

EXPERIENCES OF THE FIRST 16 HOSPITALS USING COPPER–SILVER IONIZATION FOR *LEGIONELLA* CONTROL: IMPLICATIONS FOR THE EVALUATION OF OTHER DISINFECTION MODALITIES

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ABSTRACT

BACKGROUND AND OBJECTIVES: Hospital-acquired legionnaires' disease can be prevented by disinfection of hospital water systems. This study assessed the long-term efficacy of copper–silver ionization as a disinfection method in controlling *Legionella* in hospital water systems and reducing the incidence of hospital-acquired legionnaires' disease. A standardized, evidence-based approach to assist hospitals with decision making concerning the possible purchase of a disinfection system is presented.

DESIGN: The first 16 hospitals to install copper–silver ionization systems for *Legionella* disinfection were surveyed. Surveys conducted in 1995 and 2000 documented the experiences of the hospitals with maintenance of the system, contamination of water with *Legionella*, and occurrence of hospital-acquired legionnaires' disease. All were acute care hospitals with a mean of 435 beds.

RESULTS: All 16 hospitals reported cases of hospital-acquired legionnaires' disease prior to installing the copper–silver ionization system. Seventy-five percent had previously

attempted other disinfection methods including superheat and flush, ultraviolet light, and hyperchlorination. By 2000, the ionization systems had been operational from 5 to 11 years. Prior to installation, 47% of the hospitals reported that more than 30% of distal water sites yielded *Legionella*. In 1995, after installation, 50% of the hospitals reported 0% positivity, and 43% still reported 0% in 2000. Moreover, no cases of hospital-acquired legionnaires' disease have occurred in any hospital since 1995.

CONCLUSIONS: This study represents the final step in a proposed 4-step evaluation process of disinfection systems that includes (1) demonstrated efficacy of *Legionella* eradication in vitro using laboratory assays, (2) anecdotal experiences in preventing legionnaires' disease in individual hospitals, (3) controlled studies in individual hospitals, and (4) validation in confirmatory reports from multiple hospitals during a prolonged time (5 to 11 years in this study). Copper–silver ionization is now the only disinfection modality to have fulfilled all four evaluation criteria (*Infect Control Hosp Epidemiol* 2003;24:563-568).

The source of hospital-acquired legionnaires' disease is the hospital water supply. Cases of legionnaires' disease have been prevented by disinfecting the water supply.¹ In a survey of 192 hospitals participating in the National Nosocomial Infections Surveillance (NNIS) System, 20% of the hospitals completing the survey had adopted long-term disinfection measures for the prevention of hospital-acquired legionnaires' disease.² The percentage was even higher (50%) among hospitals that had reported cases of hospital-acquired legionnaires' disease.

In 1997, the Healthcare Infection Control Practices Advisory Committee of the Centers for Disease Control and Prevention (CDC) recommended only 2 disinfection modalities for controlling *Legionella* in hospital water sys-

tems: thermal eradication (superheating the water to 65°C and flushing outlets) or hyperchlorination (1 to 2 ppm).³ Although copper–silver ionization had been introduced as a disinfection measure, the CDC did not recommend copper–silver ionization for *Legionella* in the 1997 Guidelines for Prevention of Nosocomial Pneumonia. "No recommendation" was listed for water treatment with copper–silver ionization. The reason cited for this position was that experience with ionization was too limited.³ In 1999, the CDC again stated that "the role of ionization systems in primary (*Legionella*) decontamination efforts is not yet determined."² Despite these recommendations, copper–silver ionization systems are now operational in more than 100 hospitals in the United States, and 32% (12

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of 38) of the hospitals participating in the NNIS System and surveyed in 1998 used copper–silver ionization for *Legionella* disinfection.²

Hospitals continue to struggle with the selection of a disinfection method due to conflicting and sometimes inaccurate information. Data are needed that would assist hospitals with making a decision regarding the purchase of any disinfection system for controlling *Legionella* in hospital water systems. We propose that the evaluation of any new disinfection method be an evidence-based process that includes the following steps: (1) a demonstrated efficacy in vitro against *Legionella* organisms, (2) anecdotal experience of efficacy in controlling *Legionella* contamination in individual hospitals, (3) controlled studies of efficacy in controlling *Legionella* growth and in preventing cases of hospital-acquired legionnaires' disease in individual hospitals, and (4) confirmatory reports from multiple hospitals with prolonged duration of follow-up (validation step).

