

CONTROL OF *LEGIONELLA* IN DRINKING WATER SYSTEMS: IMPACT OF MONOCHLORAMINE

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Legionella and *Legionella*-like organisms live as facultative intracellular parasites of amoebae in the biofilm that covers the inside of tanks and pipes in water systems. Most drinking-water disinfectants penetrate poorly into biofilm (20) and *Legionella* is further shielded by its amoebal host (13). In addition, *Legionella* often proliferates peripherally, while disinfectants often do not reach distant points in a distribution system.

Use of new diagnostic techniques and recent pneumonia-etiology studies have shown that the burden of disease due to *Legionella pneumophila* is large: *L. pneumophila* causes between 2 and 16% of all community-acquired pneumonias, which makes it the second to third most common causative organism (2). Non-*L. pneumophila* species and *Legionella*-like organisms that are not detected by routine diagnostic testing may cause significant additional morbidity (1, 21, 24).

Legionella-control efforts have often focused on hospitals and hotels because the outbreaks happen there. However, it should be emphasized that the great majority of Legionnaires'

disease cases are sporadic and community acquired (23). It is likely that in a large number of these sporadic cases, the disease was contracted in their homes or from other incidental sources that expose only a few persons at a time (28). A control measure that reduces *Legionella* and *Legionella*-like organism exposure in the community will therefore have great impact. Recent investigations, which will be discussed at the end of this chapter, have indicated that it is possible to prevent 90% of drinking-water-associated Legionnaires' disease (community acquired as well as nosocomial; sporadic disease as well as outbreaks) through the use of monochloramine for residual municipal water disinfection.

A selection of available *Legionella* control measures for drinking-water systems will be discussed in more detail hereunder. All of these methods have their drawbacks and none are 100% efficacious, so it may often be necessary to combine two or more. Moreover, any measure is likely to fail if it is not accompanied by a thorough analysis of the water system and correction of problems such as stagnation, cross-connections, and tepid temperatures.

HEAT

Temporarily increasing the water temperature to above 65°C and flushing all outlets for a

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few minutes (termed "superheat-and-flush") will result in a short-term reduction of *Legionella* counts. This has to be repeated regularly because the bacteria will otherwise grow back within a few weeks. In practice, this method is time-consuming, since the maximum number of outlets that can be flushed at once is limited by the capacity of the water heaters. To reduce risk of scalding, superheat-and-flush is preferably carried out at night or during weekends. The large number of staff needed for opening and closing outlets and the unusual work hours make this method expensive and impractical as a long-term solution. Superheat-and-flush was used unsuccessfully in one hospital for 13 years; *Legionella* continued to be recovered and nosocomial infection continued to occur during the entire period (27). Very few hospitals currently use this method for long-term *Legionella* control (9).

For long-term effect, the hot water temperature should be continuously maintained above 50 to 60°C in every part of the hot water system. One disadvantage of this method is the risk of scalding. Another potential problem is that an increase of the hot water temperature can lead to warming of the cold water side because of heat exchange between the two systems, resulting in an increased risk of cold water-associated *Legionella* transmission (12).

FREE CHLORINE

Supplemental chlorination is a simple method that has been proven effective in numerous instances. It is currently the most commonly used measure for U.S. hospitals (9). Standard free chlorine levels in municipal drinking water are often inadequate to kill biofilm-associated sessile *Legionella* and *Legionella*-like organisms: chlorine does not penetrate well into biofilm (6) and it often does not reach peripheral areas or areas of stagnation within the plumbing system. Nevertheless, free chlorine can be effective if the concentration is sufficiently high in all reaches of the distribution system and after necessary changes are made to prevent stagnation (10, 18, 25). Con-

centrations below 0.5 mg/liter are often not enough (Fig. 1) (16). The Centers for Disease Control and Prevention (CDC) recommends a concentration of at least 1.0 mg of free chlorine per liter (4), but some hospitals have had to go up to 3 to 4 mg/liter. The required chlorine concentration seems to depend mostly on the success that hospital staff have with maintaining temperatures and preventing stagnation. Also, free chlorine is less effective at high pH. To achieve chlorine concentrations of >1 mg/liter, facilities will usually have to install a supplemental chlorine injector. The main drawback of high chlorine concentrations is that some hospitals have reported increased corrosion of plumbing materials, with a resulting increase in operating costs (11). This corrosion apparently does not affect every hospital and some hospitals have reported that corrosion could be controlled with addition of silicates, which would form a protective "coating" (25).

