REVIEW ARTICLE

Controlling *Legionella* in Hospital Drinking Water: An Evidence-Based Review of Disinfection Methods

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Hospital-acquired Legionnaires' disease is directly linked to the presence of *Legionella* in hospital drinking water. Disinfecting the drinking water system is an effective preventive measure. The efficacy of any disinfection measures should be validated in a stepwise fashion from laboratory assessment to a controlled multiple-hospital evaluation over a prolonged period of time. In this review, we evaluate systemic disinfection methods (copper-silver ionization, chlorine dioxide, monochloramine, ultraviolet light, and hyperchlorination), a focal disinfection method (point-of-use filtration), and short-term disinfection methods in outbreak situations (superheat-and-flush with or without hyperchlorination). The infection control practitioner should take the lead in selection of the disinfection system and the vendor. Formal appraisals by other hospitals with experience of the system under consideration is indicated. Routine performance of surveillance cultures of drinking water to detect *Legionella* and monitoring of disinfectant concentrations are necessary to ensure long-term efficacy.

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The epidemiological link between presence of *Legionella pneumophila* in the hospital drinking water and the occurrence of hospital-acquired legionellosis was first made in the early 1980s by Tobin and Stout.[1,2] The first documented study of disinfection was published in 1983 using thermal eradication, which we termed "superheat-and-flush" method.[3] In 1990, the first comprehensive review of disinfection methodologies was published; definitive recommendations as to which methodology was superior were not made.[4] In 1998, two reviews on disinfection methodologies were published; one for engineers and healthcare facility managers[5] and another for physicians and infection control practitioners.[6] At that time, disadvantages of both hyperchlorination and ultraviolet light had become manifest and a new technology, copper-silver ionization, was under evaluation. Twelve years have since passed, and additional methods have been introduced: chlorine dioxide, monochloramine, and point-of-use filters. In the spirit of evidence-based medicine, we have formulated evaluation criteria with the intent of "raising the bar" for manufacturers of disinfection methodologies (Table 1). These objective criteria for demonstration of efficacy can assist hospitals in making cost-effective decisions.

SYSTEMIC DISINFECTION METHODS

Copper-Silver Ionization

Mechanism of action and application. Copper and silver are bactericidal in vitro against *Legionella* and other waterborne pathogens, including *Pseudomonas aeruginosa, Stenotrophomonas maltophilia, Acinetobacter baumannii,* and mycobacterial species. We recommend copper ion concentrations of 0.20–0.80 mg/L and silver ion concentrations of 0.01–0.08 mg/L for *Legionella* eradication. The recommended concentrations for *Legionella* eradication are 0.2–0.4 mg/L and 0.02–0.04 mg/L, respectively; lower ion concentrations have proven effective after initial installation.[7-10] Copper ion concentrations should be monitored weekly with use of a field colorimeter kit. Silver concentrations can be tested only by atomic absorption spectroscopy or inductively coupled plasma method and should be tested once every 2 months. Water samples for ion analysis should be clear and free of sediment.

Field evaluation. Copper-silver ionization is the only disinfection method for which multiple field evaluations of efficacy have been published in the peer-reviewed literature. The first installation of a copper-silver ionization system in the United States was in 1990.[11] A subsequent controlled evaluation in a hospital in Pittsburgh, Pennsylvania, showed that the percentage of distal outlets with *Legionella* colonization was reduced from 75% to 0% in 3 months. Copper and silver ion concentrations were above 0.4 mg/L and 0.04 mg/L, respectively.[12] 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 considered the basis for the prolonged bactericidal effect.[12,13] The efficacy of

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copper-silver ionization has also been well documented in long-term care facilities,[14] office buildings,[12] and apartment buildings.[15]

