Control of *Legionella* in hospital potable water systems

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4.1 Introduction

The epidemiological link between the presence of *Legionella pneumophila* in the hospital drinking water and hospital-acquired legionellosis was first made in the early 1980s by Tobin and Stout [1, 2]. However, since then, many other species of *Legionella* have been found in drinking water including *L. anisa*, *L. bozemanii*, *L. dumoffii*, *L. feeleii*, and *L. micdadei*. The genus *Legionella* contains over 50 distinct species, some with different serogroups, with approximately half of these species associated with human disease. While *L. pneumophila*, and more specifically *L. pneumophila* serogroup 1, causes the majority of cases of Legionnaires' disease, these other species are also important clinically. In immunocompromised individuals, *L. micdadei* and *L. longbeachae* are particularly problematic [3, 4]. A nosocomial outbreak of *L. micdadei* in transplant patients was reported that was linked to the hospital's water [5]. More cases of illness due to nonpneumophila species, such as *L. longbeachae*, have been reported in Europe, particularly in Scotland, than elsewhere. In addition to drinking water, *L. longbeachae* can be found in soil and compost-derived products, especially in Australia and New Zealand. In 2013, *L. longbeachae* was reported to cause 51% of Legionnaires' disease in New Zealand [6].

Numerous hospitals and long-term care facilities have reported outbreaks of healthcare-associated Legionnaires' disease [7–11]. Transmission has been consistently linked to the drinking water distribution systems. The incidence of healthcare-associated infection depends on the extent of contamination of the drinking water system and the susceptibility of the patient population to infection. The proportion of water distribution system outlets that are positive for *Legionella* has been shown to correlate with occurrence of disease, but the concentration of *Legionella* in the water obtained from these distal sites did not [12–16].

In outbreaks associated with drinking water, *Legionella* is the most frequently reported cause of infection. During the 2013–14 drinking water disease outbreak surveillance period, *Legionella* was the cause of all outbreak-related deaths. Additionally, in hospitals, healthcare facilities, and long-term care facilities all of the outbreaks

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reported were caused by *Legionella* species [17]. Two-thirds of the Legionellosis outbreaks have been reported to be in healthcare settings [18]. In the United States from 2000 to 2014, the Centers for Disease Control and Prevention (CDC) conducted 38 field investigations of Legionnaires' disease. They found that 33% of cases were healthcare-associated. These healthcare-associated outbreaks were larger and resulted in more of the deaths (86% of deaths) compared to the travel-associated outbreaks (6%) [19]. Potable water was the most frequent source of exposure, accounting for 56% of exposures, compared to cooling towers which were the source in only 22% of exposures [19, 20]. In Europe from 2011 to 2015, 29 countries reported over 30,500 cases of Legionnaires' disease with France, Germany, Italy, and Spain combined accounting for 70.3% of all European cases [21].

The first documented study of disinfection was published in 1983 using thermal eradication, which we termed "superheat-and-flush method" [14]. The first comprehensive review on disinfection methodologies was published in 1990; definitive recommendations as to which methodology was superior were not made [22]. Two reviews on disinfection methodologies were published: one for engineers and healthcare facility managers [23] and another for physicians and infection control practitioners [24]. At that time, disadvantages of both hyperchlorination and ultraviolet light had become manifest and a new technology, copper-silver ionization, was under evaluation. Over 20 years have since passed, and additional methods have been introduced: chlorine dioxide, monochloramine, and point-of-use filtration. We have previously recommended evidence-based evaluation criteria to set a standard for manufacturers of disinfection methodologies (Table 4.1). Such objective criteria assist hospitals in making cost-effective decisions.

Other waterborne pathogens including *Pseudomonas aeruginosa*, *Burkholderia cepacia*, *Stenotrophomonas maltophilia*, nontuberculous mycobacteria (NTM), *Aspergillus* species, and many more can cause healthcare-acquired infections especially in high-risk patient units and neonatal intensive care units [27–31]. These organisms have been directly linked to healthcare-associated infections that were transmitted by contaminated potable and hospital water systems [29, 30]. The scope of infections caused by these bacteria, especially *P. aeruginosa*, is not currently well understood or controlled [32].

Table 4.1 Objective criteria for disinfection methods using a four-step approach [25, 26].

– Demonstrated efficacy in vitro against *Legionella*
– Reports of anecdotal experience of efficacy in controlling *Legionella* contamination in individual hospitals
– Peer-reviewed and published reports of controlled studies of prolonged duration (years) of the efficacy of controlling *Legionella* growth and preventing cases of hospital-acquired Legionnaires' disease in individual hospitals
– Confirmatory reports from multiple hospitals with prolonged duration of follow-up (validation step)

4.2 Systemic disinfection methods

4.2.1 Chlorine dioxide

This disinfectant has been regarded as safe because it has been used for water treatment in Europe since the 1940s. Numerous chlorine dioxide systems have been installed in the United States for *Legionella* disinfection. Chlorine dioxide is a gas in solution that is typically generated on site. The two most commonly used methods for producing chlorine dioxide are controlled mixing of chemical precursors or electrochemical generation. Chlorine dioxide has been applied to both the cold and hot water systems. Chlorine dioxide does not form carcinogenic by-products such as trihalomethanes [33, 34]. Chlorine dioxide is both odorless and tasteless. It can penetrate into biofilms more effectively than chlorine. This penetration can inhibit biofilm development. Although chlorine dioxide has been shown to control *Legionella*, more time may be needed for efficacy in hot water. This is due to the breakdown of chlorine dioxide into its by-products, chlorite and chlorate [35, 36] which are less effective. The biocidal action is maintained over a wider range of pH levels than other disinfectants such as chlorine and copper-silver ionization. Corrosive effects are much less than that of chlorine, but it can cause cracking of plastic piping.

The first controlled field evaluation in the United States was conducted in a hospital that had experienced hospital-acquired Legionnaires' disease [37]. During the 15-month study, *Legionella* positivity of hot water outlets significantly decreased from 23% to 12%. *Legionella* positivity for cold water outlets approached 0%. The mean chlorine dioxide residual at cold water outlets was higher than hot water, 0.33 mg/L and 0.08 mg/L, respectively. The reduction in chlorine dioxide concentration in the hot water (0.08 mg/L) may explain why complete eradication was not achieved until after 20 months of treatment.

Zhang et al. evaluated the efficacy of chlorine dioxide in a New York hospital over a 30-month period [36]. *Legionella* positivity in hot water decreased from 60% to 10%, but this reduction took 18 months [38]. No cases of hospital-acquired Legionellosis occurred during this period. Like the previous study, significantly lower chlorine dioxide residuals were detected in the hot water (0.04 mg/L) compared to the cold (0.3–0.5 mg/L).

