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REFERENCES

1. Rupp ME, Fitzgerald T, Puumala S, et al. Prospective, controlled, cross-over trial of alcohol-based hand gel in critical care units. *Infect Control Hosp Epidemiol* 2008;29:8–15.
2. World Health Organization. WHO guidelines on hand hygiene in health care (advanced draft). Geneva: World Health Organization; 2006.
3. Rotter ML. Hand washing and hand disinfection. In: Mayhall CG, ed. *Hospital Epidemiology and Infection Control*. 3rd ed. Philadelphia. Lippincott Williams & Wilkins; 2004:1727–1746.
4. Ayliffe GA, Babb JR, Davies JG, Lilly HA. Hand disinfection: a comparison of various agents in laboratory and ward studies. *J Hosp Infect* 1988;11:226–243.
5. Kramer A, Rudolph P, Kampf G, Pittet D. Limited efficacy of alcohol-based hand gels. *Lancet* 2002;359:1489–1490.
6. Kampf G, Muscatiello M, Hantschel D, Rudolf M. Dermal tolerance and effect on skin hydration of a new ethanol-based hand gel. *J Hosp Infect* 2002;52:297–301.
7. Larson E. A causal link between handwashing and risk of infection? examination of the evidence. *Infect Control* 1988;9:28–36.
8. Kramer A, Bernig T, Kampf G. Clinical double-blind trial on the dermal tolerance and user acceptability of six alcohol-based hand disinfectants for hygienic hand disinfection. *J Hosp Infect* 2002;51:114–120.
9. Harbarth S. Handwashing—the Semmelweis lesson misunderstood? *Clin Infect Dis* 2000;30:990–991.

Not Perfect—Just Among the Best Available: Reply

To the Editor—We thank the authors of the letters for their interest in our study regarding hand hygiene¹, and we share their concern regarding the media attention and potential misinterpretation of the results.^{2–5} From an optimistic viewpoint, the widespread coverage of a study concerning hand hygiene, which would have been unfathomable a few years ago, points to the increasing recognition of the importance of nosocomial infections and infection control. We hope the profession can harness this new interest for the betterment of the field. We regret that the value of the study may have been diminished by the widespread misrepresentation of our conclusions. We have previously released notices^{6,7} to repudiate the perception that this study somehow “contradicts” Centers for Disease Control and Prevention or World Health Organization recommendations.

Many of the specific points raised in the letters to the editor simply reemphasize points we made in the article. We acknowledged that, despite the more than 2-year duration of our study, the low infection rate rendered it underpowered to dem-

onstrate a statistically significant association between hand hygiene and nosocomial infections. We also clearly noted that active surveillance cultures for methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant enterococci (VRE) were not performed, which may have precluded detection of a statistically significant effect on the acquisition of these organisms. Similarly, we noted that the pathogenesis of nosocomial infections is complex, and prevention requires a multifaceted or “bundle” approach. Indeed, we have long supported a multifaceted approach to prevention of nosocomial infections. However, major changes to this approach did not occur during the hand hygiene study, and monitoring of compliance with the bundles did not occur until more recent years.

Without belaboring the details, we respond that most of the studies cited by Mermel and colleagues,³ as well as numerous other reports purported to support the role of hand hygiene in the prevention of nosocomial infections, are even more methodologically flawed than our own study. In general, these studies were not controlled trials and often involved numerous interventions, including active surveillance cultures, isolation practices, environmental disinfection, and patient decolonization. A cautionary note, tempering somewhat unrealistic expectations of hand hygiene in the intensive care unit, has been previously sounded.^{8–10}

To more specifically address the questions raised, we wish to relate that when the various measures of nosocomial infections in our study were combined, a statistically significant association between hand hygiene compliance and infection was not detected. In addition, clustering of infections was not observed. As we noted, coagulase-negative staphylococci were by far the most common organisms recovered from the hands of nurses. *S. aureus* was recovered only once (when gel was not available in the intensive care unit); gram-negative bacilli were recovered from 7.2% of cultures of hand samples when gel was available and from 11.7% of cultures when gel was not available; yeasts were recovered from 2% of cultures when gel was available and were not observed when gel was unavailable. Although not specifically mentioned in our article, the educational program that preceded the introduction of the hand gel into the critical care units explained when and how to use the hand gel.

Several of the letters^{2–4} noted the controversy regarding the efficacy of alcohol-based hand hygiene preparations in relationship to alcohol content and formulation (gel or liquid). The hand gel used in our study contained a blend of 88% wt/wt ethanol and 4.6% wt/wt isopropanol, and the total alcohol content was 68.5% vol/vol or 60.7% wt/wt (written communication, M. Dolan, Gojo Industries, February 2008). The antimicrobial activity of alcohols is derived from their capacity to denature proteins, and they are most potent at concentrations of 60%–80%.^{11,12} At higher concentrations, they are less effective because proteins are not denatured as readily in the

absence of water.^{11,12} In general, higher-chain alcohols are more active than shorter-chain alcohols, and tertiary alcohols are less effective than primary or secondary alcohols. Alcohols have excellent *in vitro* and *in vivo* activity against vegetative bacteria, mycobacteria, a variety of fungi, and some enveloped viruses.^{11,12} The efficacy of hand hygiene preparations is influenced by a number of parameters including the type of alcohol, the concentration of alcohol, the volume used, the contact time, whether the hands are wet, and whether the hands are contaminated with organic debris. A large number of studies have documented the antimicrobial effect of alcohol-based hand rubs.^{11,12}

Contrary to the claim of Widmer and Rotter,⁴ the hand gel used in our study does meet European standard EN 1500 requirements.¹³ Hand hygiene gel formulations and antiseptic or disinfectant applications of alcohols are stringently regulated in the United States by the Food and Drug Administration and the Environmental Protection Agency, and there is some concern that the maximum alcohol content of alcohol-based hand rubs in the United States is capped at 70% vol/vol by fire codes.¹⁴ As noted by Mermel et al.³ and by Maiwald,² liquid formulations of alcohol-based hand rubs have been associated with improved *in vitro* performance compared with gels. To our knowledge, however, to date no clinical data indicate that the liquid formulations are more effective. Recently, a prospective trial in a critical care setting indicated considerably improved hand hygiene compliance when a gel formulation was available, compared with compliance when a liquid formulation was in use.¹⁵ Any increase in potency of the liquid formulation compared with that of the gel might be mitigated by a decrease in hand hygiene compliance.