Confirmatory reports. The efficacy of copper-silver ionization in eradicating *Legionella* has been documented in hospitals worldwide.[7-10,16-19] A multiple-hospital survey documented efficacy in 16 US hospitals with 5–11 years of experience (LiquiTech USA, Enrich Products, and TarnPure).[20] Seventy-five percent of these hospitals had previously applied other disinfection methods with unsatisfactory results (the superheat-and-flush method, UV irradiation, and hyperchlorination). Within 5 years after treatment with copper-silver ions, 50% of the hospitals reported a *Legionella* positivity rate of 0%, and 43% of the hospitals still reported 0% positivity 5 years later. Most importantly, no cases of hospital-acquired Legionnaires' disease had occurred in any of these hospitals since 1995. At a University of Wisconsin hospital, in the years 1985–1995, there were 10 cases of Legionnaires' disease despite use of hyperchlorination. Following installation of a copper-silver ionization system, *Legionella* was eliminated from the drinking water system, and no cases of legionellosis have been diagnosed ($P < .001$).[21]

Copper-silver ionization was used in 12 (32%) of 38 of the hospitals in the US National Nosocomial Infections Surveillance system in 1998 that had instituted disinfection measures.[22] More than 300 hospitals worldwide have since adopted ionization as the primary *Legionella* disinfection control measure. The first 3 hospitals to apply hyperchlorination for *Legionella* disinfection (Wadsworth VA Medical Center, CA; University of Vermont Medical Center, VT; and the University of Pittsburgh Medical Center, PA) ultimately converted to ionization because of failure to control *Legionella* counts and skyrocketing maintenance costs due to 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 are monitored.[18]

Advantages and disadvantages. The 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 recirculation lines. Ionization has a prolonged efficacy that provides an added margin of safety, unlike hyperchlorination, with which *Legionella* can rapidly appear in the event of system malfunction. Unlike chlorine and chlorine dioxide, the biocidal activity of copper-silver ionization is not compromised by higher water temperature.[23]

Elevated water pH[24] and low ion concentrations[25] may compromise the efficacy of ionization. High pH of the hospital water (greater than pH 8.5) may interfere with the disinfecting action of both chlorine and the copper-silver ions.[26,27] In 2 German hospitals, copper-silver ionization systems were unable to control *Legionella.*[25,28] In both hospitals, the concentrations of copper and silver ions were well below recommended levels, so as to comply with the German drinking water standard (which requires a maximum silver concentration of 0.01 mg/L); thus, the reported failure should have been expected.[29] One French hospital reported failure of ionization[30]; however, a phosphate compound was added to the water system to control corrosion, which may have interfered with the efficacy of ionization.[31]

TABLE 1. Standardized Evaluation Criteria for Disinfection Methods: A 4-Step Approach

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 efficacy in 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)

NOTE. Adapted from Stout and Yu.[20]

Emergence of *Legionella pneumophila* with resistance to copper-silver ions has been documented in a few hospitals several years after installation of copper-silver ionization systems.[32] The prevalence of resistance is unknown. Our data does indicate that resistant strains can cause hospital-acquired Legionnaires' disease. Hospitals that had monitored ion concentrations and *Legionella* positivity at hospital sites were less likely to experience this phenomenon.

The US Environmental Protection Agency (EPA) has set a maximum containment levels for drinking water of 1.3 mg/L for copper and 0.1 mg/L for silver (though this is not enforceable). The EPA now requires ionization systems to "register" as a biocide for use in potable water.[24] This registration falls under the Federal Fungicide, Insecticide and Rodenticide Act (FIFRA) for devices claiming biocidal action.

Cost. The cost of copper-silver ionization varies according to the number of systems needed and the replacement of copper-silver electrodes. For a typical 250-bed hospital, the cost for an ionization system has been estimated to be $40,000–$50,000 for a hot water recirculating line and $80,000–$100,000 for both hot and cold water treatment. The cost was $200,000 in a 1,200-bed hospital in Taiwan.[10] Some manufacturers with less experience may offer lower initial costs, but frequent replacement of the electrodes and inadequate maintenance may offset the early cost savings.

Summary. Copper-silver ionization is the only disinfection technology that has been validated by the 4-step standardized evaluation criteria we recommend.[20] Copper-silver ionization appears to be the best available technology today for controlling *Legionella* colonization in hospital water systems. Numerous vendors now offer ionization systems. Recommendations and assessments from other hospitals using ionization should be routinely sought before making a purchase. Rigorous maintenance plans with regular monitoring of both ion concentrations and the percentage of sites with *Legionella* positivity is necessary to ensure long-term success.