After 2 years of chlorine dioxide treatment (target concentration of 0.5 mg/L) in a UK hospital, the *Legionella* positivity remained unchanged. Two cases of hospital-acquired Legionnaires' disease also occurred during this period [34]. In another UK hospital with hospital-acquired Legionnaires' disease [39], chlorine dioxide was used because of repeated failures with hyperchlorination. Chlorine dioxide was injected into both the cold-water supply (0.25–0.5 mg/L) and the hot water supply (3–5 mg/L) to achieve a 0.25–0.5 mg/L residual concentration at hot water outlets. *Legionella* was not detectable from the water system after 3 years. When chlorine dioxide concentration fell below 0.25 mg/L due to mechanical failure, *Legionella* was detected in water samples within 4 days. Chlorine dioxide was injected into the water system of an Italian hospital at 0.4–0.5 mg/L at the cold-water source, which resulted in 0.2–0.3 mg/L at

the outlets. High concentrations of *Legionella* were still detected after 4 years of treatment, and 12 cases of hospital-acquired Legionnaires' disease occurred [40].

In a Scottish hospital both hyperchlorination and chlorine dioxide were used to control *Legionella*. Hyperchlorination was found to be ineffective in eradicating *L. pneumophila* from the hospital drinking water and cases of hospital-acquired legionellosis occurred. Chlorine dioxide at 0.5 mg/L was injected into the cold-water systems. Treatment was successful in controlling *L. pneumophila* serogroup 1 by week 6; however, *L. anisa* persisted in low numbers [41]. Prolonged duration of treatment with chlorine dioxide was necessary before *L. anisa* counts decreased significantly at Johns Hopkins Hospital [35]. It took 60 days to reduce positivity from 40% to 20% and 15 more months to reach the 4% level at the end of their study. *L. anisa* is a rare cause of infection and no illness was documented. In a survey from the French national *Legionella* surveillance network, 13.8% of environmental samples were positive for *L. anisa* and only 0.8% of patient samples were positive for *L. anisa* [42]. In a multicenter prospective study involving 20 hospitals across the United States, 45% of hospitals were colonized with *L. anisa*, but no infections caused by *L. anisa* were identified [15]; thus, disinfection is not recommended if *L. anisa* is the sole species isolated from the water.

When chlorine dioxide was compared to monochloramine for *Legionella* control in an Italian hospital, monochloramine was found to be more effective. Distal site positivity was reduced from 96.4% to only 45.9% in the chlorine dioxide-treated systems, whereas *Legionella* distal site positivity went from 100% to 9.5% in the monochloramine-treated building. Hot water treated with chlorine dioxide also had higher levels of chlorites and chlorates than monochloramine-treated hot water [43].

The limitations of chlorine dioxide include the following: (1) Prolonged time is required to demonstrate significant reductions in *Legionella* positivity [35–38, 44, 45]; (2) chlorine dioxide concentration in hot water is low (<0.1 mg/L) when injected into the incoming cold water at 0.5–0.8 mg/L [35, 37, 44, 46]; (3) reactions with organic material and corrosion scale in piping causes rapid conversion of chlorine dioxide to chlorite and chlorate [46], these by-products may pose health risks; (4) corrosion of galvanized pipes can cause loss of chlorine dioxide which may affect efficacy [46].

The major challenge for chlorine dioxide is maintenance of an effective residual (0.3–0.5 mg/L as ClO_2) throughout the drinking water system [46]. One New York hospital achieved success of >0.1 mg/L by direct injection into the hot water system (Stout, JE personnel communication, 2010).

Drinking water regulatory considerations include the following: (1) chlorine dioxide is a registered biocide with the US EPA; (2) the EPA has set the maximum residual disinfectant level (MRDL) for ClO_2 of 0.8 mg/L; and (3) the maximum contaminant level (MCL) for chlorite (ClO_2^-) of 1.0 mg/L [47]. Possible health effects from chlorite include congenital cardiac defects and hemolytic anemia [48]. Chlorate is currently not regulated due to the lack of health data to set an MCL. The United Kingdom Drinking Water Inspectorate specifies a limit for combined concentrations of chlorine dioxide, chlorite, and chlorate. The maximum value for total oxidants in drinking water is 0.5 mg/L. The US EPA mandates that healthcare facilities adding a disinfectant to a water system that serves at least 25 people is considered a public

water system and must comply with the Safe Drinking Water Act (SWDA) and Stage 1 Disinfection Byproducts Rule [49]. In addition, in the United States chlorine dioxide products used in hospitals must be EPA-registered and American National Standards Institute (ANSI)/National Sanitation Foundation (NSF) certified. Some states require regular monitoring of chlorine dioxide and chlorite. Such testing can be costly, and this expense is often overlooked.

Data on the efficacy of chlorine dioxide against other waterborne pathogens are promising. Chlorine dioxide was able to kill *M. avium* faster than chlorine or monochloramine [50]. Chlorine dioxide was effective in killing Gram-negative bacilli (*Pseudomonas* species, *S. maltophilia*, *Sphingomonas paucimobilis*, and others) and nontuberculous mycobacteria (NTM) [51]. A hospital building treated with chlorine dioxide had low levels of NTM, including *M. kansasii*, *M. xenopi*, *M. fortuitum*, and *M. gordonae*. A control building with no disinfection showed 70% positivity whenever the treated building was 20% [52].

4.2.2 Copper-silver ionization

Copper and silver ions are released into the hot water system from metal electrodes. The system is typically installed on the hot water recirculation system. The mechanism of action involves positively charged copper and silver ions forming bonds with negatively charged ions on the bacterial cell wall. Lysis and bacterial cell death is the result. Copper and silver ion concentrations in the ranges of 0.3–0.8 mg/L copper and 0.01–0.08 mg/L silver are typically recommended for *Legionella* control [53–56]. Copper ion concentrations should be monitored weekly with a field test kit. Silver concentrations can only be tested by a certificated reference laboratory and should be tested bimonthly. Water samples for ion analysis should be clear and free of sediment. Ions can bind to particulates and result in high readings. Monitoring ion concentrations and maintenance of equipment to reduce scale formation on the electrodes is necessary and this technology can be used for both short-term and long-term disinfection.

