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Ionization Failure Not Due to Resistance

SIR—Rohr et al. [1] report their experience with copper-silver ionization in eradicating *Legionella* in the hot water plumbing systems of a German university hospital. They report that the percentage of 1-L samples of water from distal sites that were positive for *Legionella* (the detection limit was 1 cfu/L) were as follows: before installation of the ionization unit, 100%; in year 1 after installation, 55%; in year 2, 76%; in year 3, 78%; and in year 4, 75%. From this data it appears that the copper-silver ionization system installed in this hospital did not effectively control *Legionella* in the water plumbing system, even in the first year. Although the number of cfu of *Legionella* detected decreased in the first year, the percentage of samples positive for *Legionella* remained as high as 55%. Cases of hospital-acquired legionnaires disease correlate directly with percentage of samples that are positive for *Legionella* [2, 3–4], but not with the number of *Legionella* organisms detected at each distal site.

We suspect that the copper-silver ionization system could not eradicate *Legionella* because the concentration of ions in the water system was inadequate (table 1). The efficacy of copper-silver ionization depends on maintaining adequate concentrations of both copper and silver ions in the water system. *Legionella* positivity was significantly reduced (from 70% to 0%) only after the copper and silver ion concentrations reached 400 and 40 μg/L, respectively [5]. Other studies have also shown that maintaining ion concentrations between 200–400 μg/L of copper and 20–40 μg/L of silver was crucial [6–8].

In this hospital, the background copper ion concentration was 200 μg/L, and the average copper ion concentration after installation of the ionization system was also 200 μg/L (range, 131–1159 μg/L). This suggests that insufficient copper ions were released into the plumbing system by the ionization system. In addition, the silver ion concentration applied in the water system (5μg/L) was far below the effective concentration of 20–40 μg/L recommended previously. In vitro results from our investigations [9] differ from those of Rohr et al. and show that copper and silver have synergistic activity against *Legionella* [10]; silver ions alone were inferior to the combination of copper and silver. In hospitals that use silver ions as the only disinfectant, the recommended silver concentration is 60–100 μg/L (Gunner Lyslo, personal communication), which is much higher than the 2–44.6 μg/L achieved in the hospital discussed by Rohr et al.

One possible explanation for the low concentrations of copper and silver ions in the water system has to do with the distribution of the ions within it. The ionization systems were installed on the feed line of the main hot water station and on the hot water feed line of the peripheral building (400 m away from the central hot water station). It appears that the ionization system operates on what is basically a "pass-through" mode: incoming water flows through the ionization flow cell and ions are released into the water. This system has been

Table 1. Copper and silver ion concentrations in the water of a German hospital in the 4 years after an ionization system was installed, as reported by Rohr at al. [1].

	Mean concentration, μg/L (range)				
		Year after installation			
Ion	Before installation	1	2	3	4
Copper	200	200 (131–1159)	173 (99–207)	230 (102–377)	192 (155–560)
Silver	0[a]	6 (2.3–20.8)	5 (2–14)	5 (3–23)	30 (6–44.6)

[a] Below detection limit.

described in a previous article by Rohr et al. [11]. The disadvantage of this type of installation is that the ion concentrations will fluctuate depending on the flow rate of incoming water. If a large volume of water flows through the flow cell, copper and silver ions are diluted and the concentrations will be low.

I suggest the authors collect water samples at the distal sites 10–30 s after flushing and 5 min after. Collecting water samples after a 5–10 min flush, as described in their article, may actually overestimate the concentrations in the water plumbing system, because the ion concentrations recorded are not the ion concentrations already in the hot water system, but the concentration just released from the generator: the ions generated from the feed line will probably take less than 5–10 minutes to get to the outlet for sample collection. Regardless of the timing of sample collection, the ion concentrations are too low to effectively kill *Legionella.*

Ionization systems installed in US hospitals generally place the flow cells on the hot water recirculating lines. The advantage of this approach is that it recirculates the hot water, so the ion concentrations can achieve a steady level adequate to control *Legionella.*

Given the German drinking water regulation that maximum silver concentration cannot exceed 10μg/L, electrodes of 60% silver and 40% copper will not be effective. Ionization systems installed in the United States (manufactured by Tarnpure, Pittsburgh and LiquiTech USA, Willowbrook, IL) use 30% silver and 70% copper electrodes. A solution to Germany's 10μg/L limit of silver may be to increase the copper concentration to ≥400 μg/L while maintaining a low silver concentration of <10 μg/L.

The claim of Rohr at al. that *Legionella* developed resistance to silver is unsupported by any data in their report. However, their data do document that the failure to eradicate *Legionella* is likely due to insufficient copper and silver ions in the water. A possible solution might be to increase copper ion concentration to 400 μg/L and maintain sustained copper and silver ions in the water system.