Formation of potentially carcinogenic disinfection byproducts (DBPs) has been put forward as another argument against use of free chlorine. A causal relationship between consumption of chlorinated drinking water and risk of cancer has not been confirmed. The U.S. Environmental Protection Agency did a meta-analysis in 1998 of available research on this subject. The agency concluded that among the 240 million U.S. citizens exposed to disinfected water, there may be 0 to 100 excess cases of bladder cancer per year based on toxicological data, or 0 to 9,300 based on epidemiological studies (8). To be on the safe side, authorities in many countries have put limits on the maximum concentrations of certain DBPs in drinking water. This has led many municipal water suppliers to switch from chlorine to alternative disinfectants such as monochloramine. For supplemental chlorination, however, the concern for cancer seems less relevant: any possible cancer risk will probably be negligible for short-term exposure such as for hospital patients or hotel guests.

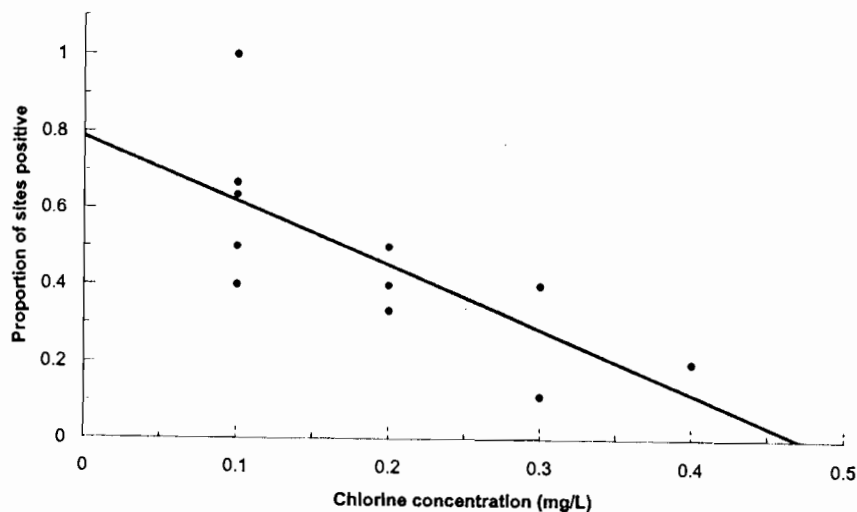


FIGURE 1 Average free residual chlorine concentration as measured in patient room tap water and proportion of sites positive for *Legionella* in 11 San Antonio hospitals. Each dot represents one hospital; a regression line is shown. Reprinted from *Infection Control and Hospital Epidemiology* (16) with permission of the publisher.

COPPER-SILVER IONIZATION

Experts disagree on the merits of this method. A review of the available literature gives the impression that *Legionella* counts generally decrease by about two logs after application of copper-silver ionization. Its effectiveness is sensitive to many parameters such as pH, water hardness, and dissolved solids. Furthermore, it is difficult to calibrate levels of copper and silver within the narrow range between minimum inhibitory levels and maximum allowable concentrations. Scale buildup may necessitate frequent replacing of the electrodes. For the above reasons, this is often a labor-intensive and expensive method. A hospital in Arizona was able to control *Legionella* with a combination of copper-silver and 0.5 mg of free chlorine per liter, but the entire process of installation and calibration of the copper-silver system was estimated to cost approximately \$1 million (15).

The first study on the effectiveness of copper and silver against *Legionella* reported that it had an effect only in the presence of at least 0.4 mg of free chlorine per liter (19). It is possible that, in some situations, this chlorine concentration could by itself achieve the reported effect. Unfortunately, later papers on the effectiveness of copper-silver have often failed to report chlorine concentrations. In addition to positive experience with copper-silver ionization (3, 22), failures have been documented frequently (5, 9, 26, 27). A hos-