The first installation of a copper-silver ionization system in the United States was in 1990 [57]. A Pittsburgh, Pennsylvania hospital showed that *Legionella* colonization of distal outlets was reduced from 75% to 0% in 3 months. Copper and silver ion concentrations were above 0.4 and 0.04 mg/L, respectively [58]. When the ionization unit was deliberately inactivated, recolonization was delayed, and the water system remained free of *Legionella* for an additional 2–3 months. Accumulation of ions inside the biofilm was demonstrated to be the basis for the prolonged bactericidal effect [58, 59]. Copper-silver ionization has been used in hospitals, long-term care facilities [60], office buildings [58], and apartment buildings [61].

Copper-silver ionization has been used to control *Legionella* in hospitals worldwide [53–56, 62–65]. Sixteen US hospitals were followed that had ionization systems in place for 5–11 years and showed success where other methods such as superheat and flush, ultraviolet light, and hyperchlorination had failed [25]. Fifty percent of the hospitals reported 0% positivity within 0–5 years after treatment with copper-silver ions, and 43% still reported 0% positivity 5 years later. More importantly, no cases of hospital-acquired Legionnaires' disease had occurred in any of these hospitals

after installing ionization systems. Ten cases of Legionnaires' disease occurred at the University of Wisconsin hospital from 1985 to 1995, despite hyperchlorination. Following installation of copper-silver ionization, *Legionella* was eliminated from the drinking water system and no cases were diagnosed [66].

A 1998 survey of US National Nosocomial Infections Surveillance hospitals showed that copper-silver ionization was used in 32% (12/38) of hospitals that had instituted disinfection measures [67]. The first three hospitals to apply hyperchlorination for *Legionella* disinfection (Wadsworth VA Medical Center, California; University of Vermont Medical Center, Vermont; University of Pittsburgh Medical Center, Pennsylvania) ultimately switched to ionization because of failure to control *Legionella* and chlorine-induced corrosion. A review of 10 published studies also concluded that copper-silver ionization is an effective method to control *Legionella* as long as ion levels were properly monitored [64]. A metadata analysis of three studies comparing copper-silver ionization to no treatment indicated a 95% risk reduction of *Legionella* distal site positivity [68]. In the United Kingdom, a new hospital compared reducing hot water temperatures (to 43°C, ranging 37–44°C) and utilizing copper-silver ionization to control *Legionella* in their water system. No *L. pneumophila* was isolated from any of the samples collected after the ionization system was installed. However, it is not clear whether there was any *Legionella* colonization or recovery prior to the installation of the copper-silver ionization system and building commissioning [69]. It should also be noted that in the United Kingdom, the Health and Safety Executive (HSE) stipulate that "Hot water should be stored at least at 60 °C and distributed so that it reaches a temperature of 50 °C (55 °C in healthcare premises) within one minute at the outlets" [70].

Advantages of copper-silver ionization include easy installation and maintenance. Oral consumption is limited since the ions are typically added only into the hot water recirculating lines. The demonstrated prolonged efficacy of ionization after an interruption provides added margin of safety. This is unlike hyperchlorination in which *Legionella* can rapidly appear in the event of system malfunction. The biocidal activity of copper-silver ionization is not compromised by higher water temperature [71], which is the case for chlorine and chlorine dioxide.

Elevated water pH [72] and low ion concentrations [73] may compromise the efficacy of ionization and so these have to be addressed at the time of installation and monitored. High pH of the hospital water (>8.5) interferes with the disinfecting action of both chlorine and the copper-silver ions [74, 75]. Copper-silver ionization was demonstrated to be effective in controlling *Legionella* in an acute care facility, previously treated with chlorine dioxide, and long-term care facility under alkaline water conditions [76]. Low ion levels in two German hospitals were responsible for copper-silver ionization systems failure to control *Legionella* [73, 77]. In both hospitals, the concentrations of copper and silver ion concentrations were well below the recommended concentrations of copper and silver so as to comply with the German drinking water standard (maximal silver of 0.01 mg/L) [78]. One French hospital also reported the failure of ionization [79]. In this case, phosphate added to the water system to control corrosion may have interfered with the efficacy of ionization [80].

Resistance of *Legionella pneumophila* to copper-silver ions has been documented in a few hospitals following installation of copper-silver ionization systems [81]; however there is no indication that resistance is frequent or widespread. Hospitals that maintain control by monitoring ion concentrations and *Legionella* distal site positivity are less likely to experience this phenomenon. Rigorous maintenance plans with regular monitoring of both ion concentrations and culturing for *Legionella* positivity are necessary to ensure long-term success.

The Environmental Protection Agency (EPA) set a maximum containment level (MCL) for copper in drinking water of 1.3 mg/L, and 0.1 mg/L for silver (nonenforceable). EPA now requires ionization systems to "register" as a biocide for use in potable water [72]. This registration falls under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) for devices claiming biocidal action. In the United Kingdom, Spain, the Netherlands, and Poland separate applications allow for these products to be used, though not authorized for the whole of the EU, whose members must use alternative methods for treatment [82].

Copper and silver ions have been demonstrated to be bactericidal in vitro and in model plumbing systems against other waterborne pathogens including *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, and *Acinetobacter baumannii* [83, 84]. One study demonstrated the inefficiency of copper-silver ionization against nontuberculous mycobacterium at levels sufficient to control *Legionella* in a hospital system [53].

4.2.3 Hyperchlorination

Hyperchlorination was one of the first approaches used to control *Legionella* in hospital water systems [22, 23]. In a 1990 review, we reviewed 17 hospitals applying hyperchlorination either alone or in combination with another disinfection method [22]. Due to costly corrosion or other problems, virtually all have since converted to other methods of disinfection. A supplemental chlorination system was installed in a medical center to stop an outbreak of *L. micdadei* infections in transplant patients. The system malfunctioned for 3 weeks and five additional culture-confirmed cases were identified [5]. A 5-year study of hyperchlorination was conducted in hospital buildings in Italy. After shock treatment with chlorine, hyperchlorination was maintained and resulted in a reduction in samples positive for *Legionella*. *Legionella* was recovered in 21.1% of samples prior to treatment, whereas during treatment only 5.5% of samples were positive [85].

The challenges most often encountered when using hyperchlorination include (1) inadequate penetration into piping biofilms, (2) resistance to chlorine by *Legionella* [86–88], (3) corrosion of the water distribution system causing pinhole leaks, and (4) the introduction of carcinogens into the drinking water. As a result, hyperchlorination is most often used as a supplementary short-term disinfection method [89].