With this study, we provide the final step in this proposed evaluation process for copper–silver ionization, a multicenter survey of hospitals in the United States to evaluate the efficacy of copper–silver ionization in eradicating *Legionella* from the water supply and in reducing the occurrence of hospital-acquired legionnaires' disease. The hospitals selected for the survey were the first 16 consecutive hospitals in the United States (and the world) to have instituted copper–silver for *Legionella* disinfection.

METHODS

We developed two surveys composed of multiple choice and short answer questions. Part of the survey was completed by the infection control practitioner and part by the engineering staff. The first survey was mailed in 1995 to the first 16 hospitals that had adopted copper–silver ionization. The survey included 30 questions related to hospital demographics, environmental monitoring of *Legionella*, identification of hospital-acquired legionnaires' disease, and disinfection practices and costs. The survey also included questions about installation, monitoring, and maintenance of the copper–silver ionization systems (LiquiTech, Inc., Bolingbrook, IL; and TARN PURE, Buckinghamshire, United Kingdom).

In 2000, a second questionnaire was mailed to the original 16 hospitals surveyed in 1995. This survey consisted of 22 questions related to the current use of the copper–silver ionization system, environmental monitoring for *Legionella*, and the incidence of hospital-acquired legionnaires' disease after the installation of the ionization system. The survey also included questions regarding monitoring for ion concentrations, maintenance of the system, and problems encountered. An overall subjective appraisal of system performance was requested from the infection control practitioner, and the engineering staff were asked to evaluate the system operation and maintenance. The appraisal was rated from 1 (poor) to 5 (excellent) by the infection control practitioner and from 1 (very difficult) to 4 (easy) by the engineering staff.

RESULTS

1995 Survey

All of the 16 hospitals surveyed responded to the questionnaire. The hospitals were in 8 different states (Table 1). The mean number of beds was 435, and 56% (9 of 16) of the hospitals performed transplant surgery. All of the 16 hospitals reported cases of hospital-acquired legionnaires' disease prior to implementing control measures. Seventy-five percent (12 of 16) of the hospitals had previously attempted other disinfection measures (Figure). Thermal eradication (superheat and flush) had been used by 50% (8 of 16) of the hospitals and hyperchlorination had been used by 31% (5 of 16) of the hospitals. The year of installation of the ionization systems in these hospitals ranged from 1989 to 1995. The mean number of ionization flow cells required per institution was 3 (range, 1 to 7). The start-up costs for installation ranged from \$6,000 to \$134,572 (mean, \$86,432). The annual maintenance costs ranged from \$240 to \$8,000.

Environmental monitoring for *Legionella* was performed by 94% (15 of 16) of the hospitals, with 56% (9 of 16) performing cultures monthly or quarterly. Forty-seven percent (7 of 15) reported that more than 30% of the samples had been positive for *Legionella* prior to the installation of the ionization systems (one hospital did not respond to this question). Isolation of *L. pneumophila* serogroups 1, 3, 5, 6, and 8 was reported from 75%, 13%, 6%, 6%, and 6% of the hospitals, respectively. Multiple serogroups were isolated from 3 of the hospitals.

After the installation of the copper–silver ionization system, 50% (8 of 16) of the hospitals reported 0% positivity of monitoring sites, 44% (7 of 16) reported 30% positivity or lower, and 6% (1 of 16) discontinued monitoring. Regular monitoring of copper and silver ion levels was performed by 94% (15 of 16) of the hospitals. Regular (monthly or quarterly) cleaning and descaling of the metal electrodes was performed by all hospitals.

2000 Survey

All of the 16 hospitals originally surveyed in 1995 responded to the follow-up survey in 2000. All were still using copper–silver ionization for *Legionella* disinfection. The duration of system operation ranged from 5 to 11 years, with a mean of 7 years. Ninety-four percent (15 of 16) of the hospitals continued to perform routine environmental monitoring for *Legionella* at various intervals. Testing was performed quarterly in 4 of the hospitals, every 6 months in 4 of the hospitals, or annually in 3 of the hospitals. In 2000, 43% (7 of 16) of the hospitals reported complete eradication (0% positivity) of *Legionella* from the water supply. No hospitals reported greater than 30% positivity of monitoring sites.

