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Author(s): María Luisa Pedro-Botet, Inma Sanchez, Miquel Sabria, Nieves Sopena, Lourdes Mateu, Marian García-Núñez and Celestino Rey-Joly
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Impact of Copper and Silver Ionization on Fungal Colonization of the Water Supply in Health Care Centers: Implications for Immunocompromised Patients

María Luisa Pedro-Botet, Inma Sanchez, Miquel Sabria, Nieves Sopena, Lourdes Mateu, Marian García-Núñez, and Celestino Rey-Joly

Infectious Diseases Unit, Hospital Germans Trias i Pujol of Badalona, Autonomous University of Barcelona, Barcelona, Spain

Copper and silver ionization is a well-recognized disinfection method to control *Legionella* species in water distribution systems in hospitals. These systems may also serve as a potential indoor reservoir for fungi. The prevalence of fungi was significantly lower in ionized than in nonionized water samples from health care facilities. The clinical consequences of this finding require further investigation.

Copper and silver ionization is now a well-recognized disinfection method to control *Legionella* species in water distribution systems in hospitals [1]. The positively charged copper and silver ions form electrostatic bonds with negatively charged sites on bacterial cell walls; this leads to cell lysis and cell death. The specific effect of this system on microorganisms other than *Legionella* species is unknown. However, some authors have demonstrated that these ions are able to penetrate the biofilms in which other bacteria, algae, protozoans, and fungi cohabit with *Legionella* species in water pipes [2, 3].

Water distribution systems in hospitals may act as potential indoor reservoirs for microorganisms other than *Legionella* species, such as *Aspergillus* species and other molds, leading to aerosolization of fungal spores and potential exposure of patients [4, 5]. Some authors recommend that hospitalized patients who are at high risk for infection avoid exposure to hospital water and use sterile water instead [6].

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Reprints or correspondence: Dr. M. L. Pedro-Botet, Infectious Diseases Unit, Hospital Germans Trias i Pujol, Carretera del Canyet s/n, Badalona, Spain (mlpbotet.germanstrias@gencat.net).

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Since a copper and silver ionization system was installed in our hospital in September 1999 for control of environmental *Legionella* species, the number of consultations to the Infectious Diseases department regarding fungal infection has markedly decreased. We hypothesized that ionization of the water supply may have reduced the level fungal colonization of the water distribution system, thereby reducing the number of patients with respiratory colonization or fungal infections in our hospital. The purpose of this study was to investigate, identify, and quantify fungi in ionized and nonionized, hot and cold water samples obtained from potable water distribution systems in different health care centers as the first step to validate this hypothesis.

Only health care centers with recirculating hot water distribution systems were included in the study. Hot and cold water distribution systems at a single health care center were examined separately. When a health care center had >1 independent hot or cold water distribution system, each system was examined separately. Sixteen ionized water distribution systems (14 hot water and 2 cold water systems) from 9 health care centers and 22 nonionized water distribution systems (8 hot water and 14 cold water systems) from 7 health care centers were included in this study. The 16 health care centers were located in 4 different autonomous regions in Spain.

Levels of copper and silver ions were determined from at least 3 samples per ionized circuit, using a photometer for copper (Spectroquant NOVA 60; Merck) and atomic absorption for silver. Environmental sampling was performed during a 1-year period (January 2006 to December 2006). Eight samples were collected from hot water circuits (7 from peripheral points and 1 from the recirculating circuit), and 7 samples were collected from cold water circuits (all from peripheral points). One liter of water was collected 10–30 s after flushing. At the peripheral points, shower and tap heads were dismantled, and the internal surfaces were swabbed. The swab was then put into the collected water sample. The samples were collected in sterile polystyrene bottles containing 1 mL of 3% sodium thiosulfate, and were filtered through sterile 0.45-μm cellulose filters (Millipore) using a filtration pump (Millipore). The filters were placed on Sabouraud glucose agar plates containing 100 mg/L chloramphenicol. Plates were incubated at 25–28°C for $\geqslant$10 days. Colonies that were thought to be likely fungal colonies were identified according to identification tables [7].

For the statistical analysis, results of the fungal investigation of ionized and nonionized water samples and water distribution systems were introduced in a database and were analyzed using the Epi Info Epicalculator, version 5.0 (Centers for Disease Control and Prevention). The concentrations of copper and silver ions were within the target levels (200–400 μg/L and 20–40 μg/L, respectively) in all evaluated circuits.