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Reply

SIR—We would like to thank Dr. E. Lin and Mr. Hayes for their comments on our article in Clinical Infectious Diseases [1] concerning the use of silver (Ag)/ copper (Cu) ionization for *Legionella* control in a German university hospital plumbing system.

As we stated in our article, our main purpose was to study the control of *Legionella* by the use of Ag/Cu ionization that produced silver concentrations within the limits of the German drinking water regulations (i.e., a maximum of 10 μg/L Ag). Long-term eradication of *Legionella* in the hot water plumbing system of our hospital under these conditions, with average Cu concentrations of 200 μg/L, was not possible. This is in contrast to the manufacturers statement that the Ag/Cu ionization units were initially set to produce correct levels "for effective disinfection"; namely, 40 μg/L Ag and 400 μg/L Cu. The ionizations units never produced levels of 40 μg/L Ag and 400 μg/L Cu.

Dr. Lin suggests that technical modifications (for example, in the composition of the Ag/Cu-electrodes that are installed within the circulation loop) may make the ionization more effective when the limitations of the German drinking water reg-

ulations must be considered. We totally agree with his arguments. His constructive, detailed technical explanations should be tested thoroughly by the manufacturers of Ag/Cu ionization systems and taken into consideration in future experiments.

Dr. Lin's main scientific point is that the data we presented in our paper do not support the claim that *Legionella* developed resistance to silver. He assumes that Ag/Cu ionization in our hospital did not effectively control *Legionella,* even in the beginning. To support this, he gives the percentages of water samples from distal sites that were positive for *Legionella* (detection limit 1 cfu/L). However, we cannot draw valid conclusions from these values alone. Our statistical evaluation is based on *Legionella* counts (cfu/L) and not on "sample points positive for *Legionella.*" The results of the multiple regression analysis that we presented in our paper clearly revealed a decreased influence of Ag ions on *Legionella* counts during the 4-year study period. But even without performing a statistical evaluation the facts are as follows: in the first year after the Ag/Cu ionization unit was installed, the percentage of samples positive for *Legionella* decreased from 100% to 55%, with an average Ag level of <10 μg/L; in the fourth year of Ag/Cu ionization, the percentage of samples positive remained at 75%, with an average Ag level of 30 μg/L.

The methods and detection limits used in various reports concerning Ag/Cu ionization are not comparable. In order to facilitate comparison [2], we gave results as counts of *Legionella* cfu/L, not as positive distal sites per swab [3, 4]. We prefer a quantitative method in reporting effective disinfection, which is a common procedure in examining any disinfection method (see, e.g., [5]). Another question is whether there is any connection between the quantity of *Legionella* (cfu/L) in water distribution systems and the incidence of legionnaires disease. Indeed, there are many unresolved questions regarding the effectiveness of Ag/Cu ioniziation for control of *Legionella* in hospitals, including the influence of chemical water composition, temperature, and circulation on metal activity.

Vigilance is necessary not only because *Legionella* may develop resistance to the activity of Ag and Cu, but also because of the question of protozoa inactivation by Ag and Cu ions. We believe that methods for disinfecting water distribution systems should be designed to control the growth of both *Legionella* and protozoa. But the investigations of Cassels et al. [6] showed that electrolytically-generated concentrations up to 80 μg/L Ag and 800 μg/L Cu did not inactivate *Naegleria fowleri* in vitro. Recently we reported that *Hartmannella vermiformis* survived at concentrations of 50 μg/L Ag and 500 μg/L Cu in vitro [7].

There was further discussion of the arguments about Ag/Cu ionization at a panel discussion on "Copper/Silver Water Ionization Systems: Pro and Con" at the Fifth International Conference on *Legionella* at Ulm, Germany, 26–29 September, 2000.

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Limitations of Plasma Human Immunodeficiency Virus RNA Testing

SIR—The studies of Mezzaroma [1] illustrate the limitations of plasma HIV RNA testing and the need for additional standardized assays to measure viral dynamics in HIV-infected patients. In a recent study [2] we compared the $CD4^+$ and $CD8^+$ cell counts and the levels of HIV DNA, HIV RNA, and infectious HIV in patients who partially responded to highly active antiretroviral therapy (HAART) and in patients for whom HAART failed completely. Patients who responded to HAART had increasing levels of $CD4^+$ cells, and patients who did not had decreasing levels of $CD4^+$ cells. Although plasma HIV RNA levels were similarly high in both groups, when compared with patients who did not respond to HAART, the patients who did respond had significant increases in $CD8^+$ cells, fewer positive plasma HIV cultures, lower frequencies of infectious HIV in $CD4^+$ cells, and lower frequencies of HIV DNA in