Mycobacteria can emerge following chlorination, despite the fact that chlorine has been demonstrated to be effective against some *Mycobacterium* species in vitro. Generally speaking, concentrations used in drinking water distribution systems are not sufficient to kill all species as some NTM are more resistant than others to chlorine

[50, 90]. In experiments using biofilm-grown *M. avium* and *M. intracellulare*, it was shown that they were more resistant to chlorine than the already relatively resistant planktonic bacteria [91]. Compared to other disinfection methods such as UV light, chlorine was less effective against *M. fortuitum* [92]. However, in one study chlorine was found to be more effective than monochloramine against *Mycobacterium* species [93]. In in vitro studies, biofilm-derived and cocultures of *B. cepacia* and *P. aeruginosa* were fairly resistant to chlorine [94]. However, when grown in suspension in pure culture *B. cepacia* [94] and *P. aeruginosa* were more susceptible [94, 95]. A laboratory study describing the disinfection kinetics of chlorine for fungal species (*Aspergillus fumigatus*, *A. versicolor*, and *Penicillium purpurogenum*) noted that these species had a similar resistance as *Mycobacterium* species and *L. pneumophila* to this treatment. Chlorine was not as effective as monochloramine against *P. purpurogenum* [96].

4.2.4 Monochloramine

Monochloramine has emerged as one of the most effective disinfectants against *Legionella*, both in laboratory and field studies [93, 97–100]. Monochloramine is stable and has the ability to penetrate biofilm more effectively than chlorine [101], and has a wider pH working range than copper-silver ionization and chlorine [102, 103]. The target concentration for monochloramine is 1.5–3.0 mg/L as Cl_2 but the target and optimal concentrations may depend on the manufacturer. The EPA MCL for monochloramine is 4.0 mg/L as Cl_2.

The ability to generate and apply monochloramine on-site for disinfection of hospital water systems has made this technology an option for hospitals. Monochloramine has been evaluated for efficacy in controlling *Legionella* in multiple healthcare facilities including four Italian hospitals and in a US hospital in Pittsburgh, Pennsylvania [104]. The system for delivering monochloramine into building hot water distribution systems was first evaluated at a hospital in Modena, Italy. A significant reduction in *Legionella* positivity was seen within 30 days of injecting 1.5–3 mg/L of monochloramine [105]. Monochloramine treatment was compared to chlorine dioxide in the same hospital system in Italy. Monochloramine was found to significantly reduce *Legionella* distal site positivity compared to chlorine dioxide (100%–9.5% vs 96.4%–45.9%) and produce fewer chlorites and chlorates overall in hot water [43]. In Catania, Italy, a monochloramine generation system was utilized to control *Legionella* in two hospitals [106]. Before the study, *Legionella* was isolated from 100% of outlets in both hospitals whereas 1 month after monochloramine treatment *Legionella* was undetectable. The speed of the reduction was noteworthy. Within 1 week, distal site positivity was down to 8% [106]. In another hospital in Catania, Italy, monochloramine treatment was effective in removing *Legionella* from the hot water system. Initially, 100% of samples were positive for *L. pneumophila* serogroup 5 but after treatment for the 3-year study no *Legionella* positive samples ($>10^3$ cfu/L) were recovered [107]. A university hospital in Pisa, Italy switched from systemic disinfection with chlorine dioxide and point-of-use filtration in high-risk wards to monochloramine treatment as part of their water safety plan. This disinfectant reduced *L. pneumophila* serogroup 1 positivity from 100% to 0%. *Legionella* was briefly isolated during malfunction of the

monochloramine generator, but all samples returned to negative after the system was adjusted [108].

Several studies have been carried out using monochloramine treatment in a hospital in Pittsburgh, Pennsylvania [109–112]. One study included 2 years of follow-up after monochloramine system installation and demonstrated a reduction in *Legionella* distal site positivity from 53% to 9% [110]. Two microbiome analyses of this system also showed *Legionella* control by monochloramine [111, 112]. Two periods of increased distal site positivity were associated with changes in chemical composition and increased pH [110]. One of these *Legionella* rebounds was observed in molecular microbiome analysis (16S rRNA sequencing) of the water system and it was perceived that *Legionella* was likely able to take over the system due to the overall reduction of bacterial richness and diversity in monochloramine-treated samples [111]. Therefore, we suggest routine monitoring for *Legionella* species and disinfectant concentration to ensure the system is operating appropriately.

If a municipality converts from chlorine to monochloramine as the primary treatment method, the hospitals in that municipality may benefit if they have a water system colonized with *Legionella* [15]. Two case-control studies suggested that hospitals in municipalities that were supplied with domestic drinking water treated with monochloramine were less likely to report hospital-acquired Legionnaires' disease [102, 113]. *Legionella* colonization decreased from 60% to 4% with conversion from chlorine to monochloramine in 53 buildings in California. The median number of colonized sites per building decreased with monochloramine disinfection [103]. The number of colonized buildings in a Florida study decreased from 20% to 6% after monochloramine was introduced into the municipal water supply [114]. The use of monochloramine at the municipal level, versus chlorine alone, was associated with a reduced risk of *Legionella* colonization of the hot water system in a study comparing 15 hospitals in Texas [115]. On the other hand, the proportion of buildings colonized by *Mycobacterium* species increased from 19% to 42% indicating that monochloramine was less effective than chlorine in controlling mycobacteria in municipal water distribution systems. Increased growth of coliforms and heterotrophic bacteria also occurred [116]. Additionally, an increase in nitrogen by-products and increased lead leaching in drinking water has been reported [61, 116]. These problems were not seen when monochloramine was applied to the hospital hot water systems [110].

Monochloramine can cause anemia in patients undergoing hemodialysis and therefore these patients must be protected. Indeed, hemodialysis and renal patients should be protected from chemicals used to treat water systems. This is something to address if applying monochloramine to the entire cold-water system and dedicated treatment and supply arrangements may be required for renal and hemodialysis units. Both where monochloramine is applied (hot vs cold water) and how it is generated can impact by-products and ammonia levels.

Monochloramine has been shown to kill *S. aureus*, *P. aeruginosa*, *A. flavus*, and *A. fumigatus*, *E. coli*, and *C. albicans* in vitro [117]. Fungal species, including *A. fumigatus*, *A. versicolor*, and *P. purpurogenum*, were determined to be fairly resistant to monochloramine in vitro though not more so than NTM or *L. pneumophila* [96]. In monochloramine systemic disinfection of hospital systems, a reduction, though not

statistically significant, of *P. aeruginosa* [105] and *Mycobacterium* species [110] was noted. Other waterborne pathogens (*P. aeruginosa*, *S. maltophilia*, and *Acinetobacter* species) were found at low concentrations before and after treatment and did not increase during continuous systemic disinfection [110]. Another study described an increase in site positivity and concentrations of *Mycobacterium* species when using 2 mg/L of monochloramine but when the concentration was increased to 3 mg/L the *Mycobacterium* species were successfully removed [108].