We appreciate the comments of the authors of the letters acknowledging that our study was well designed and well performed, because data from other prospective, controlled trials concerning the efficacy of hand hygiene are very limited. As noted, some of the finer points of the study regarding the successful conduct of this multimodal performance improvement project were lost on the media. In addition, the media largely ignored information about hand microbial ecology, drug resistance, preservation of hand hygiene compliance with increased workload, and the important effects on hand hygiene of nail length and the wearing of rings.

Unfortunately, in both the professional and the lay press we note a trend toward oversimplification of the pathogenesis and prevention of nosocomial infections. It appears that many people believe that if we would only improve our hand hygiene practices, all of our nosocomial infection problems would be resolved. In this regard, we believe our study sounds a cautionary note. We stand behind the major conclusion of our article: the prevention of nosocomial infection is a multifaceted issue, and hand hygiene is but one part of the equation.¹ As we noted, the lack of association between hand hygiene compliance and nosocomial infection incidence should not be interpreted to mean that hand hygiene is not important.¹ In fact, we believe

actions speak louder than words, and we have recently launched a hospital-wide campaign to improve adherence to hand hygiene recommendations. In the Discussion section of our article, we did not neglect to state the inherent limitations of our study, which were, to a large extent, inherent in a single-center study with limited financial support.¹ We hope governmental funding agencies will note the need to support adequately powered, multicenter, cluster-randomized studies to answer the important questions that exist in our field. Although our study was not perfect, which we pointed out in the Discussion section of the article¹ and which was again emphasized by the various letters to the editor,²⁻⁵ it is among the best studies available on the subject.

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Potential conflicts of interest. M.E.R. reports receiving a stipend from Gojo Industries to cover travel expenses associated with presentation of the study¹ at the 14th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America in 2004. Gojo Industries approved the study but did not have a role in study design, data acquisition, data analysis, or manuscript preparation.

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REFERENCES

- Rupp M, Fitzgerald T, Puumala S, et al. Prospective, controlled, crossover trial of alcohol-based hand gel in critical care units. *Infect Control Hosp Epidemiol* 2008;29:8–15.
- Maiwald M. Alcohol-based hand hygiene and nosocomial infection rates. *Infect Control Hosp Epidemiol* 2008;29:579–580.
- Mermel LA, Boyce JM, Voss A, Allegranzi B, Pittet D. Trial of alcohol-based hand gel in critical care units. *Infect Control Hosp Epidemiol* 2008; 29:577–579.
- Widmer AF, Rotter M. Effectiveness of alcohol-based hand hygiene gels in reducing nosocomial infection rates. *Infect Control Hosp Epidemiol* 2008;29:576.
- McGuckin M, Waterman R. “Cannot detect a change” is not the same as “there is not a change.” *Infect Control Hosp Epidemiol* 2008;29:576–577.
- Study demonstrates sustained infection prevention takes a comprehensive strategy. Available at: http://www.shea-online.org/Assets/files/SHEA_News_-_February_2008.pdf. Accessed May 9, 2008.
- Leading expert disputes interpretation of hand hygiene survey at University of Nebraska Medical Center. Available at: <http://www.shea-online.org/Assets/files/handgelreleaseFinal.pdf>. Accessed May 9, 2008.

8. Sebillé V, Chevret S, Valleron AJ. Modeling the spread of resistant nosocomial pathogens in an intensive care unit. *Infect Control Hosp Epidemiol* 1997;18:84–92.
9. Silvestri L, Petros AJ, Sarginson RE, de la Cal MA, Murray AE, vanSaene HKF. Handwashing in the intensive care unit: a big measure with modest effect. *J Hosp Infect* 2005;59:172–179.
10. Eckmanns T, Schwab F, Bessert J, et al. Hand rub consumption and hand hygiene compliance are not indicators of pathogen transmission in intensive care units. *J Hosp Infect* 2006;63:406–411.
11. Ali Y, Dolan MJ, Fendler EJ, Larson EL. Alcohols. In: Block SS, ed. *Disinfection, Sterilization, and Preservation*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2001:229–253.
12. World Health Organization. WHO guidelines on hand hygiene in health care (advanced draft). Geneva: World Health Organization, 2006. Available at: http://www.who.int/patientsafety/information_centre.
13. Test Report B 10988ae, Purell Hygienic Hand Rub Gel, EN 1500-Hygienic Handrub, May 19, 2006, HygCen International, Bischofshofen, Austria. Copies available from Gojo Industries.
14. International Code Council. Chapter 34. Flammable and Combustible Liquids. In: 2006 International Fire Code. Falls Church, VA: International Code Council; 2006:305–343.
15. Traore O, Hugonnet S, Lubbe J, Griffiths W, Pittet D. Liquid versus gel formulation: a prospective intervention study. *Critical Care* 2007;11:R52.