Fungi were isolated in 161 (56.1%) of 287 water samples, corresponding to 33 (86.8%) of 38 water distribution systems and to 15 (93.7%) of 16 health care centers. As seen in table 1, septated molds were the most frequently isolated fungi, followed by yeasts. The prevalence of fungi was significantly lower in samples of ionized water (36 [28.8%] of 125) than in samples of nonionized water (125 [77.1%] of 162; $P < .001$) in both hot water systems (30.6% vs. 60.9%; $P < .001$) and cold water systems (14.2% vs. 87.7%; $P < .001$). Analysis of different types of fungi showed that septated molds were significantly less prevalent in ionized water samples, compared with nonionized water samples (28 [22.4%] of 125 vs. 97 [59.8%] of 162; $P < .001$) in hot water systems (26 [23.4%] of 111 vs. 31 [48.4%] of 64; $P = .001$) and in cold water systems (2 [14.2%] of 14 vs. 66 [67.3%] of 98; $P < .001$). In particular, this difference remained significant for *Cladosporium* species and *Penicillium* species. Yeasts were significantly less prevalent in ionized water samples, compared with nonionized water samples (7 [5.6%] of 125 vs. 26 [16.04%] of 162; $P = .005$).

Fungi were significantly less prevalent in ionized water distribution systems (11 [68.7%] of 16) than in nonionized systems (22 [100%] of 22; $P = .008$). Significant differences were observed in the recovery of *Cladosporium* species and *Penicillium* species between ionized (11 [68.7%] of 16) and nonionized systems (22 [100%] of 22; $P = .008$).

The results of this study show that the prevalence of fungi was significantly reduced in ionized water samples obtained from health care centers, compared with nonionized water samples. Most of the differences observed were in fungi that are known to cause infection in immunocompromised patients [8], although the differences were more important for uncommon pathogens, such as *Cladosporium* species and *Penicillium* species, than for common pathogens, such as *Aspergillus* species and *Fusarium* species.

To our knowledge, this is the first study to have investigated the effect of copper and silver ionization on fungal colonization of water supplies in health care centers. In 2002, Anaissie et al. [6] conducted a search of the Medline database for studies of waterborne, nosocomial infections caused by microorganisms other than *Legionella* species from 1966 to 2001 and identified 29 molecularly characterized hospital-acquired infections, 3 of which were caused by fungi. Later, a 3-year prospective surveillance study at a hospital involving immunocompromised patients found that opportunistic molds (including *Aspergillus* species) can colonize water distribution systems in hospitals, leading to spore aerosolization in patient-care areas and resulting patient exposure [4]. These authors recommend providing sterile (boiled) water for drinking and sterile sponges for bathing (to avoid aerosolization associated with showering) to high-risk patients to prevent exposure to waterborne molds

Table 1. Recovery of fungi from ionized and nonionized water samples.

Fungus	Hot water samples: Ionized (n = 111)	Hot water samples: Nonionized (n = 64)	Hot water samples: P	Cold water samples: Ionized (n = 14)	Cold water samples: Nonionized (n = 98)	Cold water samples: P	Hot and cold water samples: Ionized (n = 125)	Hot and cold water samples: Nonionized (n = 162)	Hot and cold water samples: P	Total (n = 287)
Zygomycetes										
All	1 (0.9)	1 (1.5)	NS	0	1 (1)	NS	1 (0.8)	2 (1.2)	NS	3 (1)
Absidia species	1 (0.9)	0	NS	0	0	NS	1 (0.8)	0	NS	1 (0.3)
Rhizopus species	0	1 (1.5)	NS	0	1 (1)	NS	0	2 (1.2)	NS	2 (0.6)
Mucor species	0	0	NS	0	0	NS	0	0	NS	0
Septated molds										
All	26 (23.4)	31 (48.4)	.001	2 (14.2)	66 (67.3)	<.001	28 (22.4)	97 (59.8)	<.001	125 (43.5)
Tricoderma species	3 (2.7)	5 (7.8)	NS	0	1 (1)	NS	3 (2.4)	6 (3.7)	NS	9 (3.1)
Alternaria species	3 (2.7)	3 (4.6)	NS	1 (7.1)	8 (8.1)	NS	4 (3.2)	11 (6.7)	NS	15 (5.2)
Cladosporium species	2 (1.8)	6 (9.3)	.02	0	11 (11.2)	NS	2 (1.6)	17 (10.4)	.002	19 (6.6)
Paecilomyces species	6 (5.4)	5 (7.8)	NS	1 (7.1)	1 (1)	NS	2 (1.6)	6 (3.7)	NS	8 (2.7)
Penicillium species	3 (2.7)	9 (14)	.006	0	22 (22.4)	.03	3 (2.4)	31 (19.1)	<.001	34 (11.8)
Fusarium species	2 (1.8)	0	NS	0	4 (4.1)	NS	2 (1.6)	4 (2.4)	NS	6 (2.1)
Aspergillus species	1 (0.9)	2 (3.1)	NS	0	2 (2)	NS	1 (0.8)	4 (2.4)	NS	5 (1.7)
Others	6 (5.4)	1 (1.5)	NS	0	17 (17.3)	NS	6 (4.8)	18 (11.1)	NS	24 (8.3)
Yeasts	7 (6.3)	7 (10.3)	NS	0	19 (19.3)	NS	7 (5.6)	26 (16)	.005	33 (11.4)
Total	34 (30.6)	39 (60.9)	<.001	2 (14.2)	86 (87.7)	<.001	36 (28.8)	125 (77.1)	<.001	161 (56.1)

