Chlorhexidine Does Not Select for Resistance in *Staphylococcus aureus* Isolates in a Community Setting

To the Editor—Chlorhexidine gluconate (CHG) is used in decolonization protocols to prevent invasive *Staphylococcus aureus* disease in hospital and community settings.[1,2] Earlier reports have described CHG-resistant *S. aureus* in hospitals, yet evidence of this trend in the community is lacking.[3,4]

A cluster-randomized, double-blind controlled trial evaluating the effectiveness of 2% CHG body cloths (Sage Products) versus control cloths (Comfort Bath [CB] nonmedicated cleaning cloths; Sage Products) in reducing the incidence of skin and soft-tissue infection (SSTI) was performed in a cohort of military recruits.[5] Subjects used 2 cloths to cleanse their body 3 times per week. Nasal and axillary body sites were screened for *S. aureus* colonization at baseline and every 2 weeks thereafter during 6 weeks of training. Although CHG did not reduce the incidence of SSTI, it did decrease incident *S. aureus* colonization.

The substudy presented here evaluated the incidence of CHG-resistant *S. aureus* colonization among these recruits after repeated exposure. Among subjects assigned to the CHG group, those that were persistently colonized (ie, had results positive for *S. aureus* in nares and/or axilla at baseline and at each biweekly visit) and reported using greater than or equal to 50% of cloths met criteria for evaluation and had each isolate assessed for CHG resistance. The same criteria were used for selection of subjects assigned to the CB group. A random subset of recruits were selected from among subjects in the CB group who met the criteria, and the baseline and last positive biweekly isolates were assessed for CHG resistance.

CHG minimum inhibitory concentration (MIC) was determined using the agar dilution method and incorporated the use of a 3-mm Steers Replicator.[6] An ATCC #29213 *S. aureus*–positive control with a CHG MIC of 2 μg/mL was used to ensure an expected range of MICs.

No Clinical Laboratory Standards Institute MIC breakpoints exist for CHG. Although correlation of MIC with clinical outcome is unclear, several studies suggest that CHG MICs can be used as reliable indicators of trends toward decreasing biocide susceptibility.[7] Furthermore, the genes *qacA/B* and *smr* encode for drug efflux proteins that confer *S. aureus* resistance to CHG. Correlation of an elevated MIC ($\geq$4 μg/mL) with these genes has been demonstrated.[8] Polymerase chain reaction for *qacA/B* and *smr* was performed in duplicate (with positive and negative controls in each run) for isolates with increased CHG MIC as well as for a sample of other isolates from the CHG and CB groups.

Of the 781 subjects in the CHG group, 43 (5.5%) met the criteria for evaluation; all 160 isolates from these subjects (3–6 isolates per subject) were evaluated for CHG resistance. Of the 781 subjects in the CB group, 58 (7.4%) met the criteria for evaluation. A random sample of 20 of these subjects were selected, and 48 isolates from these subjects were analyzed. Of the 160 isolates from the CHG group that were tested, 25 were methicillin-resistant *S. aureus* (MRSA) and 135 were methicillin-susceptible *S. aureus* (MSSA).

Among the 48 *S. aureus* isolates obtained from 20 subjects in the CB group, none exhibited CHG MIC greater than or equal to 4 μg/mL (46 isolates [96%] had an MIC of 2 μg/mL, and 2 isolates [4%] had an MIC of 1 μg/mL). Of the 10 isolates tested for *qacA/B* and *smr*, only 1 MSSA isolate was positive for *smr*.

In the CHG group, a total of 6 isolates (3.8%) exhibited a CHG MIC of 4 μg/mL, all of which isolates were MRSA (Table 1). Two of these isolates, from 2 different subjects, were found at baseline. During the intervention, the remaining 4 isolates were again obtained from these same 2 subjects. The prevalence of CHG resistance was 4.8% (95% confidence interval, 0.57%–15.81%; 2 of 43 subjects), and no incident resistance was identified. The results of molecular analysis for *qacA/B* and *smr* were negative for the 6 isolates with an MIC of 4 μg/mL as well as for an additional sample of 24 isolates from the CHG group.

Among subjects in both the CHG and CB groups combined who were found to be colonized in both the nares and axilla

TABLE 1. Chlorhexidine Gluconate (CHG) Susceptibility of *Staphylococcus aureus* Isolates from the CHG Group

Period	No. of isolates tested	No. of isolates tested, by site		No. of isolates tested, by susceptibility to methicillin		Proportion (%) of CHG-resistant isolates[a]		
		Nares	Axilla	MSSA	MRSA	MSSA	MRSA	Total
Baseline	53	42	11	45	8	0	2/53 (3.8)	2 (3.8)
Intervention	107	82	25	90	17	0	4/107 (3.7)	4 (3.7)
Total	160	124	36	135	25	0	6/160 (3.8)	6 (3.8)

NOTE. A total of 160 isolates from 43 subjects were tested. MIC, minimum inhibitory concentration; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*.
[a] CHG resistance was defined as a minimum inhibitory concentration greater than or equal to 4 μg/mL.

at the same visit ($n = 39$), we found general MIC concordance (36 of 39 subjects had isolates with the same MIC value, 2 subjects had discordant pairs with MICs of 1 vs 2 μg/mL, and 1 subject had discordant pairs with MICs of 2 vs 4 μg/mL). The repeated application of CHG to S. aureus strains colonizing military recruits did not select for CHG resistance.