Chlorine Dioxide

Mechanism of action and method of application. Chlorine dioxide has been used for water treatment in Europe since the 1940s, and numerous systems have been installed in the United States for *Legionella* disinfection. Chlorine dioxide is a gas in solution that is typically generated on site at the facility. Methods for producing chlorine dioxide include controlled mixing of chemical precursors or electrochemical generation. A limited number of controlled prospective evaluations have been published.

Field evaluation. The first controlled field evaluation in the United States was conducted in a hospital where cases of hospital-acquired Legionnaires' disease had occurred.[33] During the 15 months following the installation, the percentage of hot water outlets with *Legionella* positivity significantly decreased, from 23% to 12%, and the *Legionella* positivity rate for cold water taps approached 0%. The average chlorine dioxide residual measured at hot water taps was 0.08 mg/L, which was 88% lower than that measured at the cold water reservoir (0.68 mg/L). The mean chlorine dioxide residual concentration at cold water outlets was 0.33 mg/L. The reduction in the 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.

In a 30-month prospective study, Zhang et al[34] evaluated the efficacy of chlorine dioxide disinfection in a New York hospital. The *Legionella* positivity rate for hot water outlets decreased from 60% to 10%. It required 18 months to achieve a significant reduction in the *Legionella* positivity rate for hot water outlets. No cases of hospital-acquired legionellosis were identified in the postdisinfection period. Significantly lower chlorine dioxide residual concentrations were detected in hot water (0.04 mg/L) than in cold water (0.3–0.5 mg/L).

Confirmatory reports. An evaluation of chlorine dioxide disinfection was conducted in a 1,000-bed hospital in the United Kingdom. After 2 years of chlorine dioxide treatment (target concentration, 0.5 mg/L), the *Legionella* positivity rate remained unchanged, and 2 cases of hospital-acquired Legionnaires' disease had occurred.[35] In a northern United Kingdom hospital where hospital-acquired Legionnaires' disease had occurred,[36] chlorine dioxide disinfection was initiated because of repeated failures with hyperchlorination. Chlorine dioxide at a concentration of 0.25–0.5 mg/L was injected into the cold water supply. However, 3–5 mg/L of chlorine dioxide injected into the hot water supply was required to achieve a 0.25–0.5 mg/L residual concentration at hot water taps. After 3 years, *Legionella* was not detectable in the water system. It is noteworthy that on 2 occasions when the chlorine dioxide concentration fell below 0.25 mg/L because of mechanical failure, *Legionella* was detected in water samples within 4 days.[36] In an Italian hospital,[37] chlorine dioxide was injected into the hospital water system at a concentration of 0.4–0.5 mg/L at the source, which resulted in a concentration of 0.2–0.3 mg/L at the water outlets. After 4 years of treatment, high concentrations of *Legionella* were still detected, and 12 cases of hospital-acquired Legionnaires' disease had occurred. The authors concluded that chlorine dioxide was not useful.[37] In a Scottish hospital,[38] hyperchlorination was ineffective in eradicating *L. pneumophila* from the hospital drinking water, and cases of hospital-acquired legionellosis occurred. Chlorine dioxide at a concentration of 0.5 mg/L was injected into the cold water system. *L. pneumophila* serogroup 1 was not detectable by week 6. However, *Legionella anisa* persisted in low numbers.[38]

Investigators from Johns Hopkins University Hospital reported that chlorine dioxide disinfection reduced the *L. anisa* positivity rate after 17 months.[39] There were caveats: a prolonged duration of treatment was necessary before the *L. anisa* positivity rate decreased significantly; it took 60 days to drop from 40% to 20% of water outlets and another 15 months to reach the 4% level achieved at the end of their study period. Moreover, Legionnaires' disease caused by *L. anisa* is extremely rare. 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*.[40] 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[41]; thus, we do not recommend disinfection if *L. anisa* is the sole *Legionella* species isolated from the water.

