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Alcohol-Based Hand Hygiene and Nosocomial Infection Rates

To the Editor—I read with great interest the study by Rupp et al., describing a crossover trial of alcohol hand gel use in critical care units.¹ I was surprised that the significant increase in compliance observed in this study did not appear to be associated with a decrease in nosocomial infection rates. I am concerned that superficial readers may conclude that alcohol-based hand hygiene does not provide a benefit in the healthcare environment compared with hand washing.

The causal role of microorganisms on hands in the pathogenesis of nosocomial infections is extremely well established.² However, the interplay between various factors involved in clinical practice (eg, availability of appropriate hand hygiene agents, correctness of their use, compliance with hand hygiene recommendations) and the outcome in terms of nosocomial infection rates is highly complex and multifactorial. Apart from the question of whether the study by Rupp et al.¹ had patient numbers sufficient in size and observation periods sufficient in length to demonstrate a difference, the authors apparently have not considered one factor that I think is important: the antimicrobial activity of a product used for hand hygiene.

The hand gel chosen by the authors has an ethanol content of only 62%. To determine the implications of this, it is necessary to look at some facts about alcohol-based hand hygiene. First, the published useful range of antimicrobial activity of alcohols is about 60%–80% for most microorganisms, with ethanol the least potent, followed by isopropanol and *n*-propanol.^{2,3} The triclosan component (0.3%) of the gel used in the study has very negligible immediate antimicrobial activity.⁴ With an ethanol content of 62%, this gel is at the very low end of the published range of activity. In addition, gel formulations often have considerably less antimicrobial activity

(about 10-fold; ie, 1 log less) than do liquid alcohol hand rubs.⁵ This has 2 implications: the antimicrobial activity is very low to start with, and it is further compromised by the gel formulation. The consequences are that there is no safety margin against handborne microbial contamination and that minor amounts of other liquids on the hands (eg, sweat, water) will render the agent inactive by dilution. Such issues have been addressed by the European EN testing standards. Hand rubs that pass EN 1500 typically produce a reduction in microbial contamination of about 4 log (about 10,000-fold) on hands within 30 seconds.^{3,5} Very few gels pass EN 1500, and the ones that do typically contain 80% or more ethanol.⁶ The World Health Organization’s standardized hand hygiene solutions contain either 75% isopropanol or 80% ethanol, and each of these formulations pass EN 1500.²

Why is the antimicrobial activity of a hand hygiene agent important? First, it is beyond doubt that microorganisms on hands are responsible for nosocomial infections and that it is the killing or elimination of microorganisms on hands that prevents these infections²; it is not the act of performing hand hygiene per se. Second, although the relationship is not a formal mathematical one, there is a quantitative dose-response relationship between microorganisms eliminated from hands and infections prevented.⁷ Third, there is no established “threshold” of microbial elimination beyond which hands can be considered “safe” from the risk of transmitting infections, such that lesser microbial reduction may be considered equally good. Fourth, with regard to user acceptability and compliance, it is important to bear in mind that antimicrobial activity per se has no negative impact on either; instead, user acceptability and compliance are influenced by overall hand rub composition and emollient additives.⁸ As a consequence, it is necessary to choose hand hygiene products that have both significant antimicrobial activity and optimized composition for the users.

Finally, we can learn from history. It is now 160 years since Semmelweis made his seminal observations.⁹ He showed clearly that soap-based handwashing—which is now known to cause only a minimal reduction in the number of microbial pathogens on hands—did not have the same beneficial effect in preventing puerperal sepsis as did hand treatment with chlorinated lime, which is now known to kill microorganisms very effectively. In essence, this study by Rupp et al.¹ appears to underline the observation by Semmelweis that very potent antimicrobial agents are most beneficial in reducing the incidence of nosocomial infections. Even high compliance with products that have limited activity may not sufficiently decrease the rate of nosocomial infections.

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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