In molecular analyses, the community composition of water treated with monochloramine was completely different than a control building. No increase in *Mycobacterium* species relative abundance was observed although an increase in *Sphingomonas* species abundance was observed [111]. During the first 6 months of treatment with monochloramine the relative abundance of *Acinetobacter* species, *Mycobacterium* species, *Pseudomonas* species, and *Sphingomonas* species increased significantly. Although it is unclear how these results relate to the presence of cultivable bacteria since the culture-based study including these samples saw an overall reduction of *Mycobacterium* species and no change in *P. aeruginosa* or *Acinetobacter* species during monochloramine application [112].

4.2.5 Point-of-use filtration

Point-of-use (POU) filters exclude microbes based on their size using the pores of the POU filter membrane and provide a physical barrier between *Legionella* and other waterborne pathogens found in hospital outlets and individuals exposed to that water. POU filters can be installed on faucets, showers, or in-line supplying ice machines. The period of approved use of these devices has continually increased from the original 7-day use period to up to 124 days of use for the faucet and shower filters depending on the manufacturer and characteristics of the filters. Some in-line filters can be used for up to 360 days or a specific number of gallons. POU filters may be affected by retrograde contamination, as reported in previous studies [118, 119]. This can limit the duration of use due to the presence of bacteria on the contaminated filter's external surface that may lead to the transfer of bacteria to other surfaces and the hands of healthcare workers.

The first controlled study of a POU faucet filter demonstrated effective removal of *Legionella* at the point of use. This filter was also able to remove or reduce NTM and total bacteria, as measured by heterotrophic plate count (HPC) [120] from the water emitted from the filter outlet. Additional studies have demonstrated the efficacy of POU faucet and shower filters in removing *Legionella* from hospital water systems [119, 121–128].

Some hospitals restrict water use during an outbreak by having patients use bottled water exclusively and restricting all patients from showering. POU filters accomplish reduced risk of exposure and allow for continued use of water and are better tolerated by patients [129]. These filters are used for both outbreak remediation and continuously on faucets and showers or in-line for ice machines in high risk units like neonatal intensive care units (NICUs), transplant units, and hematology-oncology units.

Published evaluation studies demonstrated successful removal of other waterborne pathogens including *Pseudomonas aeruginosa* [119, 122–124, 126–128, 130–136], Nontuberculous mycobacterium [118, 120, 128, 137], *Stenotrophomonas maltophilia*

[123, 124, 136], *Acinetobacter* species [123, 124], coliforms [119, 122, 132], fungi [122, 128, 132, 138], and total bacteria (HPC) [119, 120, 122, 126–128, 137].

4.2.6 UV light used alone or in combination with other disinfectants

UV light is a nonchemical option for disinfection of drinking water. Point-of-entry application does not allow eradication at outlets downstream of entry.

Two hospitals found that UV was ineffective in eradicating *Legionella* at distal sites [139, 140]. Combining UV and hyperchlorination was effective in a transplant unit for *Legionella* control [141]. In a new hospital, UV was installed on the incoming water supply. None of the 930 drinking water cultures were positive over a 13-year period and cases of hospital-acquired legionellosis were not found [142]. Unfortunately, the study was not definitive because no control sites were used. One study comparing UV light and filtration to no treatment showed a 97% risk reduction of *Legionella* positive distal sites using UV light and filtration [68]. An Italian hospital demonstrated efficacy of UV light with hydrogen peroxide injection initially and every 6 months, against *L. pneumophila* after recurrence following a thermal shock treatment [143].

Relatively few studies have been published demonstrating efficacy of UV light against other waterborne pathogens in the hospital setting. A study demonstrated *L. pneumophila* and *P. aeruginosa* removal from a respiratory hydrotherapy system using both ultrafiltration and UV light [144]. *P. aeruginosa* removal by UV light without filtration has also been described [145]. *M. avium* complex has been shown to be more resistant to UV light than other bacteria [146], but was able to be inactivated by UV light rates used in drinking water treatment [147]. UV light was demonstrated to be more effective than chlorine in the elimination of *M. fortuitum* [92]. Efficacy of UV light disinfection is affected by temperature, dose, and duration of exposure.

4.2.7 Advantages and disadvantages of systemic disinfection methods

Selection of long-term systemic disinfection methods requires consideration of many factors. As a result, it is not a one-size-fits-all approach for all facilities. The following factors should be considered during the disinfection selection process: (1) country or region-specific regulatory requirements for disinfection methods, (2) disinfectant by-products produced and their allowable limits in drinking water, (3) the efficacy against *Legionella* and other waterborne pathogens, (4) the operational and maintenance requirements for the system selected, (5) the time and training of staff needed to operate the system, and (6) cost of implementation and monitoring. The decision process must include infection preventionists and those involved in the water safety group. Both the facilities management needs and those of the patients that the healthcare facility is serving are best addressed by the infection preventionist and water safety group. For more information about application conditions, disinfection by-products, allowable chemical levels, and advantages and disadvantages of these disinfection methods, see Table 4.2.

Table 4.2 Summary of systemic disinfection methods.

Disinfection method	Typical application rate[a]	Optimal pH	Temperature	Disinfection by-products (DBP)	USEPA drinking water standard	Advantages	Disadvantages
Chlorine dioxide	0.5–0.7 mg/L ClO_2	6.0–10	Elevated temperatures accelerate decay	Chlorite	Chlorine dioxide <0.8 mg/L	• Biofilm penetration • Less corrosive than chlorine • Regulatory agency familiarity	• Extended time for efficacy • Difficult to achieve/maintain residual in hot water applications • Reactions with organic material and corrosion scale in piping • Corrosion of PEX piping
Copper-silver ionization	0.2–0.8 ppm Cu 0.02–0.08 ppm Ag	>8.5	No impact from temperature	None	Copper <1.3 mg/L Silver <0.1 mg/L	• No chemical precursors • Small equipment footprint • Prolonged efficacy if application is disrupted	• Primarily a hot water application • Laboratory measurement for silver ion concentration • Regulatory agency unfamiliarity • Anecdotal reports of corrosion in long-term applications
Hyperchlorination	2–3 mg/L Cl_2	<8.0	Elevated temperatures accelerate decay	THM and HAA5	Chlorine <4.0 mg/L	• Readily available • Regulatory agency familiarity	• Inadequate biofilm penetration • Corrosion of piping systems • Carcinogenic by-products • Studies have shown *Legionella* resistance up to 50 mg/L