Advantages and disadvantages. Chlorine dioxide has superior penetration into biofilms than chlorine. By-products, such as chlorite and chlorate, are not carcinogenic. Biocidal action is maintained over a wider range of pH than for chlorine and copper-silver ionization. Corrosive effects are much less than those of chlorine.

The limits of chlorine dioxide disinfection include the following. First, a prolonged time is necessary to demonstrate significant reductions in the *Legionella* positivity rate.[33,34,39,42,43] Second, the residual concentration in hot water is low (<0.1 mg/L) when the chlorine dioxide is injected into the incoming cold water at a concentration of 0.5–0.8 mg/L.[33,34,39,42] Third, reactions with organic material and corrosion scale in piping can cause rapid conversion of chlorine dioxide to its by-products, chlorite and chlorate.[44] These by-products may pose health risks for consumers. Fourth, corrosion of galvanized pipes can cause loss of chlorine dioxide by reaction with magnetite (Fe_30_4); this may affect efficacy.[44]

The major challenge for chlorine dioxide is maintenance of an effective residual concentration (0.3–0.5 mg/L) throughout the drinking water system.[34] One New York hospital achieved a concentration of greater than 0.1 mg/L by direct injection into the hot water system (J.E.S., personal communication, 2010).

Chlorine dioxide is a registered biocide with the EPA; it has set the maximum residual disinfectant level for chlorine dioxide at 0.8 mg/L and set the maximum contaminant level for chlorite at 1.0 mg/L.[45] Chlorite may cause congenital cardiac defects and hemolytic anemia.[46] Chlorate is currently not regulated because of the lack of health data for setting a maximum contaminant level. The United Kingdom Drinking Water Inspectorate specifies a maximum value of 0.5 mg/L for all oxidants in drinking water, which is the combined concentration of chlorine dioxide, chlorite, and chlorate. In 2004, the EPA mandated that any healthcare facility 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 and Stage 1 Disinfection Byproducts Rule.[47] All chlorine dioxide products used in hospitals must be registered with the EPA and certified by the American National Standards Institute and National Sanitation Foundation. Some states require regular monitoring of chlorine dioxide and chlorite levels. Such testing can be costly, and this expense is often overlooked.

Cost. One hospital estimated the cost of engineering measures for chlorine dioxide disinfection to be approximately $50,000 per year.[35] The annual cost for operation and maintenance of 2 chlorine dioxide units for a 438-bed hospital was approximately $34,000 per year. Installation costs were not included, because the hospital leased the chlorine dioxide units and hospital personnel installed the equipment. The annual cost for monitoring the chlorine dioxide residual concentration and the chlorite level in the hospital water system ranged from $3,000 to $5,000, with a total annual cost of $40,000.[34]

Summary. Chlorine dioxide is a promising disinfection modality; however, it has not yet fulfilled the 4 criteria required for validation of efficacy (Table 1).[34] We are optimistic that the challenges for chlorine dioxide disinfection will be overcome. For now, we would recommend it in circumstances that favor efficacy, including a smaller secondary distribution system, a low cold water temperature, nongalvanized piping, and low total organic carbon content in the hospital water. In future published studies, chlorine dioxide concentrations in concert with *Legionella* positivity rate should be reported. Given the many vendors offering varying types of chlorine dioxide generators and the marginal success experienced by so many hospitals, recommendations and assessments from other hospitals with experience with chlorine dioxide would seem mandatory.

Monochloramine

Mechanism of action and method of application. Monochloramine is effective against *Legionella* in vitro and against biofilm-associated *Legionella* in model plumbing systems.[48-50] Two case-control studies have suggested that hospitals in municipalities that were supplied with domestic drinking water treated with monochloramine were less likely to report cases of hospital-acquired Legionnaires' disease.[51,52] A 2-year prospective environmental study in a California municipality in which monochloramine replaced chlorine for water disinfection found that *Legionella* positivity of hot water systems decreased from 60% to 4% after conversion from chlorine to monochloramine disinfection in 53 buildings; the median number of colonized sites per building decreased with monochloramine disinfection.[53] The number of colonized buildings in a Florida study decreased from 20% to 6% after monochloramine was introduced into the municipal water supply.[54] On the other hand, the proportion of buildings colonized by *Mycobacterium* species increased from 19% to 42%. Increased growth of coliforms and heterotrophic bacteria also occurred.[55]