pital in Ohio reported that a copper-silver system neither reduced the number of positive samples nor terminated transmission and the system was discontinued (5). In a hospital in Pittsburgh, a copper-silver system was installed in 1994. *Legionella* counts decreased, but the bacteria continued to be recovered from the water system and at least six nosocomial Legionnaires' disease cases occurred in the 3 years after the system was installed (27). In a 4-year study in a German university hospital, copper-silver had an effect in the first 2 years, but *Legionella* counts increased thereafter. The researchers concluded that copper-silver was ineffective in the long term, perhaps because of the development of resistance, and the use of the system was discontinued (26). Another German hospital reports in these proceedings that the use of copper-silver required intensive maintenance but that it had only limited effect on *Legionella*, concluding that copper-silver cannot be recommended for control of *Legionella* in German hospitals (see chapter 84). In a survey of U.S. hospitals participating in the National Nosocomial Infections Surveillance System, 38 reported using long-term *Legionella* control measures: 22 (58%) used supplemental chlorination compared with 9 (24%) that used copper-silver. Five hospitals reported that nosocomial infection continued to occur despite the control measures, and of these five, three used copper-silver (9). The conclusion is that copper-silver is used less fre-

quently than chlorine and that it has a higher failure rate.

In view of the above evidence it seems that copper-silver alone does not reliably control *Legionella* and that it is less effective than, for example, free chlorine. However, copper-silver can be a useful addition to free chlorine because it allows for a reduction in the concentration of the latter (3, 15, 19), thereby reducing corrosion problems and improving taste and odor.

OTHER METHODS

Other disinfectants such as ozone and chlorine dioxide have been tried with limited success. These disinfectants appear to have the same problem that free chlorine has: they do not penetrate biofilm. UV light stops *Legionella* growth only at the point of application; it has no effect on peripheral *Legionella* growth and therefore has very limited value for water systems.

MONOCHLORAMINE

General Description

Monochloramine (combined chlorine) is formed when ammonia and free chlorine are mixed in water in the correct ratio (14). It penetrates better into biofilm than free chlorine and it is better at killing biofilm bacteria such as some *Pseudomonas* spp. (20). It has been used for drinking-water disinfection since 1916 (7). Municipal drinking-water disinfection has two stages: initial disinfection at the water-treatment plant, and residual disinfection to maintain biocidal activity throughout the distribution system. Monochloramine's disinfecting action is slower than that of free chlorine, so it is less useful for initial disinfection. On the other hand, it is more stable than free chlorine, so a disinfecting residual can be maintained over long distances in a distribution system, which can reduce cost (14). It is believed to form less potentially carcinogenic disinfection by products than free chlorine (8). Another advantage is that it causes fewer taste and odor problems.

A survey in 1989 and 1990 of municipal water utilities in the United States that served populations greater than 50,000 found that 23% were using monochloramine as a residual disinfectant (14), and this percentage has undoubtedly gone up since then. It is also used in other countries, such as Canada and the United Kingdom. A typical monochloramine-using water treatment plant presently uses free chlorine or ozone for initial disinfection, and monochloramine for residual disinfection (14).

Disadvantages of monochloramine are that it is toxic to some fish and it causes a febrile reaction when the water is used for dialysis. It can be removed from water by granular activated carbon filters or it can be neutralized with agents such as ascorbic acid or thio-sulphate. Although corrosion usually is not a problem associated with monochloramine, it does deteriorate some artificial rubbers.

Evidence for the Effect of Monochloramine on *Legionella*

Recent research has shown that monochloramine may be considerably more effective against *Legionella* and *Legionella*-like organisms than free chlorine. In an investigation in Texas in 1997, we did not recover *Legionella* or *Legionella*-like organisms from the water systems of hospitals in cities that treated their water with monochloramine. These hospitals also did not detect cases of Legionnaires' disease among their patients. In contrast, 11 of 12 studied hospitals in a nearby chlorine-using municipality were found to contain *Legionella* in their water system and 5 had detected nosocomial Legionnaires' disease among their patients. The only hospital in the chlorine-using city where we did not recover *Legionella* had just experienced a nosocomial Legionnaires' disease outbreak and had already implemented control measures (16). This observation led us to do a retrospective analysis of published nosocomial outbreaks of Legionnaires' disease in the United States (17). Through literature searches we identified 32 hospitals that had experienced outbreaks re-

