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 ionization 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...
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These studies suggest that measuring the levels of infectious HIV and HIV DNA may be of value to individuals with discordant immunological and virological responses to HAART. Replication of HIV continues even in individuals whose plasma HIV RNA levels have become undetectable as a result of HAART [3], and these patients may also benefit from tests that measure the cellular reservoir of HIV and/or HIV production.

Although measurement of plasma HIV RNA is currently the gold standard for predicting the likelihood of HIV disease progression, it may only be showing us only the tip of the iceberg. Microculture titrations of infectious virus provide information about the levels of replication-competent virus, but the cost of these assays makes it unlikely that they will become available for routine clinical use. The findings that patients without disease progression over many years have lower levels of HIV DNA in peripheral blood cells than do patients with rapid progression, and that the levels of cellular HIV DNA decreases after initiation of HAART, suggest that this parameter may be a useful indicator of HIV disease progression [4]. Measurement of circular forms of HIV DNA as an index of ongoing HIV replication may also prove to be useful for the clinical management of HIV-infected patients [3]. Given the apparent stability of the proviral HIV DNA levels, analysis of this marker (i.e. total HIV DNA minus the circular forms of HIV DNA) may be a useful marker of vaccine efficacy, while measurement of RNA levels will only be useful in the very short period of time between the identification of infection and the initiation of HAART. Recent studies [5] suggest that measurement of levels of peripheral blood cells expressing the gp120 envelope protein of HIV might also be useful for monitoring HIV-infected individuals. Longitudinal studies that compare the cellular reservoir of HIV, plasma HIV RNA, and immunological parameters are urgently needed to determine the best strategies for the management of HIV disease and to elucidate the viral and immunological dynamics that determine clinical end points in HIV infection.

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