



REVIEW

Surveillance of hospital water and primary prevention of nosocomial legionellosis: what is the evidence?

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Available online 21 January 2005

KEYWORDS

Legionella;
Surveillance; Water-borne infections;
Hospital-acquired infections

Summary Hospital-acquired Legionnaires' disease may be sporadic or may occur as part of an outbreak. As *Legionella* spp. are ubiquitous in many water systems, it is not surprising that hospital water may be colonized with *Legionella pneumophila* and other species. However, there is some controversy about the relationship between the presence of legionella in hospital water systems and nosocomial legionellosis. Primary prevention, i.e. measures to prevent legionella in a hospital or healthcare facility with no previous documented cases of nosocomial legionellosis, includes heightened awareness of hospital-acquired Legionnaires' disease with appropriate laboratory diagnostic facilities, and ensuring that the water system is well designed and maintained in accordance with national standards, e.g. the circulating hot water is maintained above 55 °C. Secondary prevention, i.e. preventing further cases occurring when a case has been confirmed, should include an investigation to exclude the hospital water system as a source. However, the necessity to sample hospital water routinely to detect legionella outside of outbreaks, i.e. as a component of primary prevention, is unclear. Some studies demonstrate a clear link but others do not. Differences between the patient populations studied, the methods of laboratory diagnosis of clinical cases, the analysis of hospital water and differences in the design of hospital water systems may partly explain this. Whilst further research, probably in the form of multi-centred prospective trials, is needed to confirm the relationship between environmental legionella and hospital-acquired legionellosis, including establishing the relative importance of *L. pneumophila* group 1 vs. non-group 1 and other *Legionella* spp., each hospital should consider the spectrum of patients at particular risk locally. Centres with transplant units or other patients with significant immunosuppression should, in the interim, consider routine

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sampling for legionella in hospital water in addition to other control measures. Therefore, infection control teams must work closely with hospital engineering and technical services departments and hospital management, as well as ensuring that physicians and others have a heightened awareness of hospital-acquired legionellosis.

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Introduction

Legionnaires' disease is known to cause hospital-acquired pneumonia and may occur as part of an outbreak or sporadically.^{1,2} Between 1980 and 2002, 4402 cases of Legionnaires' disease were identified in England and Wales, of which 264 were hospital acquired.³ The proportion of hospital-acquired pneumonia due to legionella has been reported as ranging from 0 to 47%.⁴ The incidence of hospital-acquired legionellosis is underestimated for a variety of reasons, including a lack of clinical awareness or a missed diagnosis, e.g. non-classical presentation especially in very ill or immunocompromised patients, infection at sites other than the respiratory tract, including soft tissue infections⁵ and endocarditis,⁶ delayed seroconversion, or lack of specialized culture facilities or urinary antigen detection tests in diagnostic microbiology laboratories. It has been shown that when an active search for legionella infection is initiated, cases are frequently confirmed.⁴

Forty-eight different species of legionella have been identified to date, although less than half of these have been linked to disease in humans.^{3,7} *Legionella pneumophila* is the most pathogenic, accounting for 90% of the cases of legionellosis, followed by *Legionella micdadei* and *Legionella longbeachae*. Although all 15 serogroups of *L. pneumophila* have been associated with disease, serogroup 1 is the most virulent and accounts for 82% of cases.³ Amongst immunocompromised patients, the proportion infected with strains other than *L. pneumophila* serogroup 1 is up to 20%.⁴ This is important in the clinical setting because one of the most widely used tests, the legionella urinary antigen test, is only specific for *L. pneumophila* serogroup 1 and there have been reports of hospital-acquired Legionnaires' disease due to species other than *L. pneumophila* serogroup 1.^{8,9} This is unsurprising as numerous species and serogroups can be present in a hospital water system. Most laboratories should be capable of determining that an isolate is a presumptive *Legionella* spp., and some will have the facility to identify the more common species and serogroups.