No cases of hospital-acquired legionnaires' disease were diagnosed after the installation of the copper–silver ionization system in 94% (15 of 16) of the hospitals. One hospital did report a case of hospital-acquired legionnaires' disease soon after the installation of the ionization system; however, no cases had occurred from 1995 to 2002 in this hospital.

TABLE 1
SURVEY RESULTS FROM 16 HOSPITALS USING COPPER-SILVER IONIZATION SYSTEMS AND RESPONDING TO THE 1995 AND 2000 SURVEYS*

Hospital No.	Location (State)	No. of Beds	Year System Installed	Environmental Monitoring (Positive for <i>Legionella</i>)			Cases of LD	
				Before Cu/Ag	After Cu/Ag		Before Cu/Ag	After Cu/Ag
					1995	2000		
1	OH	700	1989	NA	< 30%	≤ 30%	Yes	No
2	OH	400	1990	> 30%	0%	0%	Yes	Yes*
3	PA	520	1991	> 30%	< 10%	< 10%	Yes	No
4	TX	650	1992	≤ 30%	< 5%	≤ 30%	Yes	No
5	PA	542	1992	≤ 30%	0%	0%	Yes	No
6	CA	292	1993	≤ 30%	≤ 30%	≤ 30%	Yes	No
7	CA	310	1993	> 30%	≤ 30%	≤ 30%	Yes	No
8	IL	536	1993	≤ 30%	≤ 30%	≤ 30%	Yes	No
9	WI	251	1993	> 30%	0%	0%	Yes	No
10	VT	500	1994	0%	NA	NA	Yes	No
11	IL	645	1994	> 30%	0%	0%	Yes	No
12	PA	230	1994	> 30%	0%	< 30%	Yes	No
13	PA	341	1994	≤ 30%	≤ 30%	≤ 30%	Yes	No
14	WV	445	1994	0%	0%	0%	Yes	No
15	PA	337	1995	≤ 30%	0%	0%	Yes	No
16	PA	266	1995	> 30%	0%	0%	Yes	No

Cu/Ag = copper-silver ionization; NA = not available; LD = legionnaires' disease.
*No cases from 1995 to 2002.

The overall subjective appraisal of the copper-silver ionization system by the infection control practitioners and engineering personnel is listed in Table 2. Using a rating scale ranging from "poor" to "excellent," most of the infection control practitioners rated the system as excellent, based on the results of environmental cultures and the incidence of hospital-acquired legionnaires' disease. Using a rating scale ranging from "easy" to "very difficult," most of the engineering personnel rated the system operation and maintenance as average. Forty-four percent (7 of 16) of the engineering personnel reported problems with the intermittent discoloration of water or sinks in the 1995 survey, although such problems apparently had been resolved by the 2000 survey.

DISCUSSION

Disinfection modalities currently in use for *Legionella* control in hospital water distribution systems include copper-silver ionization, thermal eradication (superheat and flush), and hyperchlorination. Hyperchlorination has proven disappointing as a long-term solution due to the high expense, pipe corrosion, the introduction of carcinogenic by-products into the drinking water, and difficulty in maintaining the high concentrations (2 to 4 ppm) of chlorine needed to sustain efficacy.⁴ In the past few years, carcinogenic by-products from chlorination and increases in birth defects and spontaneous abortion have raised concerns from federal agencies and consumer interest groups. A meta-analysis of 10 case-con-

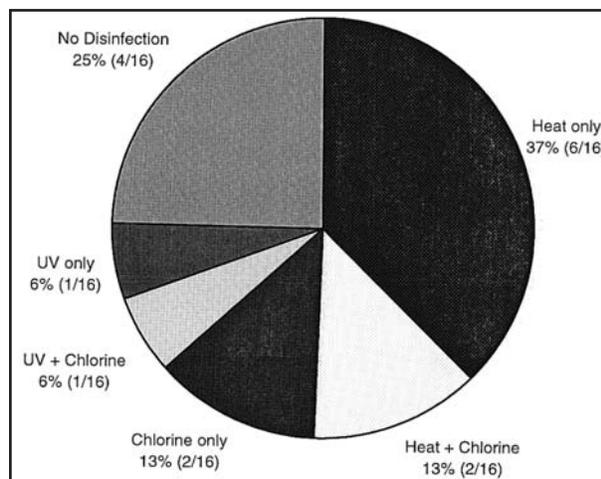


FIGURE. Disinfection methods attempted prior to the installation of copper-silver ionization systems. UV = ultraviolet light.

rol studies and 2 cohort studies concluded that the risk of cancer from the consumption of chlorinated water was significant.⁵ Spontaneous abortions have also been linked to the consumption of chlorinated water.⁶ As a result, the Environmental Protection Agency instituted stricter standards for chlorination by-products on January 1, 2002.