NOTE. Data are no. (%) of samples, unless otherwise indicated. NS, not statistically significant.

in the hospital setting. Although this recommendation has been criticized by other authors [9], new molecular typing methods [10] and the recommendation in the 2004 latest World Health Organization guidelines that a program be developed to ensure the safety of water intended for human consumption in health care facilities [11] are consistent with the risk assessment of Anaissie et al. [6].

The hypothesis that copper and silver ions may have fungicidal activity and may prevent the development of some waterborne fungal infections in immunocompromised patients is attractive and may be of utmost epidemiologic importance. To our knowledge, there have been no previous reports on the effects of this disinfection system on fungi, although silver has been used topically for the treatment of cutaneous fungal lesions for several years. Moreover, fungal sensitivity to silver seems to be genetically determined and is related to the uptake levels of intracellular silver and its ability to interact with and irreversibly denature key enzyme systems [12]. The ability to penetrate and disrupt biofilms and to destroy *Legionella* species within these biofilms might have a direct or indirect effect on fungi.

Our study demonstrates that copper- and silver-ionized water distribution systems have lower prevalences of fungal colonization, and that the greatest reductions are seen with fungi, such as septate molds and yeasts, that have been related to hospital-acquired infections in severely immunocompromised patients. In the future, more ionized cold water systems should be investigated, because only 2 of these systems were included in our analysis and fungi were observed to be more prevalent in the nonionized cold water systems. However, more data are needed to confirm the fungicidal effectiveness of this method, and further investigations are required before including this method as a preventive measure to protect immunocompromised patients from waterborne fungal infection.

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References

1. Stout JE, Yu VL. Experiences of the first 16 hospitals using copper-silver ionization for *Legionella* control: implications for the evaluation of other disinfection modalities. Infect Control Hosp Epidemiol **2003**; 24:563–8.
2. Liu Z, Stout JE, Boldin M, Rugh J, Diven WF, Yu VL. 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**; 26:138–40.
3. Exner M, Kramer A, Lajoie J, Gebel J, Engelhart S, Hartemann P. Prevention and control of health care–associated waterborne infections in health care facilities. Am J Infect Control **2005**; 33(Suppl 1):S26–40.
4. Anaissie EJ, Stratton ShL, Dignani MC, et al. Pathogenic molds (including *Aspergillus* species) in hospital water distribution systems: a 3-year prospective study and clinical implications for patients with hematologic malignancies. Blood **2003**; 101:2542–6.
5. Warris A, Klaassen CHW, Meis JFG, et al. Molecular epidemiology of *Aspergillus fumigatus* recovered from water, air and patients shows two clusters of genetically distinct strains. J Clin Microbiol **2003**; 41:4101–6.
6. Anaissie EJ, Penzak SR, Dignani MC. The hospital water supply as a source of nosocomial infections: a plea for action. Arch Intern Med **2002**; 162:1483–92.
7. Samson RA, van Reenen-Hoekstra ES, Frisvard JC, Filtenborg O. Introduction to food-borne fungi. 6th ed. Baarn, The Netherlands: Centraalbureau voor Schimmelcultures, **2000**.
8. Walsh TJ, Groll A, Hiemenz J, Fleming R, Roilides E, Anaissie E. Infections due to emerging and uncommon medically important fungal pathogens. Clin Microbiol Infect **2004**; 10(Suppl 1):S48–66.
9. Hunter PR. National disease burden due to waterborne transmission of nosocomial pathogens is substantially overestimated [letter]. Arch Intern Med **2003**; 163:1974.
10. Anaissie E. National disease burden due to waterborne transmission of nosocomial pathogens is substantially overestimated [reply]. Arch Intern Med **2003**; 163:1974.
11. World Health Organization. Guidelines for drinking-water quality. Geneva, Switzerland: World Health Organization, **2004**.
12. Lansdown AB. Silver in health care antimicrobial effects and safety in use. Curr Probl Dermatol **2006**; 33:17–34.