CORRESPONDENCE

Targeted Decolonization to Prevent ICU Infections

TO THE EDITOR: Huang and colleagues (June 13 issue)[1] report that universal decolonization was more effective than targeted decolonization or screening and isolation in reducing rates of methicillin-resistant *Staphylococcus aureus* (MRSA) clinical isolates. However, the study protocol indicates that patients with a history of MRSA infection who underwent universal decolonization were still isolated; of the patients undergoing universal decolonization, 10.6% had a MRSA history during the observation period and 3.7% had such a history during the intervention period. This suggests that one third of patients with positive tests for MRSA in this group may have been isolated and that universal decolonization meant more than simply decolonization. The protocol describes extensive training and regular input in hospitals that were randomly assigned to targeted or universal decolonization, but the facilities that were assigned to screening and isolation (standard of care) did not appear to receive this training and input. It is conceivable that training led to improved infection control and reduced infection rates that were independent of the study-specific interventions. The protocol indicates that resistance to mupirocin or chlorhexidine was a secondary outcome. These data are not reported but are required to weigh the gains from universal decolonization against the emergence of resistance.

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TO THE EDITOR: Huang et al. state that "universal decolonization . . . obviated the need for surveillance testing," a conclusion that seems to be based on a lack of change in the culture rate for MRSA in the screening-and-isolation group. However, the lack of change may have been because interventions were applied to intensive care units (ICUs) in which a screening-and-isolation program had been in place for more than 30 months. This program resulted in a 39% decline in central-catheter–associated bloodstream infections and a 54% decrease in ventilator-associated pneumonias.[1] The Department of Veterans Affairs observed a similar effect. After an initial 62% decline in health care–associated MRSA infections during the first 33 months of the Veterans Affairs MRSA Prevention Initiative,[2] rates continued to decline in the ICUs during the next 24 months. However, the difference was not significant, suggesting the effect was becoming asymptotic.[3] The effect of screening and isolation in the study by Huang et al. may have been better assessed in

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ICUs in which the intervention was novel. We agree with the authors that "hospitals that have not fully implemented a strategy of screening and isolation may derive additional benefit from this intervention."

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TO THE EDITOR: Several clarifications would be useful in the study by Huang et al. with respect to targeted versus universal decolonization of patients in the ICU. Why would one expect that hospitals already using MRSA screening and isolation (Hospital Corporation of America and Illinois hospitals) would have decreased MRSA culture rates when there was no new or additional intervention implemented at these hospitals?[1,2] MRSA culture rather than polymerase-chain-reaction (PCR) assay resulted in MRSA-positive patients remaining out of isolation in the ICU, often until discharge. Why did the intervention not reduce MRSA bloodstream infections? The rate of "MRSA-positive clinical cultures," the primary outcome, is never defined; distribution of MRSA cultures according to site would be useful. The intervention reduced the rate of bloodstream infections caused by "skin commensal organisms" (probably mostly coagulase-negative staphylococci, although the data are not shown). Subtracting the bloodstream infections caused by skin commensal organisms from those caused by "any pathogen" appears to result in a nonsignificant reduction in bloodstream infections caused by the remaining pathogens. The investigators should have evaluated resistance to mupirocin and chlorhexidine, and such resistance should remain an important concern and caution for those contemplating universal decolonization of patients in the ICU.[3,4]

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TO THE EDITOR: Huang et al. state that universal decolonization with the use of chlorhexidine is more effective than other strategies for MRSA decolonization, screening, and isolation in reducing rates of MRSA clinical isolates and bloodstream infections from any pathogen. The latter was mainly caused by a reduction in the rate of bloodstream infections caused by coagulase-negative staphylococcus, but the rate of MRSA bloodstream infections did not change significantly. Even though the investigators used the criteria of the Centers for Disease Control and Prevention for skin commensal organisms causing bacteremia, it is not clear which specimen collection technique was used (e.g., central vs. peripheral-blood cultures).[1] Therefore, a reduction in the contamination rate for coagulase-negative staphylococcus blood cultures rather than in the rate of true bacteremia cannot be ruled out. The authors do not provide data on the minimum inhibitory concentrations for chlorhexidine in cultures of organisms obtained from patients before

and after bathing with chlorhexidine-impregnated cloths. This is of particular importance, since in one study, the continuous use of chlorhexidine increased the rate of chlorhexidine-resistant MRSA isolates by up to 47%.[2] We conclude that on the basis of the vague collection techniques for blood cultures, the absent effect on MRSA bloodstream infections, and the threat of chlorhexidine resistance, great caution should be exercised in transferring the study's results into clinical practice.