Thermal eradication (70°C flush for 30 minutes), a

TABLE 2
RATING BY INFECTION CONTROL PROFESSIONAL AND ENGINEERING PERSONNEL OF THE PERFORMANCE OF THE COPPER-SILVER IONIZATION SYSTEM

Respondent	Evaluation	Percent of Respondents Giving Rating				
		1	2	3	4	5
ICP	Overall appraisal	0	6	0	6	88
ENG	Operation and maintenance	0	13	63	25	-

ICP = infection control professional; ENG = engineering personnel.
Overall Appraisal: 1 = poor; 2 = adequate; 3 = good; 4 = very good; 5 = excellent.
Operation and Maintenance: 1 = very difficult; 2 = difficult; 3 = average; 4 = easy.

method developed by our group,⁷ has been efficacious; however, contamination with *Legionella* will often recur within months. Furthermore, it is tedious and labor intensive to implement. Although ozonation, instantaneous heating systems, and ultraviolet light were conceptually attractive solutions in field trials, failures have outweighed successes.⁴ Moreover, no controlled studies of 5 years or longer have been reported for any of the three methods.

Randomized comparative trials are considered the gold standard for assessing therapeutic modalities in evidenced-based medicine. Such an approach is not practical for the evaluation of hospital disinfection systems due to the diversity and type of water distribution systems in different hospitals, the environmental variability of *Legionella* contamination and water quality, the nonfeasibility of having a control group in an urgent situation requiring an immediate solution, and the absence of any established disinfection method to serve as a standard for a comparison.

Despite the limitations in evaluation, it becomes increasingly important to devise a scientific method of evaluation of any disinfection method. The current basis of decision making for most hospitals in determining which type of system to implement and which commercial product to purchase includes anecdotal reports of success without corroborating data and unsubstantiated testimonials from commercial vendors. We propose that any new disinfection method undergo a standardized evaluation with the following steps: (1) a demonstrated efficacy in vitro against *Legionella* organisms, (2) anecdotal experience of efficacy in controlling *Legionella* contamination in individual hospitals, (3) controlled studies of prolonged duration (years, not months) of the efficacy of controlling *Legionella* growth and preventing cases of hospital-acquired legionnaires' disease in individual hospitals, and (4) confirmatory reports from multiple hospitals with prolonged duration of follow-up (validation step).

What is the current status of copper-silver ionization in controlling *Legionella* in hospital hot water systems

according to the above four steps? In laboratory assays, copper and silver ions have been shown to effectively kill *Legionella* in vitro.⁸⁻¹⁰ These positively charged ions form electrostatic bonds with negatively charged sites on bacterial cell walls. This action, coupled with protein denaturation, leads to cell lysis and death. Numerous anecdotal reports of the efficacy of ionization systems have been presented, although controls and consistency in surveillance were variable in these studies.¹¹⁻¹⁷ More rigorous controlled studies of the efficacy of ionization have also been reported for both hospitals and nursing homes during a prolonged period.¹⁸⁻²² This study represents the final step in the evaluation of copper-silver ionization: a confirmatory multicenter survey of 16 hospitals that have been using ionization for *Legionella* control for 5 to 11 years.

After the installation of the ionization system, 50% of the hospitals surveyed in 1995 reported that *Legionella* contamination had dropped to 0% positivity at the distal monitoring sites, and when surveyed again in 2000, 43% of the hospitals still reported 0% *Legionella* contamination. The remainder reported 30% positivity or lower. Complete eradication of *Legionella* may be unreasonable to expect with any disinfection method; however, it is noteworthy that 94% (15 of 16) of the hospitals reported no cases of hospital-acquired legionnaires' disease during the follow-up period. The one hospital that reported a case has not experienced another case in the subsequent 7 years.