The patient population, the mode of transmission and potential environmental reservoirs are key issues when considering the likely occurrence of hospital legionellosis. Recognized patient risk factors include chronic lung disease and immunosuppression.^{1,10,11} Patients are also at risk after surgery; in one study of patients following surgery for head and neck cancer, 30% of postoperative pneumonia was confirmed as being due to *Legionella* spp.⁶

The most frequently described route of transmission is by inhalation of contaminated aerosols;¹² transmission occurs when water containing the bacterium is aerosolized in droplets small enough to be inhaled (1-5 µm). Transmission has also been reported, however, via aerosol-generating devices such as nebulizers which used contaminated water,^{13,14} whirlpool spas¹⁵ and showers.¹⁶ Micro-aspiration is another known route of transmission, with some authors believing it to be the most common route of transmission.¹⁷⁻¹⁹

Over the last 20 years, our understanding of the reservoir and ecology of *Legionella* spp. has increased substantially. Manmade aquatic environments that become colonized with *Legionella* spp. serve as the principal reservoirs for dissemination of the organism. Factors that most enhance colonization of water environments include the water temperature, obstruction and stagnation of the flow of water, biofilm formation in plumbing systems and the presence of other micro-organisms that support the growth of *Legionella* spp.²⁰ Cooling towers were originally thought to be the main reservoir for *Legionella* spp. However, from 1982 to 1985, potable water supplies were identified as the major source of hospital-acquired Legionnaires' disease,²¹ and the UK Communicable Disease Surveillance Centre (CDSC) reported that from 1982 to 1990, 19 of 20 nosocomial outbreaks of Legionnaires' disease in the UK were attributed to this source.²²

There have been numerous reports of hospital-acquired Legionnaires' disease over the last 20 years, and reports with detailed testing and follow-up of hospital water systems for legionella.^{1,13,23-26} Testing of hospital water supplies may occur as part

of either primary or secondary preventive programmes. Primary prevention refers to environmental testing for legionella in an institution with no background or documented cases of hospital-acquired legionellosis. Secondary prevention refers to measures undertaken in institutions with previous nosocomial legionellosis to prevent further cases.^{24,27} Unlike environmental surveillance for legionella as part of an outbreak investigation, surveillance for primary prevention remains controversial. This article will review the evidence for the surveillance of water systems for legionella as a component of the primary prevention of nosocomial legionellosis. A literature search of publications in English on hospital-acquired legionellosis between 1980 and 2004 was conducted. Key words used to search the Medline database were: legionella; *L. pneumophila*; nosocomial infection; and environmental screening.

Hospital water and legionella

The investigation of sources of sporadic cases of hospital-acquired Legionnaires' disease is often unrewarding, partly because of the ubiquitous nature of the organism. However, our understanding of the ecology and epidemiology of legionella within hospital water systems²⁸ has improved. As a result of previous outbreaks of Legionnaires' disease, guidelines are available on the control of *Legionella* spp. in water systems.²⁹ These preventive programmes should be part of the maintenance schedule of good engineering practice which, in turn, should minimize water colonization and prevent outbreaks or sporadic cases in hospitals.³⁰ Some of the main recommendations for the prevention of multiplication of legionella in health-care premises are summarized in Table I.

One of the conclusions of the investigation of an outbreak of Legionnaires' disease in Stafford, UK in the mid 1980s was that once legionella is established within a system, it is eradicated with great difficulty, if at all.³¹ This is largely due to the development of a biofilm in the water system and also the symbiotic relationship between legionella and certain free-living protozoa. The bacteria can persist intracellularly in amoebae and this impairs the efficacy of most disinfection processes.^{28,32,33}

It has been shown that the most beneficial method of preventing colonization of water systems is by keeping the circulating water temperature below 20 °C or above 55 °C.^{24,34} Darelid *et al.* showed that when water temperature was maintained above 55 °C following a nosocomial outbreak

of Legionnaires' disease, the prevention of Legionnaires' disease was possible.²⁴ In a similar study by Liu *et al.* over a three-year period, legionella was isolated from only 12% of the water systems of 17 hospitals sampled, and the authors concluded that the low incidence of positive water samples compared with that found in other studies was due to the effective implementation of legionella control measures.³⁰