Two hospital-based studies found similar results and reported that no CHG-resistant S. aureus isolates were identified after 5- and 7-day treatment courses of daily washes.[9,10] However, Wang et al[3] identified an increase in the incidence of CHG-resistant MRSA (MIC $\geq$4 μg/mL) over a 20-year period during which a routine in-hospital CHG hand hygiene program was implemented (the percentage of MRSA isolates with resistance to CHG increased from 1.7% to 46.7%).

Differences in the incidence of CHG-resistant strains in the hospital versus community setting may be a reflection of the S. aureus isolates evaluated. In our community setting, we evaluated predominantly MSSA isolates colonizing recruits, whereas Wang et al[3] described MRSA isolates associated with blood stream infections in inpatients. Additional studies should investigate potential variability in CHG susceptibility among different strains of S. aureus (MSSA vs MRSA, pulsed-field type, colonizing vs infecting, and hospital- vs community-acquired strains).

Our study has several limitations. CHG was used 3 times per week, which differs from the daily application more commonly seen in hospital settings. Adherence to CHG cloths was self-reported, and only 25 (23%) of the 107 isolates that colonized recruits after enrollment day were isolated from the axilla and therefore directly exposed to CHG.

We identified few prevalent and no incident CHG-resistant S. aureus strains in a military recruit setting despite repeated exposure to CHG over time. These data support the safety of CHG use as part of a community-based decolonization and SSTI-prevention program.

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Retrospective Analysis of Culture-Positive Peripherally Inserted Central Catheter Infections at an Academic Medical Center

To the Editor—Long-term intravenous (IV) access is often necessary for the administration of medication in the form of antibiotics, total parental nutrition (TPN), and chemotherapy. The trend in long-term IV access has been shifting toward the use of peripherally inserted central catheters (PICCs) instead of surgically placed catheters. PICCs are inserted without the use of general anesthesia and with a lower risk of hemothorax or pneumothorax. Although the convenience of insertion is an advantage, published studies have described various complications such as infection, phlebitis, thrombosis, catheter fracture, and catheter malposition. The intent of this retrospective pilot study was to identify potential modifiable risks associated with culture-documented PICC infections.

The current literature reports no difference in infection rates between central venous catheters and PICCs in hospitalized patients. However, the average life of a PICC in the study was only 11.3 days.[1] The quoted infection rate for PICCs in all types of patients is reported as approximately 7%.[2]

The Ohio State University (OSU) Wexner Medical Center (OSUWMC) is a 980-bed tertiary-care center in Columbus, Ohio. OSUWMC includes the James Cancer Hospital, an active transplantation program, and a level-1 trauma center. The center has an average of 45,000 admissions annually. The OSUWMC PICC team comprises specifically trained registered nurses (RNs) who are board-certified in vascular access.

A query of the OSUWMC Information Warehouse (IW) database was performed to identify positive culture results for samples collected from all intravenous catheters, including PICCs, during the period July 1, 2008, to June 30, 2009. The cases identified in this search were then screened to evaluate whether the infection was a true PICC infection. Infection was defined as (1) a positive PICC blood culture result and a negative peripheral blood culture result; (2) a time differential between a positive PICC blood culture result and a positive peripheral blood culture result, with a positive PICC blood culture result occurring first; or (3) a positive PICC or unrecorded site blood culture result and a positive catheter tip culture result (>15 colony forming units).[3] Clinical patient data were collected and descriptively analyzed for possible risk factors. The OSU Office of Responsible Research Practices Institutional Review Board approved this study.

The search of the IW database identified 126 culture results as indicating possible catheter infections. Results for prisoners were excluded. After screening, 20 PICC infections were identified in 18 evaluable patients. Eleven patients were female. Three (15%) of 20 of the PICCs involved were placed at an outside facility, the RN PICC team at OSUWMC placed 15 PICCs (75%), and the interventional radiology team placed 2 (10%). Three (17%) of 18 patients had active malignancies (Epstein-Barr virus [EBV]–associated Burkitt's lymphoma, appendiceal carcinoma, and leiomyosarcoma). The patient with EBV-associated Burkitt's lymphoma was also HIV positive.

The average period from PICC placement until time of infection was 50 days (median, 33 days). In 15 (75%) of the 20 cases we evaluated, patients had been discharged from the hospital with a PICC in place when the infection occurred. A urinary catheter was present in 13 patients (65%) during their hospital stay. Four patients (20%) were on a ventilator when their infection occurred, and 4 PICC infections occurred in 3 patients (19%) who were receiving active chemotherapeutic agents. In addition, 2 other infected patients (10%), 1 who had multiple sclerosis and 1 who had Castleman disease, were treated with immunosuppressive agents including cyclophosphamide, prednisone, intravenous immunoglobulin, rituxan, and methylprednisolone. Eight (40%) of the 20 infections occurred in patients who were receiving TPN. The most common bacterial species isolated was coagulase-negative *Staphylococcus* species, followed by other gram-positive organisms: *Enterococcus* species and *Staphylococcus aureus*.

During a 1-year retrospective review, 20 cases of culture-positive PICC infection were identified at a large academic medical center. In this limited data set, the majority of patients who had PICC infections either had a PICC but were no longer in the hospital or had a urinary catheter in place when their infection developed. About one-third of infections occurred in patients receiving TPN; surprisingly, this is a lower rate than observed in those who were out of the hospital or who had a urinary catheter. TPN has historically been identified as a risk factor for PICC-related infections. In a study by Marra et al[4] of 47 patients receiving long-term TPN, 38 (80.9%) of patients developed a catheter-related blood-