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Major Article

Successful control of a methicillin-resistant *Staphylococcus aureus* outbreak in a burn intensive care unit by addition of universal decolonization with intranasal mupirocin to basic infection prevention measures

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Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) is frequently implicated in health care–associated outbreaks in burn intensive care units, incurring substantial morbidity and mortality to these high-risk patients and excess costs to health care systems.

Methods: MRSA health care–associated infections (HAIs) were noted before and after the implementation of basic infection prevention measures and the subsequent implementation of universal decolonization with intranasal mupirocin. Pulsed-field gel electrophoresis was used to determine the relatedness of clinical isolates. A case-control study was conducted to characterize the risk factors for MRSA HAIs.

Results: Basic interventions failed to decrease the rate of MRSA HAIs, although compliance with these interventions was high throughout the study. MRSA HAIs decreased from 8.53 HAIs per 1,000 patient days before the implementation of intranasal mupirocin to 3.61 HAIs per 1,000 patient days after the implementation of intranasal mupirocin ($P = .033$). Pulsed-field gel electrophoresis disclosed 10 unique clones with no large clusters. The case-control study revealed a significant association between MRSA HAIs and lengths of stay, body surface area burned, intubation, pressor requirement, leukocytosis, lactic acidosis, development of pneumonia, MRSA colonization, and death.

Conclusions: Basic environmental and behavioral interventions fell short of controlling a low-count, sporadic, and multiclonal MRSA outbreak in the burn intensive care unit of a tertiary medical center. However, the added implementation of universal decolonization with intranasal mupirocin was effective. Burn victims with greater disease severity were at higher risk for MRSA HAIs.

Burns represent a major challenge to infection prevention. Breakdown of the skin barrier and the impact on the innate and acquired immune systems predispose patients with burns to infectious complications. Health care–associated infections (HAIs) originating from endogenous or exogenous sources are a feared complication of burn injury affecting 7% of patients, with mortality rates of up to 33% in 1 large retrospective study.[1] Several outbreaks of multidrug-resistant organisms have been described in burn unit settings, with many of these owing to methicillin-resistant *Staphylococcus aureus* (MRSA).[2] MRSA is the leading cause of invasive infections, accounting for >50% of the infections in burn patients.[3] Prolonged hospitalization, complications such as pneumonia or graft loss, and high mortality rates are associated with MRSA.[4-6]

Between 2014 and 2015, the standard infection ratio of laboratory-identified (LabID) MRSA bacteremias in our hospital increased

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from 0.797 (25 actual of 31.35 predicted) to 1.84 (44 actual of 23.9 predicted).[7,8] Our burn intensive care unit (BICU) accounted for 11 of the 44 events in 2015, which was the basis for evaluating the MRSA HAIs for this location. We report the impact of prevention measures subsequently introduced in the BICU to successfully reduce and prevent these infections.

METHODS

Located in an 885-bed tertiary care university hospital, our BICU has 8 beds in private rooms, with an average daily census of 5 patients and approximately 300 admissions annually (Fig 1). At any given time, the unit is staffed with 3-4 nurses, 2 physicians, 3 physician's assistants, 1 nursing assistant, 1 wound care specialist, 1 respiratory therapist, 1 physical therapist, and 1 occupational therapist.

BICU MRSA HAIs were followed from May 2016-April 2018. We implemented a combination of basic and intensive infection prevention interventions (Fig 2). Basic interventions included: (1) improvement of hand hygiene adherence, (2) improved cleaning of patient rooms by environmental services, with spot checks to monitor for adherence using the adenosine triphosphate cleaning verification system and fluorescent tagging, (3) reorganization of the hydrotherapy room (ie, where burn victims undergo shower therapy to aid wound healing by the removal of skin debris) and intensification of the cleaning protocol for this room and its equipment by environmental services (eg, re-engineering the ventilation system of the room, relocating a mechanical ventilator to a designated storage area, and replacing curtains immediately after a MRSA-colonized patient occupied the room or at least weekly), (4) re-implementation of targeted contact isolation (ie, gowns and gloves) for patients known to be MRSA-colonized, previously not required in our hospital, (5) staff education and training, and (6) development and implementation of a BICU infection prevention policy, previously not in place.

Intensive interventions included universal decolonization with 2% intranasal mupirocin in polyethylene glycol twice daily for 5 days, as well as the active surveillance of nasal colonization by MRSA for all BICU admissions. Active surveillance was already in place prior to the study period. Universal decolonization was implemented by May 2017. All other interventions were fully implemented by November 2016.

