occasion in September 1989, after the member of staff became infected. On the first occasion 183 responded; most worked in South block and complained of recent respiratory symptoms. On the second occasion 64 responded from all areas of the hospital. Most of these were involved in maintenance or engineering work. Two of the 242 screened had a titre of 16 and one of 64. None gave a history of severe illness, or had evidence of a rising titre.

Control of the outbreak

The potential of the 43 °C hot water system as a source of infection was appreciated when HALD was first recognized. Limited water sampling in November 1988 failed to detect legionellae. However, after a further case in February 1989, it was decided to disinfect the system in South block. Initially shower heads were disinfected in hypochlorite, and the circulating hot water temperature raised to 60 °C over a weekend. Staff were instructed to flush hot water outlets for 5 min. This was repeated on three weekends before the temperature was permanently raised, in both South and East blocks, to 60 °C on 17 April 1989. It was not possible to show if the outbreak was ended by the pulsed thermal disinfection, or the permanent rise in temperature. The last outbreak case

was in early April. To avoid scalding injuries over 300 thermostatic mixer valves were then fitted to showers and baths. Further engineering measures were completed over the subsequent months. These involved identifying and removing underused water outlets. Dead legs in the pipework were reduced to a minimum length. Staff were encouraged to report outlets that failed to run hot, or that had poor flow, and these were modified. Lastly a programme of regular weekly flushing by nursing and domestic staff was introduced.

Monitoring

To gauge the effectiveness of the control measures routine bacteriological monitoring for *Legionella* spp. was introduced in October 1989. Between October 1989 and March 1991 three isolates were made on the top two floors of South block from 296 samples. Positive samples were collected early in this period from little used points which were removed. Throughout the same period 64 isolates were made from 293 samples collected on the lower two floors, which are both supplied from the same void. Colony counts were low, 10–200 colony forming units per litre. Most of the isolates were from one arm of the circulating system within that void. No reason for the persistent colonization was identified. Temperature records were satisfactory [8], no excessive 'dead legs' or stagnant sections within the pipework could be identified, which might have accounted for the continued isolation of legionellae.

During this 18-month monitoring period five cases of LD were diagnosed in in-patients in the University hospital. Only one of these, a non-fatal case, was probably nosocomially-acquired, the remaining four were unequivocally community-acquired. The nosocomially infected patient had been nursed on a persistently colonized ward in South block during the probable incubation period.

In March 1991 a commercial disinfection system using an electrolytic process to produce silver and copper ions (Tarn Pure Ltd, High Wycombe, England) was installed in the domestic hot water system of South block. This produces ions at low concentrations, within the limits for potable water [9]. In the following 12 months no further isolations of legionella were made in South block, and only a single case of community-acquired LD was diagnosed within the hospital.

DISCUSSION

Although investigations confirmed the initial suspicion of the hot water system as the outbreak source, other options were also considered. The cooling towers were all in good repair, maintained according to guidelines and culture negative for legionella at that time. There had been extensive excavations in the vicinity of the hospital due to a road improvement project. The distribution of cases made this air-borne spread from this source unlikely.

Domestic hot water systems are a well recognized source of HALD [10–14]. Colonization of hot water systems with legionellae is usually associated with circulating water temperatures less than 50 °C. It is recommended that water is stored at a minimum of 60 °C, with the temperature at outlets above 50 °C after running for 1 min [8]. Problems may arise for several reasons, for example stratification within calorifiers, long dead legs within the distribution, or blending

of hot and cold water [14–16]. In this case water was circulated at 43 °C, a temperature selected, before Legionnaires' disease was described, to avoid scalding injuries in frail, confused or young patients. Raising the temperature was a costly operation, for example over 300 thermostatic mixing valves were required to comply with regulations and avoid scalding injuries at the higher circulating temperature. Therefore action to raise the temperature to recommended levels had been delayed, in the absence of any problems, until the funds for the required engineering work were available. The outbreak precipitated an immediate response.