Surveillance of hospital water for legionella

The engineering components of legionella control in water systems are defined for the UK,²⁹ but there is no consensus on the role of routine water sampling for legionella as a primary preventive strategy. In 1997, as part of guidelines on the prevention of nosocomial pneumonia, the Centers for Disease Control and Prevention (CDC) in the USA recommended culture of hospital water and the environment only in the event of cases of hospital-acquired Legionnaires' disease.²⁷ The CDC justified this at that time because it considered that as legionella are ubiquitous in water systems, the relationship between the results of water cultures and risk of legionellosis remained undefined.

Studies such as that by Alary and Joly, which involved 84 hospitals in Quebec and found that 6% of hospitals were colonized with *Legionella* spp. (26% were colonized at more than 30% of sites sampled) but there were few cases of hospital-acquired Legionnaires' disease, tend to support that view.³⁵ Similarly, a study by Marrie *et al.*, in which culture for *Legionella* spp. was undertaken together with case finding, detected no cases of Legionnaires' disease on a urology ward over three and a half months when 70% of water samples were culture positive for *L. pneumophila* serogroup 1.³⁶ However, as Yu pointed out when commenting on this study, 52 cases of Legionnaires' disease were diagnosed on other wards in the same hospital over a four-year period, 1983-1987.³⁷

The CDC claimed that there were insufficient data to correlate the risk of infection with the quantity (colony forming units) of *Legionella* spp. isolated from environmental samples.²⁷ When routinely culturing water samples for legionella, there is an obligation to try to eradicate legionella if *Legionella* spp. are recovered. Legnani *et al.* studied 11 private healthcare facilities in Italy over a 12-month period, and *Legionella* spp. and *L. pneumophila* were recovered from 87% and

Table I Control of legionella in hot water systems

1. Physical	
a) Heat	Raising calorifier temperatures Instantaneous steam heat systems Self-regulating trace heat systems
b) Ultraviolet irradiation	
c) Sonication	
d) Draining and flushing pipes with compressed air	
2. Chemical	
a) To prevent scale formation and maintain sediment in suspension	
b) Biocides	Sodium hypochlorite Ozone
c) Charcoal filters	
3. Good plumbing practice	
a) General maintenance	
b) Pumps and calorifiers should be in series not parallel	
c) Dead spaces in calorifiers should be eliminated	
d) Dead legs should be removed	
e) Regular flushing of outlets	
f) Use of Water-Research-Centre-recommended components	

82.6% of water samples, respectively. However, during this period, no cases of hospital-acquired Legionnaires' disease were confirmed.³⁴ The authors acknowledge, however, that hospital-acquired Legionnaires' disease is underdiagnosed in their region. Also, it is not clear if, during the study period, any of the healthcare facilities had immunosuppressed patients who would be at particular risk of acquiring hospital-acquired legionellosis due to *L. pneumophila* or other legionella species.

Timbury *et al.* demonstrated that regular environmental surveillance for legionella may not predict future cases.³⁸ Three and five months before an outbreak of hospital-acquired Legionnaires' disease, when the water system was cultured, the water system was deemed to be legionella free. When the outbreak was detected, however, a cooling tower and related system were confirmed as heavily colonized with legionella. This suggests that surveillance of water systems may not always predict an outbreak or assist in preventing Legionnaires' disease. However, details of the water sampling undertaken before the outbreak were not provided. A design fault within the cooling towers was ultimately thought to be the source of the outbreak.³⁸ Hoge and Breiman argued, in a review, that factors influencing a decision to undertake preventive procedures, including whether or not to carry out routine environmental screening, include the apparent frequency or infrequency of hospital-acquired Legionnaires' disease, the ubiquitous nature of the organism, the

difficulty in eradicating the organism from water sources, and the lack of data on the effectiveness of preventing disease.²⁰

In contrast, several other studies have shown that hospital-acquired Legionnaires' disease can be directly related to colonized hospital water systems. Therefore, others advocate routine surveillance of hospital water systems for legionella^{6,12,26,39,40} to heighten physicians' awareness of the infection and to initiate enhanced eradication measures when samples become positive for *Legionella* spp.