Monochloramine	1.5–3 mg/L as Cl_2	7.0–9.0	Minimal impact by elevated temperature	Reduced THM and HAA5 compared with chlorine	Chloramine <4.0 mg/L as Cl_2	• Biofilm penetration • Less corrosive than chlorine • Regulatory agency familiarity • Rapidly effective against *Legionella* • Reduced DBP formation	• Cold water application can impact hemodialysis and fish • Cold water application could impact water quality (i.e., nitrification)
POU filters	Applied to faucets, showers, or in-line	2.0–12.0 depending on manufacturer	Temperature range of use dependent on manufacturer	None	N/A	• Complete microbiological barrier • Quick implementation • No water restrictions required • Good for high-risk patients	• Barrier only: does not eradicate • Requires periodic filter replacement • Filters might reduce flow over time, especially in turbid waters • Ongoing cost to replace
UV light	UV reactor on-site	N/A	Some components may be impacted by elevated temperatures	None	N/A	• Easily installed • Effective against *Legionella* • Water taste and odor not affected	• No residual protection • Affected by turbid water • More operational and maintenance requirements • Does not affect biofilm formation

HAA5, Haloacetic acids including monochloroacetic acid, dichloroacetic acid, trichloroacetic acid, monobromoacetic acid, and dibromoacetic acid; *THM*, trihalomethanes.

[a] Typical application rate concentrations should be in accordance with the system manufacturer's specifications.

4.3 Emergency disinfection methods

Immediate measures are needed to minimize panic among patients and employees and to manage public relations when cases of hospital-acquired Legionnaires' disease are identified. Some Legionnaires' disease prevention regulations and guidelines require immediate use of a short-term control measure if the distal site's positivity for *Legionella* exceeds 30% [148] or if a threshold value of concentration is reached. During an outbreak, superheating and flushing or hyperchlorination are generally recommended by the public health authority having jurisdiction. In this situation, the hospitals may use superheat-and-flush plus/minus shock hyperchlorination as a short-term, systemic control measure [23]. This method is logistically tedious, and the benefits are short-term; re-colonization invariably occurs. Hot water temperatures are elevated to >70°C (158°F) for 3–5 days with flushing of each hot-water faucet and showerhead for 30 min [149]. A 5- to 10-min flush was recommended by the CDC [150], but such shorter flush times have been shown to be ineffective [149, 151]. The advantage of this method is that disinfection of the water distribution system can be instituted rapidly. However, temperatures at the distal site must be rigorously maintained and monitored [152]. Superheating at distal taps where thermostatic mixer valves are installed may not reach the required temperature. These thermostatic mixer valves need to be bypassed in order to achieve the desired temperature. Caution is advised when superheating water due to risk of scald injury.

Shock chlorination may be the only option in some hospitals where superheat-and-flush cannot be used [151]. Shock chlorine dioxide is theoretically feasible but may pose health risks due to gassing off of the disinfectant. Clinical experience as a short-term measure is very limited [153]. A short course of copper-silver ionization may also be an option for some facilities [59, 154]. Point-of-use water filters are a cost-effective measure if a limited patient area can be targeted. They can be applied immediately and are better tolerated by patients and staff when compared to the alternative of restricting showering and providing bottled water [129]. See Table 4.3 for information about these emergency disinfection methods.

4.4 Selection and validation of disinfection method

Making decisions about what type of disinfection system may be appropriate for the facility and selection of the supplier warrants careful consideration. Objective assessments from other hospitals that have used the supplier's product may provide information to help facilities. The necessity and ongoing requirement for maintenance and monitoring following installation are often underestimated. Regulatory compliance and possible permitting requirements must be considered in each of the countries in which the disinfectants are used. Allowable levels of chemicals, especially chlorine and chlorine dioxide, and the applicability to either hot or cold-water systems depends on the country or region and may impact the choice of disinfection system. In Europe, generally thermal treatment is recommended followed by physical measures (UV light or POU filters), then electrochemical disinfection (copper-silver

Table 4.3 Summary of emergency disinfection methods.

Emergency disinfection method	Method of application[a]	Advantages	Disadvantages
Thermal (superheat and flush)	• Increase hot water generation temperature to ≥160°F • Flush every outlet for minimum of 30 min, maintaining outlet temperature between 150°F and 160°F	• No chemicals required • No special equipment required • Quick implementation • Relatively inexpensive	• Scald potential • Labor and energy intensive • Reduced temperature or flush duration impacts efficacy • Water restrictions during application • High temperatures can impact plumbing system • Temporary solution
Shock hyperchlorination	• Achieve 20–50 mg/L free chlorine in tanks • Flush every outlet until chlorine ≥2 mg/L is detected • Hold for a minimum of 2 h • Flush outlets until chlorine is <2 mg/L	• Reagents are readily available • Effective against *Legionella* and viruses • Used with mixing valves	• Labor intensive • Accelerated piping corrosion, especially with repeat applications • Water restrictions during application • Does not penetrate biofilms well • Must be performed by a qualified water treatment professional
Short-course copper-silver ionization	• Portable copper-silver ionization cells installed on hot water system • Operated within drinking water for 30–60 days	• Small equipment footprint • Prolonged efficacy compared with thermal or hyperchlorination • No water restrictions during application	• Rental of equipment during application • Plumbing modifications to pipe in • Laboratory measurement for silver ion concentrations • Permitting may be needed depending on regulatory agency
POU filters	• Install filter on outlet or on the water supply to appliance • Replace filter per manufacturer's instructions	• Complete microbiological barrier • Quick implementation • No water restrictions required	• Barrier only: does not eradicate • Requires periodic filter replacement • Filters might reduce flow over time, especially in turbid waters • Ongoing cost to replace

[a] Method of application is abbreviated for the purposes of the table. Actual application should include consideration for water restrictions during implementation, precautions during implementation, methods for returning the system to operation, and documentation requirements.

ionization), and finally chemical disinfection (hyperchlorination, chlorine dioxide, and monochloramine) [155]. Initial installation costs are often low, but easily offset by the need for maintenance, repairs, and ongoing chemical costs. In addition to installation costs, the experience and service commitment by commercial suppliers varies and must be reviewed in detail by the water management team. Service and monitoring of the system postinstallation and records to be kept must be documented in writing before purchase.