The 1984 survey alluded to in the introduction showed that some of the hospital's water systems were colonized at that time. Since the outbreak was investigated *L. pneumophila* has been isolated from all the blocks in the building. We can only speculate why cases did not occur until 1988, and why, in spite of potentially susceptible populations, only one block has been implicated as a source of HALD.

Whereas outbreaks of LD caused by cooling towers can be explosive, with cases presenting over a short period [17, 18], those due to domestic water systems tend to be more insidious, and may only be revealed after active surveillance is introduced [12, 13]. If there had been a long-standing unrecognized problem in Nottingham, we would have hoped to expose it in the case finding exercise. In fact cases were found in other blocks and another Nottingham hospital. The most likely source of infection in all these patients proved to be an in-patient stay in South block. The staff seropositive rate of 1·2% is low compared with that seen in control populations without a history of exposure [17, 18]. This suggests that there has not been significant long-term exposure. A seropositivity rate of 6·3% was seen in staff working in Kingston District Hospital in a building with HALD and a positive domestic water system [10]. Much higher rates, e.g. 30%, are seen in cooling tower associated outbreaks [17]. Nevertheless hospitals with well-documented colonization of domestic water may fail to show high seropositivity amongst staff [13].

Using two typing schemes it was clearly shown that there were several types of *L. pneumophila* serogroup 1 in the hospital. Only one, Benidorm RFLP 14, was found in areas where HALD occurred, and was isolated from a case. This type was never found to be mixed with other types. In hot water systems colonized with several serotypes of *L. pneumophila*, the predominant serotype appears to cause the majority of disease if an outbreak occurs [14, 16]. In this case all the isolates were of serogroup 1. Some subtypes of serogroup 1 are most likely to be associated with LD [19–21], particularly those reacting with Mab 2, or equivalent monoclonals [20, 22]. The factors which determine which strain causes disease are not well understood. In Nottingham the outbreak strain has the Mab 2 marker. In addition the Philadelphia, RFLP 1, strain isolated in East block possesses this marker. This latter strain has only been identified from one outlet in low numbers. As the at-risk population exposed to the non-outbreak strains contained few patients with profound immunosuppression, the type of individual more likely to become infected with non-Mab 2 strains [21, 22], it is possible that HALD did not occur until a 'virulent' strain colonized the building in sufficient numbers to infect patients. The circumstantial evidence suggests that this event may have occurred

in South block in the period before July 1988. If this were the case it would explain why no HALD was detected before then, even though there was *Legionella pneumophila* serogroup 1 within the domestic hot water.

The outbreak was terminated by raising the circulating water temperature. Bacteriological monitoring in South block showed that low numbers of *L. pneumophila* persisted, especially in one area, in spite of care to eliminate excessive dead legs, ensuring that the temperature was satisfactory, and having a programme of flushing outlets. Persistent low numbers of *Legionella* spp. are not unusual in these circumstances, and it has been suggested that they may not represent a significant risk [23]. Sixteen months after the outbreak another case of probable HALD was detected in the area in which persistent isolations were made. As no clinical isolate was made in this case, it is not possible to be certain that the infection was caused by the serotype present on the ward in question. It may be that any detectable numbers of *L. pneumophila* in a ward's water supply can be shown to be important if a sufficiently sensitive surveillance scheme is applied for a long enough period. However the evidence from this particular outbreak, though incomplete, would suggest that the strain involved is an important part of the risk assessment equation. At present there are no useful markers with which to judge the potential virulence of a strain when present in domestic water supplies in low but detectable numbers. Over 30 *Legionella* species have been described to date and 16 have been associated with disease in man [24]. It would be prudent to aim to eliminate detectable legionellae from water supplies in hospitals.

In outlets that had been persistently positive for *Legionella pneumophila*, negative cultures followed the introduction of copper and silver ions into the hot water system. In the 1 year period of surveillance that has followed, cultures have remained negative for *Legionella* spp. and no further cases of HALD have been detected. At present we are investigating the microbiology of domestic hot water systems with silver and copper electrolytic units installed. If these and other novel biocidal treatments prove effective, it might be possible to reduce the temperature of circulating hot water safely. This would result in a reduction in the risk of scalding injuries, and savings in energy and construction costs.

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