Discarded blood, tracheal, and bronchial cultures positive for MRSA were retrieved. These samples had been collected in the BICU based on clinical suspicion of HAIs, as defined by the National Healthcare Safety Network. Pulsed-field gel electrophoresis (PFGE) was performed after digestion of total MRSA DNA with the restriction endonuclease Sma1. DNA fragments were fractionated alongside known standards in a 1% agarose gel for 20 hours at a voltage of 6 volts per cm, an initial switch time of 5 seconds, and a final switch time of 40 seconds. Sequences were aligned and their relatedness (defining clonality as >90%) determined using BioNumerics version 7.6 (Applied Maths, Sint-Martens-Latem, Belgium) cluster analysis with Dice's coefficient (0.5% optimization and 1% position tolerance) and converted into a dendrogram using the unweighted pair group method with arithmetic mean algorithm.

MRSA HAI rates pre- and postuniversal decolonization, expressed as HAIs per 1,000 patient days, were compared using the lower-tailed z test for 2 proportions. Various characteristics of patients with MRSA HAIs were compared to controls using a case-to-control ratio of 1:2, matched by month of the study period. The χ^2 test of independence was used for categorical variables and the 2-tailed Student t test for continuous variables. Univariate odds ratios were derived to identify potential drivers of MRSA HAIs. The alpha level was set at 0.05 for all statistical tests.

Cost savings pre- and postmupirocin for LabID MRSA bacteremia events were estimated using institutional diagnosis-related group rates from fiscal year 2017 (July 2016-June 2017).

RESULTS

Fifteen cases of MRSA (ie, 8 blood, 3 tracheal, and 4 bronchial) were identified during a span of 1,758 patient days between May 2016, and implementation of universal decolonization in May 2017

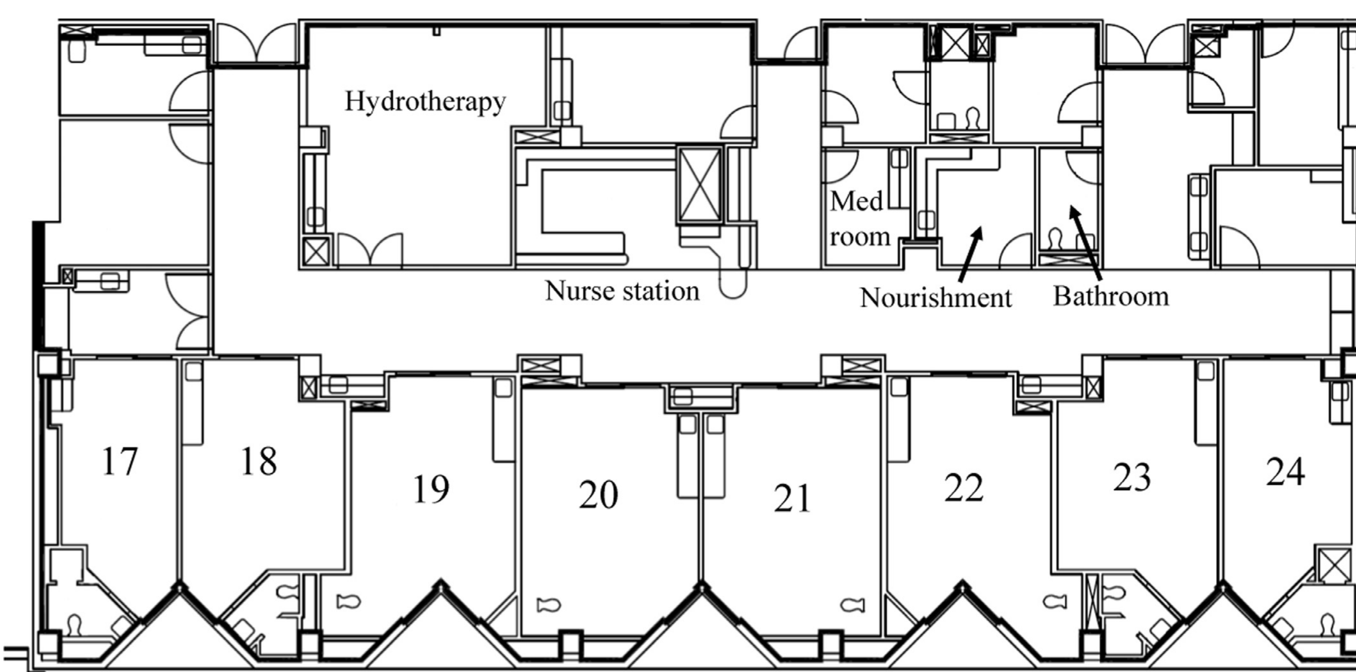

Fig 1. Floor plan of the burn intensive care unit. *Med*, medication.