Yu *et al.* prospectively studied three hospitals that did not have a previous record of endemic nosocomial Legionnaires' disease.²⁶ Two of the three hospital water systems were colonized with *L. pneumophila*; three cases of Legionnaires' disease were diagnosed in one of these during the study period. Subtyping using monoclonal antibodies showed that the patient isolates were of a similar serogroup to those isolated from the water system. This study, although describing small numbers of cases, provides support for the routine sampling of hospital water systems for legionella.

Following several local outbreaks of Legionnaires' disease in healthcare institutions in the early 1990s, the Allegheny County Health Department in Pennsylvania, USA issued comprehensive guidelines in 1997 on the prevention and control of legionellosis, including environmental surveillance and decolonization measures.⁴¹ In contrast to the CDC guidelines at the time, routine environmental screening of hospital water systems for legionella and the implementation of a specialized protocol of

eradication if the hospital water system was colonized with legionella were strongly recommended.

UK guidelines recommend periodic sampling, e.g. quarterly, for the presence of legionella in cooling towers, and the sampling method should be in accordance with ISO 11731.²⁹ It is also recommended that hot and cold water systems should be monitored if there are difficulties with maintaining hot water storage and distributing temperatures greater than 60 °C and 50 °C, respectively, if an outbreak is suspected or if 'at-risk' patients are present. Irish guidelines, which were published in 2002 and which draw on both the UK and 1994 CDC documents, present the arguments for and against routine sampling (i.e. as part of primary prevention), but do not definitively make a specific recommendation on this issue.⁴²

Goetz *et al.* performed environmental cultures of hospital water systems in six healthcare facilities. When cultures yielded legionella, intensive monitoring for legionella infection was carried out in all cases of hospital-acquired pneumonia.³⁹ Three centres completed the study and legionella was recovered from the hospital water system of all three; in two of the three hospitals where a patient isolate was available, these were found to be identical to the environmental isolates by molecular subtyping.

An important issue in any debate on the routine testing of hospital water systems for legionella as a component of a primary preventative strategy is to consider those patients at particular risk of legionellosis, particularly immunosuppressed patients. Two recent studies highlight the importance of routine cultures in regional transplant centres.^{1,28} A study by Kool *et al.* confirmed nosocomial acquisition of *Legionella* spp. amongst immunosuppressed patients in a regional transplant centre over a 17-year period; 18 of 25 culture-positive cases were due to possible or definite nosocomial legionellosis.¹ Subsequent aggressive control measures successfully interrupted hospital acquisition.

The most recent guidelines for prevention of healthcare-associated pneumonia published by the CDC in 2003 state that because severely immunosuppressed patients (e.g. stem cell transplant recipients) are at much higher risk for disease and death from Legionnaires' disease compared with other patients, periodic water sampling for *Legionella* spp. from the transplant unit's potable water supply can be done as part of a comprehensive strategy to prevent Legionnaires' disease.⁴³ However, the optimal method of sampling and the most cost-effective approach has not been defined for primary prevention. Due to the higher incidence of non-*L. pneumophila* serogroup 1 infection in these patients, the aim of environmental sampling would

be to maintain water systems free of all detectable *Legionella* spp. Physicians at these centres must be aware of the risk of Legionnaires' disease in this group of patients and undertake the appropriate diagnostic testing.

Laboratory methods to detect legionella in water systems

The CDC have outlined procedures for collection and processing environmental specimens for *Legionella* spp. if there is evidence of healthcare-associated transmission of Legionnaires' disease.⁴⁴ These recommendations include collecting 1-L samples of water in sterile containers, taking culture swabs of internal faucets, aerators and shower heads to be placed in sterile containers, having previously submerged each swab in 5-10 mL of sample water, and finally culturing samples for the presence of *Legionella* spp. by using semi-selective culture media. However, no recommendations are specifically provided for environmental surveillance cultures as part of a primary prevention programme. Since the number of legionella bacteria in hospital water may be relatively small outside an outbreak, the above recommendations may not be optimal for primary prevention surveillance.