One possible weakness of this study is that the conditions of the two study periods may not have been comparable, although none of the hospitals reported any overt change in patient management or prophylactic antibiotic therapy.

Controlled studies have supported the biologically plausible concept that the single most important factor in decreasing the incidence of hospital-acquired legionnaires' disease is the eradication of the reservoir for this microorganism.²³⁻²⁷ The uniform finding of disappearance of hospital-acquired legionnaires' disease in 16 diverse hospitals catering to different patient populations in different geographic areas confirms the primary importance of the reservoir in the causation of legionnaires' disease.

Minimizing the risk of hospital-acquired legionnaires' disease may not require complete eradication (0% positivity) of *Legionella* from water outlets. Our experience with ionization at the Pittsburgh Veterans Affairs Medical Center was also consistent with that of the 16 hospitals surveyed. When using thermal disinfection, we found that cases rarely occurred in our hospital when distal outlet positivity was below 30%.^{7,28} We have periodically isolated *L. pneumophila* serogroup 1 from a few of the outlets (fewer than 30%) since installing the copper-silver ionization system¹⁹ (our system was not listed in this study). However, the incidence of hospital-acquired legionnaires' disease was dramatically reduced following installation. The average number of cases of hospital-acquired legionnaires' disease decreased significantly from 6 per year prior to installation to an average of only 1 per year in the 7 years following installation ($P < .05$)¹⁹

(J. E. Stout, PhD, unpublished data, May 2002). In fact, there were no cases of hospital-acquired legionnaires' disease during the 4 years from 1999 to 2002.

Sixty-three percent and 25% of hospital engineers rated the overall maintenance of the copper–silver ionization system as average or easy, respectively, and 88% of the infection control practitioners rated the overall performance of the system as excellent (Table 2). One reason for the success of these systems in the hospitals is that adequate maintenance was routinely performed, including follow-up surveillance culture and monitoring of copper–silver concentrations. The primary problem in the initial phases following installation was the appearance of discolored (gray) hot water (44%, 7 of 16). Six percent (1 of 16) also experienced discoloration of sink basins. These problems occur when silver levels are above the recommended range of 20 to 40 µg/L. Silver concentrations must be tested by either atomic absorption spectroscopy or inductively coupled mass spectroscopy. This testing is usually performed by a reference laboratory, which necessitates the shipment of specimens. As a result, this testing may not be performed at optimal intervals. By 2000, the problem of sink discoloration had been resolved at the affected hospitals.

Seventy-five percent (12 of 16) of the surveyed hospitals reported the failure of previous attempts to control *Legionella* by other methods. This included 5 hospitals that used hyperchlorination. Failure to maintain long-term disinfection of *Legionella* by hyperchlorination is commonplace, and high costs due to corrosion are often cited as the main reason for its discontinuation. Similarly, although superheat and flush is effective, long-term use can become logistically tedious.¹⁹ For many hospitals, copper–silver ionization was installed as a more convenient and cost-effective approach.

It is not unusual for a hospital to try many options for *Legionella* control. For example, *Legionella* persisted in a Finnish hospital despite thermal disinfection (75°C with a 30-minute flush), the removal of hot water tanks, and setting the hot water temperature to 60°C.²⁰ After a copper–silver ionization system was installed, there was a significant ($P < .05$) reduction in *Legionella* contamination. Other failures of thermal disinfection have been reported; however, in some of the hospitals, the distal outlets were flushed for only 5 minutes instead of the recommended 30 minutes, an error in the CDC guidelines.²⁹ A hospital in Ohio had installed an ionization system because of a previous failure to control *Legionella* with hyperchlorination,²⁹ but ionization also proved unsuccessful in controlling *Legionella* in the water system. It was subsequently determined that the high pH (higher than 8.5) of the water may have interfered with the disinfecting action of both chlorine and copper–silver ions.³⁰ In a similar scenario, a hospital in Wisconsin reported success with copper–silver ionization after adding acid to the water system to lower the pH.¹⁶

In a study performed in Germany, the failure of copper–silver ionization to control *Legionella* was attrib-

uted by the authors to the emergence of *Legionella* resistant to copper–silver ionization.³¹ However, careful analysis of the article showed that resistance to copper or silver ions was never demonstrated for any *Legionella* strains isolated following copper–silver disinfection. The apparent failure to control *Legionella* was more likely due to suboptimal ion levels and not to the development of resistance.³²

Advantages of copper–silver ionization are that it is more cost-effective than hyperchlorination, is easier to maintain, and does not corrode piping or plumbing fixtures, and in the event of mechanical failure, recontamination is delayed for weeks, allowing a safety buffer.³³⁻³⁵ In contrast, if a chlorinator fails, recontamination occurs rapidly. Copper–silver ionization systems proved effective in 75% (12 of 16) of the institutions in which thermal eradication, hyperchlorination, or both had proven unsatisfactory.