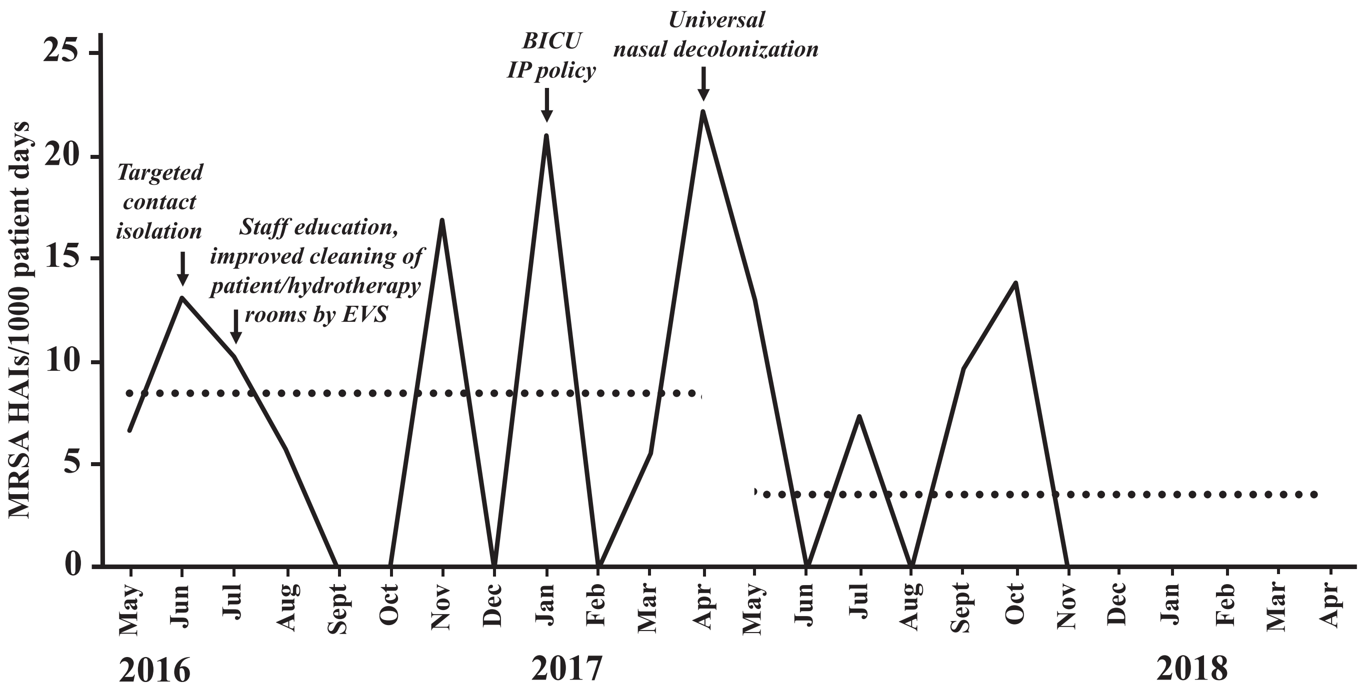

Fig 2. Monthly MRSA HAI rates (eg, number of HAIs divided by patient days from May 2016) are denoted by solid lines. Cumulative infection rates of the pre- and postuniversal decolonization periods (eg, total number of HAIs divided by total patient days from May 2016-April 2017) are denoted by dotted lines. The various interventions are presented by month of implementation. *BICU*, burn intensive care unit; *EVS*, environmental services; *HAI*, health care–associated infection; *IP*, infection prevention; *MRSA*, methicillin-resistant *Staphylococcus aureus*.