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TO THE EDITOR: In their editorial discussing inpatient MRSA screening and decolonization, Edmond and Wenzel[1] question the wisdom of targeted detection and isolation of carbapenem-resistant Enterobacteriaceae (CRE). We disagree. The decision to pursue "vertical" or "horizontal" interventions versus multidrug-resistant organisms (MDROs) should be made while considering the pathogens, their prevalence, and the resources available to implement control measures. Unlike MRSA, CRE has no established decolonization protocol; the effect of selective digestive decontamination on antimicrobial resistance has been understudied. A horizontal intervention in a population in which CRE must be considered would therefore require placing every patient in contact isolation, a costly proposition unlikely to be met with high compliance. Moreover, targeted interventions to prevent the spread of a sporadic MDRO have been shown to be effective.[2] In the Israeli CRE outbreak, a vertical national intervention, which was aimed at detecting and isolating carriers, was necessary to contain spread.[3] The Israeli approach has since been incorporated into international guidelines.[4,5] Horizontal and vertical approaches are not mutually exclusive. A comprehensive strategy of MDRO prevention should use both approaches, with periodic evaluation of target attainment.

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THE AUTHORS REPLY: Cartwright et al. inquire whether training and routine input produced unanticipated changes that reduced infection. This is unlikely. First, training was limited to intervention implementation (e.g., how to warm and apply cloths). Second, we monitored and restricted new practices that would conflict with the trial. Third, all study groups received routine input through monthly coaching calls. Fourth, Hospital Corporation of America continued its usual campaigns in all hospitals, emphasizing adherence to best-practice guidelines.

We agree with Evans et al. and Jarvis that our study provides no information about the absolute effect of screening and isolation. We published evidence suggesting that a strategy of screening and isolation reduces infection.[1] Regardless of whether such a strategy produces benefit, the finding that universal decolonization produced sizable and significant incremental reductions in the MRSA burden and in rates of all-cause bloodstream infections suggests that

universal decolonization is the more effective strategy. Furthermore, the use of PCR would be unlikely to change the study's findings. The use of chromogenic agar provided next-day results in our trial. Recent evidence suggests that the additional isolation time gained by PCR is insufficient to reduce transmission or infection.[2]

With regard to the comments by Jarvis and Krause et al.: our study had the power to determine a relative reduction of 60% in the rate of MRSA bloodstream infections with universal decolonization. Thus, it is not surprising that the observed 28% reduction was not statistically significant. However, the direction of this reduction is similar to the statistically significant change in MRSA clinical cultures (our primary outcome) and all-cause bloodstream infections. Therefore, our finding is consistent with a positive effect on MRSA bloodstream infections. Certainly, the lack of a significant difference in this trial is not evidence against an effect.

Furthermore, the larger proportion of bloodstream infections caused by coagulase-negative staphylococcus and *Staphylococcus aureus* is consistent with the usual distribution of bloodstream pathogens. We did not test the effect on gram-positive, gram-negative, and fungal pathogens, since such testing was not prespecified in our analysis plan. However, the reduction in these types of pathogens in the group receiving universal decolonization appears to be proportional to their prevalence.

As we state in our article and as many of the correspondents note, it will be important to monitor the effect of universal decolonization on the emergence of resistance to chlorhexidine and mupirocin.

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THE EDITORIALISTS REPLY: We agree with Schwaber et al. that vertical infection-control interventions, such as active detection and isolation, are useful in outbreak settings. However, for control of endemic pathogens, we conclude that horizontal interventions should be the cornerstone of prevention. Given the high direct and opportunity costs associated with vertical strategies, basic horizontal practices, such as hand hygiene, may not be sufficiently emphasized. Lastly, we agree that horizontal and vertical interventions are not mutually exclusive. However, the key question remains: given an optimally functioning horizontal program (i.e., near perfect compliance with hand hygiene and chlorhexidine bathing), what is the incremental benefit of a superimposed vertical strategy?

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Treatment of Acute Promyelocytic Leukemia

TO THE EDITOR: Lo-Coco et al. (July 11 issue)[1] report that a combination of all-*trans* retinoic acid (ATRA) and arsenic trioxide as an induction and consolidation therapy was not inferior and was possibly superior to ATRA plus chemotherapy in patients with low-to-intermediate-risk acute promyelocytic leukemia (APL).[1] It is notable that the advantage of ATRA plus arsenic trioxide therapy was mainly its lower mortality from toxicity. We assume that the advantage of the less