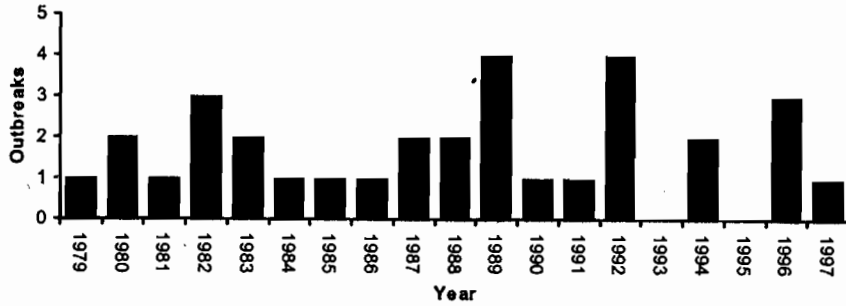


FIGURE 2 Potable water-associated nosocomial Legionnaires' disease outbreaks identified through literature review in the United States, by year. Solid bars represent hospitals supplied with free chlorine-containing water; the shaded bar is the hospital that was supplied with monochloramine-containing water. Reprinted from *The Lancet* (17) with permission of the publisher. © by The Lancet Ltd., 1999.

lated to their water system (Fig. 2). Forty-eight control hospitals were randomly selected and matched by hospital size and the presence of a transplant program. We then collected information on the type of water disinfection by interviewing the local water-treatment authorities. A total of 31 of the 32 case hospitals were supplied with water containing free chlorine. Only one, a hospital in Denver, was supplied with water that was disinfected with monochloramine (Fig. 3). This hospital experienced a small outbreak of three cases in 1981. At the time, it had an unusual water system configuration: large hot water storage tanks were in turn taken off-line but were

kept warm and full of water for weeks at a time before being reconnected. After the hospital corrected this problem by replacing the tanks with instantaneous heaters, no nosocomial Legionnaires' disease cases were detected in the following two decades in spite of intensive surveillance. Of the control hospitals, 12 (25%) were supplied with drinking water containing monochloramine. Interestingly, the Denver hospital with the outbreak received water with a lower monochloramine concentration (1 mg/liter) than all control hospitals (1.5 to 4.3 mg/liter; Table 1). Denver later increased the monochloramine level because the municipality had difficulty main-

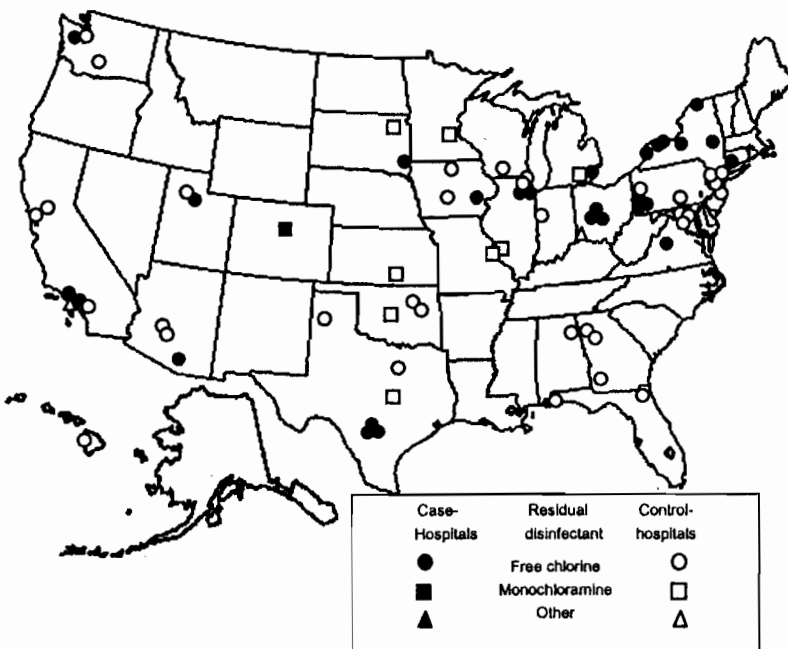


FIGURE 3 Geographical distribution of hospitals with reported Legionnaires' disease outbreaks associated with potable water and of randomly selected control hospitals. Some overlapping points were dispersed to improve legibility. Reprinted from *The Lancet* (17) with permission of the publisher. © by The Lancet Ltd., 1999.