(8.53 HAIs per 1,000 patient days). Six cases of MRSA (ie, 2 blood, 3 tracheal, and 1 bronchial) were identified during a span of 1,662 patient days between May 2017 and April 2018 (3.61 HAIs per 1,000 patient days), indicating a significant decrease of 58% ($P = .033$) (Fig 2). The rate of MRSA HAIs did not significantly differ after the complete adoption of basic infection prevention interventions by November 2016. A total of 8 cases were noted during a span of 1,042 patient days between May 2016 and November 2016 (7.68 HAIs per 1,000 patient days), whereas 7 cases were noted during a span of 716 patient days between December 2016 and April 2017 (9.78 HAIs per 1,000 patient days; $P = .32$). Compliance with the basic infection prevention methods was excellent throughout the entire study period (eg, 96.8 ± 3.9% for hand hygiene and 99.1 ± 3.1% for contact isolation), and no significant differences between compliance pre- and postbasic intervention or pre- and postuniversal decolonization were noted (data not shown). Among cases, nasal colonization with MRSA on admission was similar before (20%) and after (33.3%, $P = .52$) the implementation of universal decolonization.

PFGE revealed 10 unique clones with 3 clusters (Fig 3). Of note, 3 of the samples were not available for analysis. In cluster C, 3 cases of MRSA occurred during April 2017, with 2 of them in neighboring rooms. In cluster A, 2 infections occurred during May 2017, but not in neighboring rooms. In cluster B, both infections occurred during January 2017 in neighboring rooms. With 1 exception (ie, room 22 in cluster A), no 2 patients occupying the same room at different points in time were infected by the same strain of MRSA.

The case-control study revealed a significant association between MRSA cases and lengths of stay in the hospital and in the BICU, significant association is shown between the body surface area burned, intubation on admission, the requirement of pressor support during admission, leukocytosis, lactic acidosis, the development of pneumonia, MRSA colonization, and death (Table 1). Multivariate analysis led to complete separation of cases and controls (ie, this set of predictors separated individuals perfectly into their respective case and control groups), thus precluding calculation of the multivariate odds. No significant differences in patient characteristics were noted between the pre- and postuniversal decolonization populations (data not shown).

Universal decolonization with intranasal mupirocin in the BICU resulted in approximately 6 fewer LabID MRSA bacteremia HAIs per year. At $33,486 per infection, the annual cost savings amounted to $200,916.

DISCUSSION

Strict adherence to comprehensive basic environmental and behavioral interventions failed to reduce the occurrence of MRSA HAIs in our BICU. However, the adjunctive treatment of all new admissions with intranasal mupirocin, while maintaining the basic interventions, effectively controlled this outbreak. The failure of these basic interventions may have been attributable to the low count, sporadic event clusters in a small unit, and the presence of multiple sources of MRSA strains as identified by PFGE. MRSA colonization status on admission was notably similar among cases before and after the implementation of universal decolonization.

MRSA decolonization strategies in burn patients are only sparsely described, although the current paradigm is to treat the skin or wounds with agents such as chlorhexidine gluconate or bleach solutions, in addition to intranasal mupirocin.[9-11] In contrast, we used only intranasal mupirocin for the decolonization of all admissions to the BICU. To our knowledge, this is the first account in which a MRSA outbreak in a BICU was ultimately controlled by universal decolonization with intranasal mupirocin alone. The improved infection rate without any explicit treatment of the skin or wounds appears counterintuitive, although evidence has been mounting that nasal decolonization alone might lead to a reduction in MRSA infections in