Field evaluation. The efficacy of on-site monochloramine treatment in individual hospitals has not yet been studied over a prolonged period. In a hospital in Washington, DC, a monochloramine concentration of 0.31 mg/L (with a free chlorine concentration of 0.39 ± 0.38 mg/L and an ammonia concentration of 0.045 mg/L) was effective in reducing *Legionella* counts.[56] The effects on the percentage of sites positive for *Legionella* were not reported. Concurrent presence of monochloramine, free chlorine, and ammonia may have indicated an incomplete mixing of chemicals during monochloramine generation.[56] A system for delivering monochloramine into building water distribution systems was evaluated at a hospital in Italy, and investigators found a significant reduction in the *Legionella* positivity rate within 30 days after injection of monochloramine at a concentration of 1–2 mg/L.[57]

Confirmatory reports. Controlled evaluation of monochloramine treatment in hospitals over time has not been performed.

Advantages and disadvantages. Monochloramine provides a stable residual that penetrates biofilms and has a wider working pH range than copper-silver ionization and chlorine. Monochloramine can cause anemia in patients undergoing hemodialysis. The on-site generation of monochloramine can be complicated; injecting hypochlorous acid upstream and ammonia downstream in a flow-through pipe could result in concurrent presence of free chlorine, ammonia, and monochloramine because of incomplete mixing of the reactants. The smell of ammonia in drinking water is unpleasant.

If a municipality converts from chlorine to monochloramine as the primary treatment method, the hospitals in that municipality become inadvertent beneficiaries if they have a water system colonized with *Legionella*.[41] The adverse effects have been increased populations of other microorganisms (*Mycobacterium* species), presence of nitrogen by-products, and increased lead leaching in drinking water.[55,58] Wide-scale conversion to monochloramine treatment of municipal water supplies appears unlikely today.

Summary. Monochloramine disinfection appears to be a promising approach for decreasing *Legionella* colonization. Long-term studies remain to be reported.

Hyperchlorination

Systemic continuous hyperchlorination has been reviewed in detail elsewhere.[4,5] Of the 17 hospitals applying hyperchlorination as the sole modality or in combination with another modality in our 1990 review,[4] virtually all have since converted to other methods of disinfection. Hyperchlorination was found to be the most unreliable and also the most expensive disinfection modality. It has met with increasing disfavor because of inadequate penetration of the agent into biofilms in piping, persistence of *Legionella* organisms in hyperchlorinated systems,[59] corrosion of the water distribution system leading to pinhole leaks over time, and the introduction of carcinogens into the drinking water.[60]

Point-of-Use Filtration

Point-of-use filters (0.2-μm pore size) (AquaSafe; Pall Medical) have been used for prevention of nosocomial infections due to *Legionella* and *Pseudomonas aeruginosa,* particularly in high-risk areas such as intensive care units and transplant units.[61-63] In a controlled study, the filter completely eliminated *Legionella* and *Mycobacterium* organisms from the water.[62] Some hospitals restrict water use during an outbreak by having patients use bottled water exclusively and restricting all patients from showering. Use of filters is usually more cost-effective and better tolerated by patients.[64]

UV Light

UV light is an attractive option for disinfection since no chemicals are added to the drinking water. Its point-of-entry application does not allow distal eradication if *Legionella* within the biofilms of the water distribution system are distal to the point of entry.

Field evaluation. Two hospitals have shown that UV was ineffective in eradicating *Legionella* at distal sites.[65,66] Combination of UV with other treatment modalities was effective for individual hospital units.[67-69] In a new hospital, a UV disinfection system was installed on the incoming water supply. None of 930 cultures of drinking water over a 13-year period cultures were positive for *Legionella,* and cases of hospital-acquired legionellosis were not found.[70] No control sites were sampled, so the study was not definitive.