Numerous companies now offer disinfection systems. Failures have become more commonplace with patients contracting Legionnaires' disease despite installation of an expensive disinfection system that may have been purchased based on the sales literature from the company concerned. Any new disinfection method that is being considered for purchase should undergo an objective and standardized evaluation by the infection control team and the water safety group. The following steps have been proposed previously: (1) demonstrated efficacy in vitro against *Legionella* organisms, (2) previous recorded and preferentially published experience of efficacy in controlling *Legionella* contamination in individual hospitals, (3) controlled studies of prolonged duration (years, not months) of the efficacy of minimizing *Legionella* growth and preventing cases of Legionnaires' disease in individual hospitals, and (4) confirmatory reports from multiple hospitals with prolonged duration of follow-up or validation [25].

When hospital-acquired Legionnaires' disease recurred after a disinfection system had been installed, we have noted one consistent finding: the decision for purchase of the disinfection system was made by the engineers within the facilities management team with minimal input from the Infection Prevention department. To avoid this mistake, we strongly advocate that the infection control team and water safety group take the lead and coordinate the effort in both selecting the disinfection method and the vendor. Infection control leads are healthcare professionals dedicated to preventing healthcare-associated infections. An infection preventionist's highest priority is keeping patients, healthcare providers, employees, and visitors free from healthcare-associated infections. These responsibilities contribute to preventing Legionellosis in a healthcare facility. Timely surveillance and accurate analysis of clinical test results identify healthcare-associated Legionellosis and prompt outbreak investigation response to prevent additional cases. Infection control leads and the water safety group will also serve as liaisons to local and state health departments.

Infection preventionists also play a key role in the education of patients and healthcare workers on the basic principles of infection prevention and control as relates to prevention of Legionnaires' disease. There continues to be confusion and misconception about Legionellosis. Therefore, it is critical that infection preventionist provide accurate information to patients and all healthcare workers in a facility or during community outbreaks [156].

An infection preventionist actively serves on multiple interdisciplinary teams to provide their expertise. Infection preventionist provides an understanding of evidence-based best practices and current infection prevention guidelines to the teams. Their role on a healthcare facility's water safety group and product evaluation committee is essential in preventing healthcare-associated cases of *Legionella*. This is particularly important in matters related to products that could grow and spread *Legionella* in the

building water system and equipment that may contain or consume water. For example, hands-free electronic sensor faucets are designed to limit hand contamination and to reduce water usage. In recent years, however, there have been reports of increased recovery of *Legionella* and *Pseudomonas aeruginosa* from these water fixtures [157–160]. Therefore, recommendations to restrict their use in high-risk areas have been made. The advent of waterless hand cleansers has decreased water usage in many hospitals. The reduced exposure of water fixtures to the disinfectant has resulted in increased colonization rates by *Legionella*. This can be reversed by periodic (monthly 20 min) flushing of the outlets to increase disinfectant exposure [161].

Additional committees that require an infection preventionist's expertise to prevent infections due to *Legionella* are the facility construction and renovation committee and the water management program team (or water safety group). Hospital units that have been closed for renovation are vulnerable to recolonization. Such units should not house patients until all water pipelines are flushed and monitored for the presence of *Legionella*. As part of the water management program team in a healthcare facility, an infection preventionist provides the knowledge of areas where medical procedures may expose patients to aerosols; areas where the most vulnerable patients are housed, and confirm that the appropriate diagnostic tests for Legionnaires' disease are being used by clinicians testing patients with healthcare-associated pneumonia. Other members of the water safety group should include hospital engineers and members of the administration. However, decisions made by the water management group concerning the consideration of implementation of a secondary disinfection, selection of the secondary disinfection system to implement, and the testing method used to monitor and validate this system must include the infection preventionist.

There is the potential for the emergence of *Legionella* with resistance to any of these disinfectants. This has been previously demonstrated with copper-silver ions in a few hospitals with such system. Therefore, we recommend that any institution that installs a systemic disinfection system should save *Legionella* isolates from before installation and periodically thereafter to monitor for emergence of resistance.

Legionella distal site positivity and disinfectant concentrations need to be routinely monitored for the life of the system. Routine environmental cultures of *Legionella* are necessary to assess the risk of disease since *Legionella* colonization will vary over time [15] (Fig. 4.1). The Allegheny County (Pittsburgh, Pennsylvania) Health Department recommends once a year culturing of water sites in patient units and wards housing high risk patients [162], while the Maryland Guidelines recommend flexibility with four time a year culturing if an outbreak has occurred [163]. For those hospitals using systemic disinfection, the World Health Organization (WHO) recommends *Legionella* culture of the drinking water be performed every 3 months to verify efficacy [164]. The only way to monitor a disinfection system's effectiveness in reducing the *Legionella* colonization is to culture the water system for *Legionella* using standard ISO methods. Physicochemical parameters (pH, free chlorine, Ca, Mg, TOC, etc.) have not consistently demonstrated predictive relationships with *Legionella* colonization in the literature. The total bacterial count, as measured by adenosine triphosphate (ATP) or heterotrophic plate count (HPC) concentrations, does not correlate with *Legionella* distal site positivity [165].

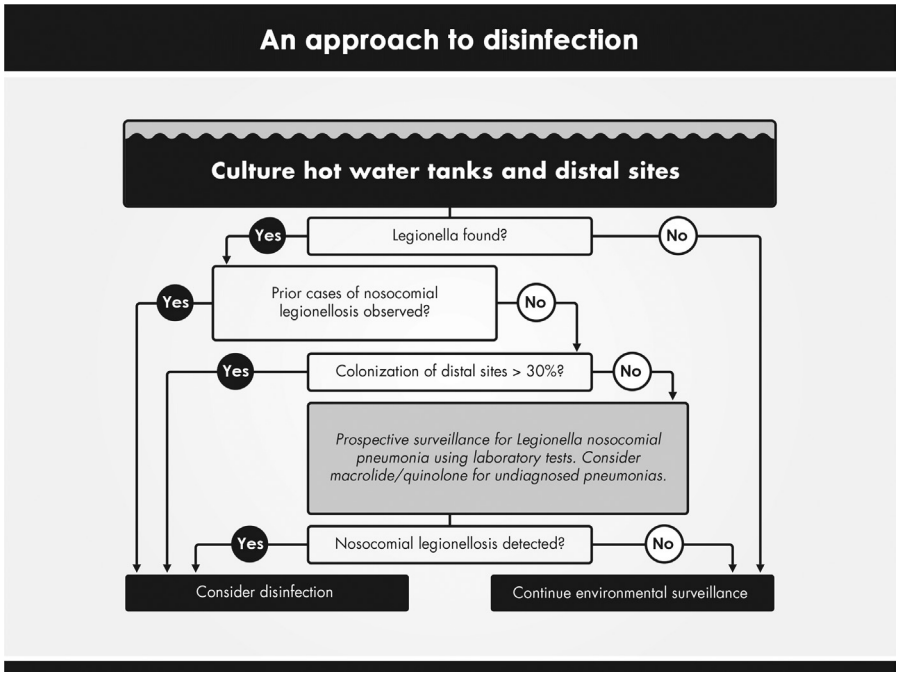

Fig. 4.1 Guidelines for *Legionella* environmental cultures and clinical surveillance. Modified from Allegheny County Health Department. Approaches to prevention and control of Legionella infection in Allegheny County Health Care Facilities. 2nd ed. Pittsburgh, PA: Allegheny County Health Department; 1997. p. 1–15.