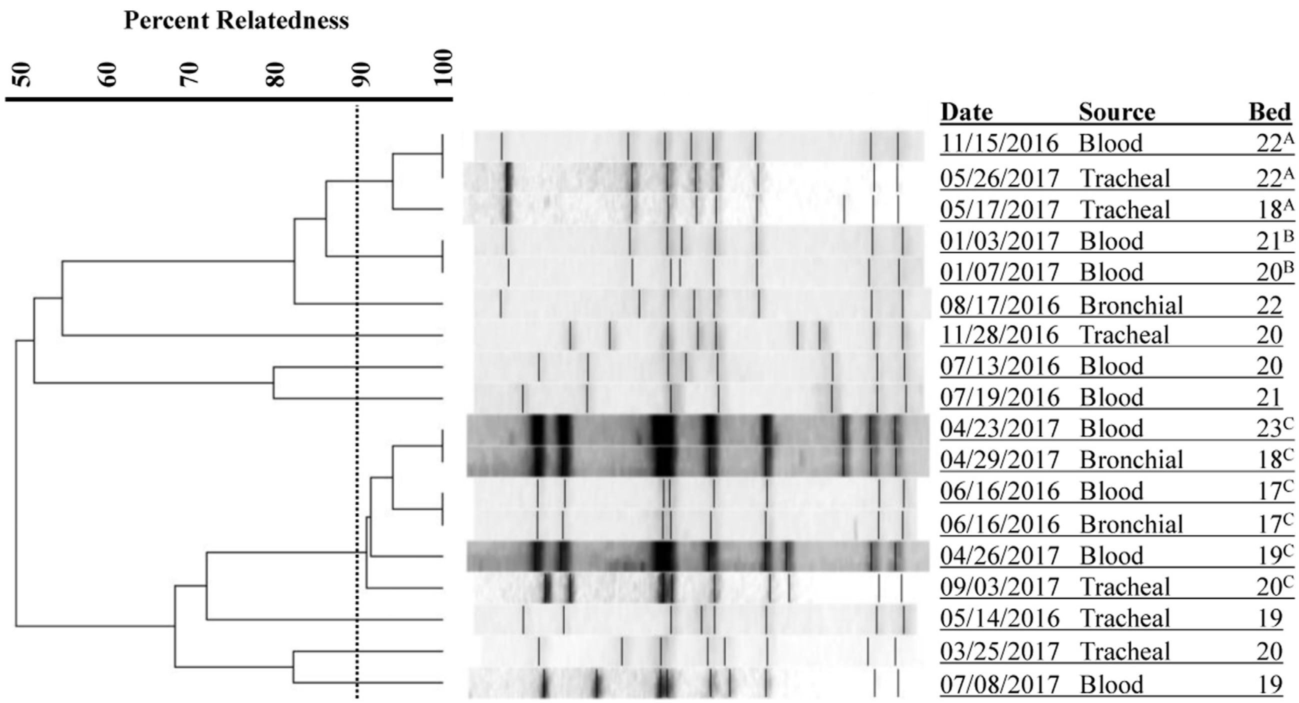

Fig 3. BioNumerics-generated dendrogram of percent relatedness of PFGE profiles from the MRSA isolates of this BICU outbreak, with corresponding culture dates, culture sources, and patient room numbers. A dotted line is provided at 90% (our definition of clonality) to guide the eye. Clusters are denoted by capital letter superscripts. *BICU*, burn intensive care unit; *MRSA*, methicillin-resistant *Staphylococcus aureus; PFGE*, pulsed-field gel electrophoresis.

similarly high-risk populations (eg, dialysis patients, postoperative patients, and long-term facility residents).[12]

We observed 10 unique clones by PFGE throughout the study period, making a point source less likely. In 2 of the 3 clusters, 2 different patients in neighboring rooms developed MRSA HAIs, which suggests transmission from patient, to provider, to patient. Moreover, across the clusters, the neighboring beds were localized to rooms 18-21, most central to the BICU, directly across from high-traffic locations such as the hydrotherapy room, the nurse's station, the medication room, and the restroom. Among all cases reported during the study period, the majority occurred in rooms 18-22. It is possible that patients were preferentially placed in more central locations when the unit was not at full capacity, although review of the BICU bed assignments throughout this period did not demonstrate a clear pattern to support this. Notably, there were no apparent lapses in compliance with isolation during any of the months in which a cluster was observed (ie, January, April, and May 2017). Whereas April 2017 experienced the lowest observed compliance with handwashing (85%), the observed compliance was excellent during January 2017 (100%) and May 2017 (95%). Although our score cards might overestimate compliance rates, little variation was noted throughout the entire study period; therefore, a more rigorous monitoring system would be required to attribute this outbreak to hand washing and contact precaution nonadherence. As the infection of 2 patients, by the same strain at different times, in the same room was a rare occurrence, it is unlikely that this outbreak can be attributed to inadequate