The four evaluation criteria listed earlier have now been fulfilled for copper–silver ionization. We recommend that this process of evaluation be applied to other newer disinfection approaches such as those involving chlorine dioxide and monochloramine. It may be several years before sufficient controlled trials of these modalities are available for scientific scrutiny. This study documents the long-term efficacy of copper–silver ionization in reducing *Legionella* in hospital hot water distribution systems, as well as reducing or eliminating cases of hospital-acquired legionnaires' disease.

REFERENCES

- Lin YE, Stout JE, Yu VL. Disinfection of water distribution systems for *Legionella*. *Semin Respir Infect* 1998;13:147-159.
- Fiore AE, Butler JC, Emori TG, et al. A survey of methods to detect nosocomial legionellosis among participants in the National Nosocomial Infections Surveillance System. *Infect Control Hosp Epidemiol* 1999;20:412-416.
- Centers for Disease Control and Prevention. Guidelines for prevention of nosocomial pneumonia. *MMWR* 1997;46(RR1):1-79.
- Lin YE, Vidic RD, Stout JE, et al. *Legionella* in water distribution systems. *Journal of the American Water Works Association* 1998;90:112-121.
- Morris RD, Audet AM, Angelillo IF, et al. Chlorination, chlorination by-products, and cancer: a meta-analysis. *Am J Public Health* 1993;82:955-963.
- Swan SH, Waller K, Hopkins B, et al. A prospective study of spontaneous abortion: relation to amount and source of drinking water consumed in early pregnancy. *Epidemiology* 1998;9:126-133.
- Best M, Yu VL, Stout J, et al. Legionellaceae in the hospital water supply: epidemiological link with disease and evaluation of a method of control of nosocomial legionnaires' disease and Pittsburgh pneumonia. *Lancet* 1983;2:307-310.
- Landeem LK, Yahya MT, Gerba CP. Efficacy of copper and silver ions and reduced levels of free chlorine in inactivation of *Legionella pneumophila*. *Appl Environ Microbiol* 1989;55:3045-3050.
- Lin YE, Vidic RD, Stout JE, et al. Individual and combined effects of copper and silver ions on inactivation of *Legionella pneumophila*. *Water Res* 1996;30:1905-1913.
- Rohr U, Senger M, Selenka F. Effect of silver and copper ions on survival of *Legionella pneumophila* in tap water [in German]. *Zentralbl Hyg Umweltmed* 1996;198:514-521.
- Thompson RB, File TM, Plouffe J, et al. Use of Tarn-Pure to eradicate *Legionella pneumophila* from a hospital hot water system. In: *Proceedings of the Annual Meeting of the American Society for Microbiology (Anaheim, CA)*. Washington, DC: American Society for Microbiology; 1990.
- Lumish RM, Stout JE, Fleming J, et al. New approach to controlling nosocomial Legionnaires' disease: copper/silver ionization treatment in hot water system. Presented at the 11th Annual Interscience