4.5 Regulatory requirements, standards, and guidelines

Outbreaks and increased incidence of Legionnaires' disease across the United States have led to the development of guidelines, standards, and laws to prevent exposure to *Legionella* in water systems. International *Legionella* regulations and guidelines have existed for decades, but only in 2015 was a voluntary standard published in the United States. ASHRAE (formally the American Society of Heating, Refrigerating and Air-Conditioning Engineers) published Standard 188, "Legionellosis: Risk Management for Building Water Systems" in 2015. This standard was updated in 2018 [166]. Normative Annex A for Healthcare Facilities in ASHRAE Standard 188 describes specific tasks for the risk management plan for healthcare facilities. Construction in healthcare facilities is a known risk for healthcare-acquired Legionnaires' disease. ASHRAE Standard 188, Section 8—Requirements for Designing Building Water Systems deals with construction-related issues including delayed occupancy. The risk is greatest when high risk patients are placed in newly constructed or renovated spaces [167]. ASHRAE has also published Guideline 12, "Managing the Risk of Legionellosis Associated with Building Water Systems" [168]. Implementation of specific Legionellosis risk management and a water management program are described in this guideline.

The US Centers for Disease Control and Prevention (CDC) published a toolkit on how to implement the ASHRAE Standard 188 water management program entitled "Developing A Water Management Program to Reduce Legionella Growth and Spread in Buildings: A Practical Guide to Implementing Industry Standards" [169]. This guidance includes instruction for water management program teams to establish procedures to provide evidence that the water management program is effective, initially and on an ongoing basis. This validation step for water management demonstrates that control measures have effectively limited *Legionella* growth and spread from the building water systems. Again, the only way to validate control of *Legionella* is to test for it.

The US Centers for Medicare and Medicaid Services (CMS) issued a memorandum "Requirements to Reduce *Legionella* Risk in Healthcare Facility Water Systems to Prevent Cases and Outbreaks of Legionnaires' Disease (LD)" in 2017 [170]. This memorandum requires covered healthcare facilities to develop a water management program, as described in ASHRAE Standard 188, with the assistance of the CDC's toolkit document. While this document focuses on the prevention of Legionnaires' disease, it also required facilities to develop and adhere to procedures that would inhibit the growth of *Legionella* and other waterborne organisms (including *Pseudomonas*, *Acinetobacter*, *Burkholderia*, *Stenotrophomonas*, nontuberculous mycobacterium (NTM) and fungi) in building water.

The US Veterans Health Administration (VHA) in the Department of Veterans Affairs issued VHA directive 1061: Prevention of Healthcare-associated *Legionella* Disease and Scald Injury from Potable Water Distribution Systems, following a large outbreak of Legionnaires' disease. This directive requires facilities to conduct a risk assessment, develop a water management plan, and test water samples for *Legionella* quarterly [171, 172]. This directive applies only to facilities that are run by the Department of Veterans Affairs.

The first law in the United States for *Legionella* prevention was passed in 2016 in New York State. The New York State Department of Health passed regulation in the New York State Sanitary Code Title: Part 4—Protection Against *Legionella* that requires registration of cooling towers and assessments and sampling of cooling towers and healthcare facilities for *Legionella* colonization [148]. The city of New York also passed Local Law 77, requiring cooling tower assessment and testing [173]. Currently these are the only legally enforceable *Legionella* regulations in the United States and they only apply to those healthcare facilities and cooling towers in New York State.

Internationally, the World Health Organization (WHO) provides information on *Legionella* prevention using a water management approach in their "*Legionella* and the prevention of Legionellosis" [164]. The WHO also has several other documents that provide guidance on *Legionella* in potable and nonpotable water [155]. In 1986, European Working Group for *Legionella* Infections (EWGLI), now the ESCMID Study Group for *Legionella* Infections, was formed by members of the European Commission [155]. The working group's technical guidelines establish required water temperatures, critical *Legionella* concentration limits, and when action is required to reduce the concentration to below the critical level, including through the use of disinfection [174]. Some countries in the EWGLI have considered critical levels of

Legionella that are divergent from the overall guidance including Belgium, France, Germany, and the Netherlands [155]. Several other countries and regions, not included in the EWGLI, have their own guidance on *Legionella* prevention including Africa, Australia, China, Dubai, New Zealand, Russia, Singapore, South America [155], and Ireland [175], which are summarized elsewhere. These guidance documents generally specify if *Legionella* testing is recommended or required, the action level for *Legionella* concentration or positivity, preventative maintenance for systems, and information about methods of disinfection. In the United Kingdom, the HSE has published a number of legislative and guidance documents for dutyholders, which includes employers, those in control of premises, and those with health and safety responsibilities for others, to help them comply with their legal duties and includes documentation on evaporative cooling towers [176], hot and cold water systems [70], and other water systems [177]. In addition, in the United Kingdom the Department of Health and Social Care (DHSC) (England) has also published guidance documents that relate to the use of "Safe water in healthcare premises" through the design, installation, commissioning, testing, monitoring, and operation of water supply systems in healthcare premises [178]. In this guidance, the DHSC has proactively encouraged users toward a holistic management of water systems via water safety groups (WSGs), water safety plans (WSPs), and other initiatives. In addition, WSPs are a risk management tool that identify potential microbiological hazards and establish effective practices in local water usage, distribution, supply, and controls. It is important to consider that WSPs are working documents that need to be reviewed to ensure adequate assessment and control of risks from *Legionella* and other waterborne pathogens in healthcare and care home settings.

4.6 Conclusion

Healthcare-acquired Legionnaires' disease continues at an alarming rate and with high mortality. Proactive prevention requires risk assessment that includes testing for *Legionella*. The disinfection approaches reviewed here have had some measure of success in preventing further illness from *Legionella* and may also reduce infections from other opportunistic waterborne pathogens. Through these proactive measures, we can end Legionnaires' disease!

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