Table 1
Characteristics of cases and controls

Characteristic	Cases (N = 19)	Controls (N = 38)	*P* value	Univariate odds ratio (95% CI)
Age (y)	47.0 ± 23.0	39.7 ± 26.4	.31	1.35 (0.76-2.41)
Male sex, no. (%)	73.7	65.8	.54	1.46 (0.43-4.94)
Body mass index (kg/m^2)	25.4 ± 8.91	26.7 ± 9.06	.59	0.85 (0.48-1.52)
Chronic obstructive pulmonary disease, no. (%)	21.1	10.5	.28	2.27 (0.5-10.29)
Diabetes, no. (%)	10.5	7.89	.74	1.37 (0.21-9.00)
Heart disease, no. (%)	21.1	5.26	.067	4.80 (0.79-29.07)
Chronic kidney disease, no. (%)	10.5	10.5	1.0	1.00 (0.17-6.02)
Surface area burned (%)	31.4 ± 20.9	17.8 ± 15.5	.007	2.22 (1.16-4.24)
Temperature (°F)	97.0 ± 2.43	98.0 ± 1.47	.062	0.59 (0.33-1.05)
Systolic blood pressure (mmHg)	130 ± 27.0	131 ± 27.9	.85	0.95 (0.54-1.65)
Pressors during admission, no. (%)	57.9	13.2	<.001	9.08 (2.45-33.61)
White blood cell count ($10^3/\mu L$)	21.3 ± 9.82	14.2 ± 5.00	.001	2.79 (1.37-5.67)
Lactic acid (mmol/L)	3.89 ± 2.50	2.59 ± 1.65	.035	1.93 (1.01-3.68)
Intubation on admission, no. (%)	68.4	31.6	.008	4.69 (1.44-15.35)
Pneumonia during admission, no. (%)	57.9	7.89	<.001	16.0 (3.62-71.17)
Positive nasal surveillance culture on admission, no. (%)	31.6	7.89	.021	5.38 (1.17-24.75)
Total length of stay (d)	54.9 ± 51.1	16.6 ± 17.1	<.001	5.33 (1.81-15.71)
Burn unit length of stay (d)	41.8 ± 45.6	10.1 ± 12.1	<.001	8.13 (1.95-33.86)
Mortality, no. (%)	36.8	5.26	.002	10.5 (1.92-57.58)

CI, confidence interval.

cleaning of the rooms between consecutive patient admissions. Although limited by sample size, our PFGE analysis suggests that sporadic person-to-person transmission might account for this multiclonal outbreak of MRSA.

The case-control study revealed that patients who were sicker at presentation (eg, with worse burns, respiratory compromise, hemodynamic instability, tissue ischemia, and an increased inflammatory response) were at greater risk of acquiring a MRSA HAI. MRSA colonization on admission was unsurprisingly significantly greater among cases. These patients also had more complicated illness trajectories, as cases were significantly associated with increased lengths of stay, the development of pneumonia, and death. However, because of their wide confidence intervals, the odds ratios can only be interpreted cautiously, although respiratory compromise (ie, from inhalation injury or subsequent infection) and prolonged exposures to the health care setting may be the major drivers of developing MRSA HAIs.

Our study is limited by the small size of the unit and rarity of events, and the implementation of universal nasal decolonization in a larger outbreak situation or among multiple centers would be necessary to generalize this result. The sporadic appearance of low-count clusters poses a challenge to the confirmation or ruling out of a common source. Whereas nasal swabs alone are a relatively insensitive measure of MRSA colonization, compared to the testing of multiple anatomic sites (eg, axilla and groin),[13] these surveillance data did not ultimately influence our successful management of this outbreak via a universal decolonization protocol. It would, however, be informative to ascertain the true frequency of MRSA colonization in this population, whose prior exposure to the health care system is typically minimal. We did not test staff for MRSA carriage, although larger single-strain clusters might have been expected if any staff member was a significant and consistent source of infection. Although we did not test for mupirocin resistance in our MRSA isolates, increased resistance has not been observed in the setting of similarly short-term perioperative intranasal mupirocin prophylaxis in patients undergoing a variety of surgical procedures (eg, orthopedic, general, gynecological, neurological, or cardiothoracic).[14-16] In contrast, increased resistance has been observed in populations undergoing repeated applications of mupirocin to the skin over long periods of time (eg, to the exit sites of chronic peritoneal dialysis catheters, decubitus ulcers).[17-19]

CONCLUSIONS

MRSA poses a major threat to burn patients. Although a wide range of basic infection prevention interventions did not control this outbreak, treatment of all new admissions with intranasal mupirocin —in addition to the basic interventions, but without additional treatment of skin or wounds—successfully reduced the occurrence of MRSA HAIs and led to substantial cost savings. This approach should be taken into consideration when attempting to reduce the MRSA burden in burn settings. Further mechanistic and outbreak investigations are warranted to better understand the efficacy of interventions in the burn patient population.