- Conference on Antimicrobial Agents and Chemotherapy; October 17-20, 1993; New Orleans, LA.
13. Nouri K, Posey K, Ruben F, et al. Installation of metal ionization system for the reduction of *Legionella pneumophila* at a university hospital: black water and other complications. *Infect Control Hosp Epidemiol* 1996;17:16.
 14. Biurrun A, Caballero L, Pelaz C, et al. Treatment of a *L. pneumophila*-colonized water distribution system using copper-silver ionization and continuous chlorination. *Infect Control Hosp Epidemiol* 1999;20:426-428.
 15. Colville A, Crowley J, Dearden D, et al. Outbreak of Legionnaires' disease at a university hospital, Nottingham: epidemiology, microbiology, and control. *Epidemiol Infect* 1993;10:105-116.
 16. Bowler WA, Bresnahan J, Bradfish A. A "vitrilic" solution to the problem of *Legionella* contamination of a hospital water system. *Soc Health Care Epidemiol Assoc* 1999.
 17. Mietzner S, Schwille RC, Farley A, et al. Efficacy of thermal treatment and copper-silver ionization for controlling *Legionella pneumophila* in high-volume hot water. *Am J Infect Control* 1997;25:452-457.
 18. Selenka F, Rohr U, Volker M. Studies on reducing the *Legionella* load of a hospital warm-water system by using the Tarn-Pure procedure. *Hyg Med* 1995;20:292-302.
 19. Stout JE, Lin YSE, Goetz AM, et al. Controlling *Legionella* in hospital water systems: experience with the superheat-and-flush method and copper-silver ionization. *Infect Control Hosp Epidemiol* 1998;19:911-914.
 20. Kusnetsov J, Ilvanainen E, Elomaa N, et al. Copper and silver ions more effective against legionellae than against mycobacteria in a hospital warm water system. *Water Res* 2001;35:4217-4225.
 21. States S, Kuchta J, Young W, et al. Controlling *Legionella* using copper-silver ionization. *Journal of the American Water Works Association* 1998;90:122-129.
 22. Reynaga E, Garcia-Nunez M, Pedro-Botet M, et al. Copper-silver ionization system water disinfection, and nosocomial legionellosis. Presented at the 41st Annual Interscience Conference on Antimicrobial Agents and Chemotherapy; December 16-19, 2001; Chicago, IL.
 23. Johnson JT, Yu VL, Best M, et al. Nosocomial legionellosis uncovered in surgical patients with head and neck cancer: implications for epidemiologic reservoir and mode of transmission. *Lancet* 1985;2:298-300.
 24. Yu VL, Beam TR, Lumish RM, et al. Routine culturing for *Legionella* in the hospital environment may be a good idea: a three-hospital prospective study. *Am J Med Sci* 1987;294:97-99.
 25. Joly J, Alary M. Occurrence of nosocomial Legionnaires' disease in hospitals with contaminated potable water supply. In: Barbaree JD, Breiman RF, Dufour AP, eds. *Current Status and Emerging Perspectives*. Washington, DC: American Society for Microbiology; 1994:39.
 26. Goetz AM, Stout JE, Jacobs SL, et al. Nosocomial Legionnaires' disease discovered in community hospitals following cultures of the water system: seek and ye shall find. *Am J Infect Control* 1998;26:6-11.
 27. Modol JM, Pedro-Botet ML, Sabria M, et al. Environmental and clinical legionellosis in hospitals in Catalonia, Spain. Presented at the 38th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy; September 24-27, 2002; San Diego, CA.
 28. 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; 1997:1-15. Available at www.legionella.org.
 29. Centers for Disease Control and Prevention. Transmission of nosocomial Legionnaires' disease. *JAMA* 1997;277:1927-1928.
 30. Lin YE, Vidic RD, Stout JE, et al. Negative effect of high pH on biocidal efficacy of copper and silver ions in controlling *Legionella pneumophila*. *Appl Environ Microbiol* 2002;68:2711-2715.
 31. Rohr U, Senger M, Selenka F, et al. Four years of experience with silver-copper ionization for control of *Legionella* in a German university hospital hot water plumbing system. *Clin Infect Dis* 1999;29:1507-1511.
 32. Lin YE. Ionization failure not due to resistance. *Clin Infect Dis* 2000;31:1315-1316.
 33. Liu Z, Stout JE, Tedesco L, et al. Controlled evaluation of copper-silver ionization in eradicating *Legionella pneumophila* from a hospital water distribution system. *J Infect Dis* 1994;169:919-922.
 34. Liu Z, Stout JE, Boldin M, et al. Intermittent use of copper-silver ionization for *Legionella* control in water distribution systems: a potential option in buildings housing individuals at low risk of infection. *Clin Infect Dis* 1998;26:138-140.
 35. Mathys W, Hohmann CP, Junge-Mathys E. Efficacy of copper-silver ionization in controlling *Legionella* in a hospital hot water distribution system: a German experience. In: Marre R, Kwaiq YA, Bartlett C, et al., eds. *Legionella*. Washington, DC: ASM Press; 2002:419-424.