The Allegheny County Health Department has proposed a methodology for environmental sampling as part of a primary prevention programme⁴¹ which has been supported by others.² In these guidelines, the suggested number of outlets to be sampled for a 500-bed hospital is a minimum of 10 distal sites plus the hot water storage tanks. If the bed size is greater than 500, two distal sites per 100 beds is the recommendation. The distal sites should be taken from units housing patients at higher risk for acquiring Legionnaires' disease. These guidelines recommend that all hospitals should carry out environmental surveillance yearly, but this should be performed more often in a transplant centre, although the exact frequency is not defined.

Identification of *Legionella* spp. takes three to 10 days by conventional culture techniques. There is concern that culture may underestimate the presence of *Legionella* spp. in water samples due to the presence of legionella in amoebae or clumps, high levels of contaminating organisms, damage to legionella by concentration steps, or the presence of viable but non-culturable organisms.⁴⁵

Molecular typing methods, particularly monoclonal antibody typing, DNA sequence amplification using polymerase chain reaction (PCR) and

pulsed-field gel electrophoresis, have proved invaluable as epidemiological tools in the investigation of outbreaks of Legionnaires' disease.^{23,26,45,46} It seems likely that molecular methods, particularly PCR, will probably supplant culture as a first-line laboratory technique for surveillance of legionella in hospital water samples.⁴⁷ PCR circumvents the difficulties of detecting *Legionella* spp. associated with free-living amoebae and can be adapted to detect different species and serogroups using multiplex PCR. With results potentially available within one day, water decontamination and engineering modifications of the water system can be implemented more rapidly than when culture is the sole detection method, as routine culture takes up to 10 days to confirm a positive result. However, more information regarding the sensitivity and specificity of molecular techniques is needed before conventional culture can be replaced.⁴⁴ In the meantime, it seems prudent to use culture and PCR together in surveillance studies of water systems until the superiority of PCR is confirmed. However, amplification-based assays, such as PCR, do have a role in the outbreak setting where there is a need to screen large numbers of water samples for *Legionella* spp. in as short a time as possible.⁴⁵

Conclusion

Since the question of testing hospital water for legionella was first raised more than 20 years ago,⁴⁸ there remains controversy on this issue as a component of primary prevention of hospital-acquired legionellosis. Yu's³⁷ argument in favour of a large-scale multi-centre prospective study over two to three years, comparing the incidence of hospital-acquired Legionnaires' disease in colonized hospital water systems with non-colonized hospital water systems, using the same clinical case definitions and similar laboratory techniques, is convincing but the feasibility of conducting such a trial would be challenging. Furthermore, there might be an ethical issue over detecting legionella in hospital water and not taking measures to ensure that the water system is rendered legionella free as soon as possible, even in hospitals with no confirmed cases. It is also not clear whether both conventional culture and molecular detection approaches should be used in such a study.

While we await definitive evidence regarding environmental testing for legionella as part of a primary prevention programme, each hospital should assess preventive strategies in the light of the published evidence, the engineering

specifications of the local hospital water system, and the spectrum of patients cared for in the institution, especially their immunological status.

It is also essential to raise the general awareness of nosocomial Legionnaires' disease amongst all healthcare workers and to facilitate laboratory diagnosis. In one study, only 19% of hospitals routinely performed sputum culture for Legionnaires' disease in at-risk patients with hospital-acquired pneumonia.⁴⁹ In particular, the use of urinary antigen detection tests for legionella should be routine in the diagnosis of community- and hospital-acquired pneumonia possibly caused by *L. pneumophila* serogroup 1.^{50,51} Finally, infection control teams must work closely with hospital engineers and technical services departments as well as with hospital management to minimize the risk. Furthermore, an increased awareness of hospital-acquired legionellosis amongst physicians and others will lead to earlier diagnosis and may result in more appropriate and cost-effective interventions.

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