References

1. Duin DV, Strassle PD, Dibiase LM, Lachiewicz AM, Rutala WA, Eitas T. et al. Timeline of health care−associated infections and pathogens after burn injuries. Am J Infect Control 2016;44:1511-6.
2. Girerd-Genessay I, Bénet T, Vanhems P. Multidrug-resistant bacterial outbreaks in burn units. J Burn Care Res 2016;37:172-80.
3. Prasanna M, Thomas C. A profile of methicillin resistant *Staphylococcus aureus* infection in the burn center of the Sultanate of Oman. Burns 1998;24:631-6.
4. Cook N. Methicillin-resistant *Staphylococcus aureus* versus the burn patient. Burns 1998;24:91-8.
5. Bunnell KL, Zullo AR, Collins C, Adams CA. Methicillin-resistant *Staphylococcus aureus* pneumonia in critically ill trauma and burn patients: a retrospective cohort study. Surg Infect 2017;18:196-201.
6. Robson MC, Heggers JP, Krizek TJ. Biology of surgical infection. Chicago (IL): Year Book Medical Publications; 1973.
7. Available from: https://epi.publichealth.nc.gov/cd/hai/figures/hai_apr2015_providers.pdf. Accessed December 18, 2018.
8. North Carolina Surveillance for Healthcare-Associated and Resistant Pathogens Patient Safety (SHARPPS) Program. Healthcare-associated infections in North Carolina; 2016. Available from: https://epi.publichealth.nc.gov/cd/hai/figures/2015/2015Q4_Hospital_Specific_Quarterly_Report.pdf. Accessed December 18, 2018.
9. Patel M, Thomas H, Room J, Wilson Y, Kearns A, Gray J. Successful control of nosocomial transmission of the USA300 clone of community-acquired methicillin-resistant *Staphylococcus aureus* in a UK paediatric burns centre. J Hosp Infect 2013;84:319-22.
10. Johnson AT, Nygaard RM, Cohen EM, Fey RM, Wagner AL. The impact of a universal decolonization protocol on hospital-acquired methicillin-resistant *Staphylococcus aureus* in a burn population. J Burn Care Res 2016;37:e525-30.
11. Gray D, Foster K, Cruz A, Kane G, Toomey M, Bay C, et al. Universal decolonization with hypochlorous solution in a burn intensive care unit in a tertiary care community hospital. Am J Infect Control 2016;44:1044-6.
12. Septimus EJ, Schweizer ML. Decolonization in prevention of health care-associated infections. Clin Microbiol Rev 2016;29:201-22.
13. Lee CS, Montalmont B, O'Hara JA, Syed A, Chaussard C, McGaha TL, et al. Screening for methicillin-resistant *Staphylococcus aureus* colonization using sponges. Infect Control Hosp Epidemiol 2015;36:28-33.
14. Pérez-Fontán M, Rosales M, Rodríguez-Carmona A, Falcón TG, Valdés F. Mupirocin resistance after long-term use for *Staphylococcus aureus* colonization in patients undergoing chronic peritoneal dialysis. Am J Kidney Dis 2002;39:337-41.
15. Upton A. Mupirocin and *Staphylococcus aureus*: a recent paradigm of emerging antibiotic resistance. J Antimicrob Chemother 2003;51:613-7.
16. Vasquez JE, Walker ES, Franzus BW, Overbay BK, Reagan DR, Sarubbi FA. The epidemiology of mupirocin resistance among methicillin-resistant *Staphylococcus aureus* at a Veterans' Affairs hospital. Infect Control Hosp Epidemiol 2000;21:459-64.
17. Perl TM, Cullen JJ, Wenzel RP, Zimmerman MB, Pfaller MA, Sheppard D, et al. Intranasal mupirocin to prevent post-operative *Staphylococcus aureus* infections. N Engl J Med 2002;346:1871-7.
18. Wilcox M, Hall J, Pike H, Templeton PA, Fawley WN, Parnell P. et al. Use of perioperative mupirocin to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) orthopaedic surgical site infections. J Hosp Infect 2003;54:196-201.
19. Fawley W, Parnell P, Hall J, Wilcox M. Surveillance for mupirocin resistance following introduction of routine peri-operative prophylaxis with nasal mupirocin. J Hosp Infect 2006;62:327-32.