Costs. In a 2003 report, the cost of the UV system in a 700-bed hospital was US$22,973; the annual cost of supplies and electricity was approximately US$3,000.[70]

Summary. The efficacy of UV disinfection is optimized if the system is installed on the incoming water main of a virgin hospital in which no biofilm has been established. It may play a role if the area for disinfection is limited (eg, a transplant unit) and if a systemic disinfection system is also used concurrently.

emergency disinfection methods

Cases of hospital-acquired Legionnaires' disease often generate media publicity. Immediate measures are needed to minimize panic among patients and employees. In this situation, the hospitals may use superheat-and-flush disinfection, with or without shock chlorination, as a short-term systemic control measure.[5] Water temperatures at distal sites must be rigorously maintained and monitored.[71] Shock chlorination may be the only option in some hospitals where superheat-and-flush disinfection cannot be used because hot water lines are not available at every distal site.[72] Shock chlorine dioxide disinfection is theoretically feasible, but clinical experience with this method as a short-term measure is limited.[73] Point-of-use water filtration is a cost-effective measure if a limited patient area can be targeted. Filters can be installed immediately and are cost-effective, compared with the alternative of restricting showering and providing bottled water.[64]

risk assessment and selection of disinfection method

Routine performance of environmental cultures to detect *Legionella* is necessary to assess risk, because *Legionella* colonization will vary over time.[41] The Allegheny County (Pittsburgh) Health Department recommends annual culturing of water outlet sites in patient units and wards housing high-risk patients,[74] whereas the Maryland Department of Health guidelines recommend flexibility, with culturing 4 times per year if an outbreak has occurred.[75] For hospitals using systemic disinfection, the World Health Organization recommends that drinking water cultures for *Legionella* be performed every 3 months, to verify the efficacy of disinfection.[76]

Given the emergence of *Legionella* strains resistant to copper-silver ions in a few hospitals that have such systems, we recommend that any institution that installs a systemic disinfection system save *Legionella* isolates obtained before installation and periodically thereafter to monitor for the emergence of resistance.

The advent of waterless hand cleansers has decreased water usage in many hospitals. The reduced exposure of water fixtures to disinfectant has resulted in increased *Legionella* colonization rates. This can be reversed by periodic flushing of the outlets (20 minutes once per month) to increase disinfectant exposure.[77] In addition, hospital units that have been closed for renovation are vulnerable to recolonization. Such units should not house patients until all lines are flushed and cultured to detect *Legionella.*

Selection of the vendor for installation of a systemic disinfection method warrants careful consideration with intense scrutiny. Objective assessments from other hospitals that have used the vendor's product are mandatory. The necessity for maintenance and monitoring after installation is often underestimated. The *Legionella* positivity rate for water outlet sites and the disinfectant concentrations need to be routinely monitored for the life of the system. Low costs for initial installation are easily offset by the need for maintenance and repairs (requiring the system to be shut down) because of flawed design, improper installation, or poor service. Given the proliferation of companies that offer disinfection systems, failures have become commonplace, with patients contracting Legionnaires' disease despite installation of an expensive disinfection system. Review of our experience, in which cases of hospital-acquired Legionnaires' disease occurred after a disinfection system had been installed, revealed one consistent finding: the decision for purchase of the disinfection system was made by the engineers within the facilities management team and there was minimal input from the infection control department. As a result, we strongly advocate that the infection control practitioner, not healthcare facilities personnel, lead the task force in selecting the disinfection method and in selecting the vendor. The critical contribution of the infection control practitioner is the insistence that evidence-based data be used in making the selection. Other members of the task force should include hospital engineers and members of the administration. In addition to installation costs, the experience and service commitment by the commercial vendors must be reviewed in detail by the infection control practitioner. Specifics regarding the service and monitoring of the system after installation must be put in writing before purchase.

Finally, *Pseudomonas aeruginosa, Stenotrophomonas maltophilia,* and *Chryseobacterium* and *Aspergillus* species can also colonize drinking water. *Legionella* disinfection may also lead to suppression of these other waterborne pathogens[78,79]; this remains to be confirmed in controlled studies.

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