Statistics of 32 hospitals with drinking water-associated Legionnaires' disease outbreaks, 42 their municipal water suppliers^a

	Outbreak hospitals (n = 32)	Control hospitals (n = 48)	Adjusted OR (95% CI) ^b	P
Water	26	45		
Chlorine	31	46		
Monochloramine	23 (72%)	35 (73%)		0.89 ^c
Year	1988.5 (1979–1997)	1988 (1979–1997)		
Age	31	36	10.2 (1.4–460)	0.007 ^c
Sex	1	12 ^c	1.0 ^d	
Temperature	0.55 (0.0–1.8)	0.6 (0.0–2.1)		0.34 ^c
Humidity	1.0 (1.0–1.0)	2.7 (1.5–4.3)		0.11 ^c
Time	31	43	2.1 (0.16–11.4)	0.46 ^c
Time	1	3	1.0 ^d	
Time	0	1	Excluded	
Time	0	1	Excluded	
Time	22	33		0.91 ^c
Time	5	10		
Time	5	5		
Time	242,500 (5,000–4,000,000)	198,000 (3,500–9,000,000)		0.28 ^c
Time	7.6 (7.0–10.0)	7.8 (7.0–10.5)		0.82 ^c

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OR, odds ratio.

^aWater supplied with water that contained free chlorine for 2 weeks per year.

^bOR for those water systems that used this disinfectant and are the water-treatment specialist's estimate of the population of the hospital. Free chlorine concentration is in mg/liter, monochloramine concentration is expressed in mg/liter.

^cOR

^dMonochloramine concentration surface water as a continuous variable.

residual in warm summer

the above case-control study
of 10.2 (95% confidence
0). In other words, the like-
an outbreak of nosocomial
associated Legionnaires' dis-

ease was 10 times higher for hospitals in
chlorine-using municipalities than for those
in monochloramine-using cities. This result
suggests that 90% of drinking-water-
associated outbreaks would not have occurred
if all hospitals had been supplied with
monochloramine-disinfected water. Apart

from the municipal residual disinfection method, no other parameters were associated with risk of outbreaks (Table 1). Because we collected data on water treatment at the time of the beginning of each Legionnaires' disease outbreak, none of the hospitals in our study were implementing control measures against *Legionella*.

The protective effect of monochloramine was confirmed in a survey of more than 300 hospitals, which found that hospitals supplied with chlorinated water were 3.6 times more likely to experience a problem with nosocomial Legionnaires' disease. This result suggested that 72% of occurrences of nosocomial transmission could have been prevented if all municipalities had used monochloramine as a residual disinfectant (J. D. Heffelfinger, S. K. Fridkin, J. L. Kool, V. Fraser, J. C. Hageman, E. R. Zell, B. Kupronis, and C. G. Whitney, 4th Decennial Int. Conf. Nosocomial Healthcare-Associated Infections, May 2000). A pilot study of monochloramine injection in the water system of one wing of a Washington, D.C., hospital showed promising results (Shelton, B. G., N. Donegan, W. D. Flanders, J. Kool, L. Pic-Aluas, and L. Witherell, Efficacy of point of use monochloramine treatment to control *Legionella* in colonized building water system. 5th International Conference on Legionella, Ulm, Germany, 2000). The municipal water supplier of that hospital later switched to monochloramine, and since then, no *Legionella* could be recovered from any of the other hospital wings (personal communication, L. Pic-Aluas, February 2001). A laboratory study on the effect of monochloramine on *Legionella* in a biofilm model is described in chapter 82. Monochloramine was more effective at killing biofilm-associated *Legionella* than free chlorine.

It is likely that the superior effect of monochloramine is mostly due to its better penetration into biofilm. This effect may be further enhanced by its higher chemical stability, enabling it to penetrate the far reaches of a distribution system and to persist longer in areas of stagnation. An interesting hypothesis is that

monochloramine may also be better at killing the amoebae that serve as hosts to *Legionella* and *Legionella*-like organisms. More research is needed to elucidate the mechanisms by which monochloramine inhibits *Legionella* colonization.

CONCLUSIONS

To this author's knowledge, monochloramine is the only disinfectant that has been shown to reduce the incidence of Legionnaires' disease when used at the municipal level. This finding is not just important for control of nosocomial infections. More than 75% of cases of Legionnaires' disease acquire their infection in the community (23). Residual disinfection of municipal drinking water with monochloramine seems an inexpensive and efficient way to prevent many of these cases. In addition, supplemental injection of monochloramine may become one of the preferred methods for control of *Legionella* and *Legionella*-like organisms in hospitals, hotels, and similar institutions.

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